HORMONE REPLACEMENT IN PERIMENOPAUSE AND MENOPAUSE

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DEFINITIONS

• MENOPAUSE: THE PERMANENT CESSATION OF MENSTRUATION THAT OCCURS AFTER THE LOSS OF OVARIAN ACTIVITY
  • 1 YEAR AFTER LAST MENSES
  • SURGICAL REMOVAL OF THE OVARIES
  • AVERAGE AGE 51

• PERIMENOPAUSE, CLIMACTERIC OR MENOPAUSAL TRANSITION: FLUCTUATIONS IN HORMONE LEVELS AND BLEEDING PATTERNS PRIOR TO CESSATION OF MENSES. OFTEN WITH VASOMOTOR SYMPTOMS.
DEFINITIONS

• PREMATURE OVARIAN INSUFFICIENCY: LOSS OF OVARIAN FUNCTION BEFORE AGE 40 THAT MAY WAX AND WANNE. CAN BE IDIOPATHIC, AUTOIMMUNE, METABOLIC OR GENETIC (FRAGILE X)

• INDUCED MENOPAUSE: CESSATION OF OVARIAN FUNCTION INDUCED BY CHEMOTHERAPY, RADIOTHERAPY, OR BILATERAL OOPHORECTOMY

• EARLY MENOPAUSE: CESSATION OF OVARIAN FUNCTION OCCURRING BETWEEN AGES 40 AND 45 IN THE ABSENCE OF OTHER ETIOLOGIES FOR SECONDARY AMENORRHEA (PREGNANCY, HYPERPROLACTINEMIA, AND THYROID DISORDERS).


SYMPTOMS OF MENOPAUSE

• VASOMOTOR SYMPTOMS (VMS): HOT FLASHES OR HOT Flushes IN UP TO 75% OF WOMEN

• NIGHT SWEATS

• SLEEP DISTURBANCES:  
  • 1) INCREASE IN EPISODES OF WAKING AFTER SLEEP-ONSET, 2) A DECREASE IN PERCEIVED SLEEP EFFICIENCY; AND 3) A CORRELATION BETWEEN NOCTURNAL VMS AND SLEEP DISRUPTION

• GENITOURINARY SYNDROME OF MENOPAUSE- OCCURS LATE IN MENOPAUSE  
  • VULVOVAGINAL ATROPHY-DYSpareunia, thinning of mucosa  
  • URINARY TRACT DYSFUNCTION

• OTHER: MOOD CHANGES, LOSS OF LIBIDO, ANXIETY AND DEPRESSION, MENTAL FOgginess, Fatigue, ARTHRAGIAS, PALPITATIONS

SYMPTOMS VARY IN FREQUENCY, DURATION AND SEVERITY FROM WOMAN TO WOMAN. SYMPTOMS LAST ON AVERAGE 7 YEARS BUT MAY BE SHORTER OR LONGER. ETHNICITY, EXCESSIVE WEIGHT, SMOKING MAY BE FACTORS IN SEVERITY. USUALLY START IN PERIMENOPAUSE AND GRADUALLY DIMINISH OVER TIME.
GENITOURINARY SYNDROME OF MENOPAUSE

- Vulvar pain, burning, or itching
- Dyspareunia
- Spitting or bleeding after intercourse
- Dysuria, urinary frequency, urgency, recurrent urinary tract infections
- External genitalia changes:
  - Decreased labial size
  - Loss of vulvar fat pads
  - Vulvar fissures
  - Receded or phimotic clitoris
  - Prominent urethra with mucosal eversion or prolapse signs
- Vagina changes:
  - Pale or erythematous dryness, thinning of epithelium
  - Introital narrowing
  - Loss of elasticity
  - Thin vaginal epithelial lining

HYPOACTIVE SEXUAL DESIRE DISORDER

- Definition: Persistent or recurrent deficiency or absence of sexual thoughts and fantasies and/or desire for, or receptivity for, sexual activity causing personal distress or interpersonal difficulties.
- Multifactoral
  - Decreased androgen levels
  - Low libido, decreased arousal, decreased orgasmic response
  - Psychosocial-quality of relationship, cultural expectations, personal prior history of physical or sexual abuse, stress, fatigue
  - Dyspareunia; endometriosis, vulvitis or vestibulitis
  - Health issues- ex: hypothyroidism, hypopituitaryism, adrenal insufficiency, HTN
  - Psychiatric and neurologic disease; medication side effects
  - Pelvic floor and bladder dysfunction; injury related to childbirth
DIAGNOSING MENOPAUSE

• 1 YEAR WITHOUT A MENSES
• SURGICAL MENOPAUSE WITH OOPHORECTOMY
• HYSTERECTOMY; OVARY SPARING
  • OVARIES MAY CONTINUE TO PRODUCE HORMONES UNTIL AVERAGE AGE OF MENOPAUSE BUT ON AVERAGE FAIL 1.9 YEARS EARLIER
  • FSH >25 BUT MAY FLUCTUATE IN PERIMENOPAUSE AND EARLY MENOPAUSE, SERIAL LEVELS BEST
• PREMATURE OVARIAN INSUFFICIENCY (< AGE 40)
  • FSH ELEVATED
  • LOW ANTIMULLERIAN HORMONE INDICATING DECREASED FOLLICLE RESERVE AND DECREASED FERTILITY

Diagram:

- Hypothalamus
- Pituitary
- Ovary
- Estrogen + Progesterone

- (+) Gonadotropin-Releasing Hormone (GnRH)
- (+) Luteinizing Hormone (LH)
- (+) Follicle-Stimulating Hormone (FSH)
HORMONE REPLACEMENT

- ESTROGENS - MOST EFFECTIVE IN MANAGEMENT OF VASOMOTOR SYMPTOMS
  - 17 βESTRADIOL (E2)
  - CONJUGATED EQUINE ESTROGENS (CEE)
  - ESTRIFIED ESTROGENS
- PROGESTERONE/PROGESTINS
  - MICRONIZED PROGESTERONE
  - PROGESTINS-MEDROXYPROGESTERONE (MPA), NORENTHINDRONE
- COMBINATION OF AN ESTROGEN AND PROGESTIN PRODUCT (PROGESTINS AS ABOVE OR SIMILAR TO CONTRACEPTIVES)
- TESTOSTERONE
  - TESTOSTERONE TOPICAL (COMPounded)
  - TESTOSTERONE CYPIANATE INJECTABLE
  - METHYLTESTOSTERONE GIVEN IN COMBINATION WITH ESTRIFIED ESTROGENS

MANAGEMENT OPTIONS

- HORMONE REPLACEMENT (HRT)
  - SYSTEMIC
  - VAGINAL
  - ESTROGEN
  - PROGESTERONE OR PROGESTIN
  - TESTOSTERONE
- CONTRACEPTIVES IN PERIMENOPAUSE (MORE EFFECTIVE THAN HRT)
- SSRI/SSNI
- NON-HORMONAL SUPPLEMENTS
- LIFESTYLE CHANGES-EXERCISE, WEIGHT LOSS, DRESSING IN LAYERS, AVOIDING SPICY FOODS, COOLER ROOM TEMPERATURE OR FANS
HORMONE REPLACEMENT ROUTES, PROS AND CONS

- **ORAL - ESTROGEN ALONE USED POST HYSTERECTOMY (ET)**
  - Most common and with generics most cost effective for management of vasomotor symptoms
  - Increased serum triglycerides and C-reactive protein with oral estrogen
  - Prothrombic effect due to first pass effect
  - Increased sex hormone-binding globulin (SHBG), thyroid binding globulin (TBG) and cortisol-binding globulin (CBG)
    - Lower free testosterone (lower libido not proven), increased TBG with lower bioavailable T4 and increased CBG increasing serum cortisol.

- **ORAL ESTROGEN AND PROGESTERONE OR PROGESTIN COMBINATIONS (EPT)**
  - With an intact uterus, a progestosterone is needed to prevent hyperplasia and endometrial carcinoma
  - Micronized progestosterone – no adverse effects on lipids and blood pressure, enhances onset of sleep
  - Progestins may increase cell division in mammary tissue and both ET and EPT increase density
  - Cyclic 12 days a month vs continuous of progestin with continuous estrogen

HORMONE REPLACEMENT ROUTES, PROS AND CONS

- **TRANSDERMAL**
  - Least risk for VTE, MI, diabetes and obesity; avoids first pass effect and interactions with anticonvulsants, thyroid medication
  - Patches (estradiol or estradiol/progestin)
  - Gels (estradiol); may transfer skin to skin
  - Lotions/creams

- **VAGINAL ESTROGENS**
  - Local-cream or tablet; tablet has the least systemic absorption
  - Systemic-ring

- **INJECTION** – depo-estradiol, estradiol valerate and testosterone cypionate
  - Peak and trough effect

- **SUBCUTANEOUS PELLETS** – compounded estradiol or testosterone
  - Last 4-6 months
  - Slow release for long action
  - Not FDA approved
ANDROGEN THERAPY

• TESTOSTERONE
  • ORAL/TRANSDERMAL- NO FDA APPROVED PREPARATION FOR WOMEN
  • COMBINATION OF ESTRIFIED ESTROGENS AND METHYLTESTOSTERONE ONLY FDA APPROVED ORAL THERAPY
  • TESTOSTERONE CYPIONATE INJECTABLE
  • COMPOUNDED ORAL, TOPICAL OR PELLET
• DHEA (DIHYDROEPiANDROSTERONE) AND DHEA-S (SULFATE)
  • PROHORMONES FROM ADRENAL GLANDS THAT MAY BE CONVERTED TO ACTIVE ANDROGENS

TESTOSTERONE

• GIVEN BY INJECTION, ORAL METHYLTESTOSTERONE /ESTRIFIED ESTROGENS (ESTRATEST BRAND DISCONTINUED) OR COMPOUNDED PRODUCT
  • METHYLTESTOSTERONE MAY HAVE INCREASED RISK OF HEPATOTOXICITY
• COMPOUNDED TESTOSTERONE ROUTES BY CREAM, PELLETS, ORAL
• RECOMMENDATION IS FOR USE IN HYPOACTIVE SEXUAL DESIRE DISORDER ONLY
  • 6 MONTH TRIAL RECOMMENDED. IF NO IMPROVEMENT, DISCONTINUE
• FEW STUDIES IN WOMEN IDENTIFYING RISKS OR BENEFITS
• SERUM TESTOSTERONE DOES NOT DIRECTLY CORRELATE WITH EFFECT AT RECEPTOR SITES
• PRIMARY BENEFIT IS FOR LIBIDO
• CLAIMS MADE THAT IMPROVES ENERGY, MOOD AND QUALITY OF LIFE

CONTRAINDICATIONS TO HORMONE THERAPY

ESTROGEN

• HISTORY OF BREAST OR HIGH RISK ENDOMETRIAL CANCER
• CORONARY HEART DISEASE
• PREVIOUS THROMBOEMBOLIC EVENT OR STROKE
• ACTIVE LIVER DISEASE
• UNEXPLAINED VAGINAL BLEEDING
• TIA

• HYPERTRIGLYCERIDEMIA
• ACTIVE GALL BLADDER DISEASE
• THROMBOPHILIAS – LEIDEN V, PROTEIN S OR C DEFICIENCIES
• UNCONTROLLED HYPERTENSION
• UNCONTROLLED DIABETES WITH VASCULAR INVOLVEMENT

Postmenopausal Estrogen Therapy; Route of Administration and Risk of Venous Thromboembolism. ACOG Committee Opinion; No. 556, April 2013, Reaffirmed 2015

CONTRAINDICATIONS TO HORMONE THERAPY

PROGESTINS

• RISK FOR VTE WITH SYNTHETIC PROGESTINS
• MICRONIZED PROGESTERONE MAY BE PREFERABLE AS NOT ASSOCIATED WITH INCREASED RISK OF VTE
• MAY NOT BE TOLERATED-MOOD SWINGS WITH PROGESTINS
• WOMEN’S HEALTH INITIATIVE (WHI) SHOWED INCREASED BREAST CANCER INCIDENCE IN CEE/MPA GROUP VS PLACEBO AND CEE ALONE.
  • INCIDENCE OF BREAST CA DROPPED IN IMMEDIATE 5 YEARS AFTER TREATMENT STOPPED BUT OVERALL HAS BEEN SLIGHTLY ELEVATED.
CONTRAINDICATIONS TO HORMONE THERAPY
TESTOSTERONE

• ACNE, HIRSUTISM, ANDROGENIC ALOPECIA
• CARDIOVASCULAR DISEASE-POSSIBLE INCREASED RISK. MOST OF THE DATA IS IN MEN AND INCONCLUSIVE
• CHANGES IN LIPID PROFILES HAVE BEEN SEEN WITH DECREASED HDL AND ELEVATED LDL
• DEEPENING OF VOICE, CLITOROMEGALY MAY OCCUR


HORMONE REPLACEMENT OPTIONS

• ESTRADIOL
  • ORAL
    • ESTRADIOL (ESTRACE) .5, 1 MG AND 2 MG; START AT 1 MG
    • ESTERIFIED ESTROGEN (MENEST) .3, .625, 1.25, 2.5 MG; START AT .625 MG
    • CEE (PREMARIN) .3, .45, .625, 9, 1.25 MG; START AT .625 MG
    • ESTROPIRATE, .75, 1.5, 3 MG (.75 = .625 MG ESTRONE SULFATE)
    • SYNTHETIC CONJUGATED ESTROGEN (ENJUVIA) 3 AND .45 MG WITH DOSING UP TO 1.25 MG (HIGHER DOES MAY BE DIFFICULT TO FIND) START AT LOWER DOSES.
  • TRANSDERMAL PATCH
    • ESTRADIOL PATCH (ALORA, CLIMARA, VIVELLE-DOT, MINIVELLE) 0.025, .0375, .05, .075, .1 MCG/DAY; DOSES VARY BY BRAND
    • MENOSTAR (LOW DOSE 14 MCG ESTRADIOL FOR OSTEOPOROSIS PREVENTION)
  • INJECTION-
    • DEPO-ESTRADIOL (ESTRADIOL CYPIONATE) 5 MG/ML; START AT 5 MG EVERY 4 WEEKS IM
    • DELESTROGEN (ESTRADIOL VALERATE) 10 TO 40 MG/ML; GIVE 10-40 MG EVERY 4 WEEKS IM
HORMONE REPLACEMENT OPTIONS

• ESTRADIOL
  • GEL - ESTROGEL TOPICAL (1 PUMP = 0.75 MG ESTRADIOL), DIVIGEL (.25, .5 AND 1 MG PACKETS), ELESTRIN (1 PUMP + 0.52 MG/.87 GM)
  • LOTION – ESTRASORB (4.35 MG/1.74 GM; APPLY 1-2 PACKETS)
  • SPRAY – EVAMIST (1.53 MG/SPRAY; 1-3 PER DAY)
  • COMPOUNDED BIEST (20% ESTRADIOL, 80% ESTRIOL; START AT 2 MG AS A TOPICAL CREAM OR CAPSULE); TRIEST (10% ESTRADIOL, 10% ESTRONE, 80% ESTRIOL). CAN ALSO BE GIVEN AS A TROCHE OR DROPS

HORMONE REPLACEMENT OPTIONS

• VAGINAL ESTROGEN
  • PREMARIN CREAM - CONJUGATED ESTROGENS (.625 MG/GM; START AT .5 GM DAILY X 7-14 DAYS THEN 2 X WEEK)
  • ESTRACE CREAM – ESTRADIOL (0.01%, START 1 GM DAILY X 7-14 DAYS THEN 1 GM 2 X WEEK)
  • VAGIFEM TABLETS – ESTRADIOL (10 MCG; START DAILY X 7-14 DAYS THEN 2 X WEEK)
  • ESTRING VAGINAL 90 Day Ring- ESTRADIOL (2 MG=7.5 MCG/24 HOURS). LOCAL AND SYSTEMIC ABSORPTION
  • FEMRING VAGINAL 90 Day Ring-ESTRADIOL (.05 OR .1 MG/DAY) LOCAL AND SYSTEMIC ABSORPTION
  • ESTRIOL VAGINAL CREAM (COMPOUNDED AT 1 MG/GM). LESS EXPENSIVE OPTION

• PELLETS-SUBDERMAL IMPLANTATION
  • COMPOUNDED ESTRADIOL OR TESTOSTERONE PELLETS
  • LONG ACTING, 4-6 MONTHS DURATION. DISADVANTAGE: CANNOT BE REMOVED
HORMONE REPLACEMENT OPTIONS

• PROGESTERONE/PROGESTIN
  • MICRONIZED PROGESTERONE
    • PROMETRIUM (BRAND) OR GENERIC-100 AND 200 MG IN PEANUT OIL
    • COMPOUNDED CAN BE MADE WITHOUT THE PEANUT OIL IN A CAPSULE OR IN A CREAM
  • MEDROXYPROGESTERONE ACETATE (PROVERA) 2.5 AND 5 MG FOR HRT, 10 MG FOR BLEEDING CONTROL
  • NORETHINDRONE (AYGESTIN) 5MG

• COMBINATION THERAPY
  • COMBINATION ESTRADIOL/PROGESTIN PATCH (COMBIPATCH, CLIMARA PRO)

HORMONE REPLACEMENT OPTIONS

• COMBINATION THERAPY-ORAL
  • NORETHINDRONE ACETATE/ETHINYL ESTRADIOL (FEMHRT-.5MG/2.5 MCG, 1 MG/5MCG-, FYAVOLV-.5MG/2.5 MCG, 1 MG/5MCG-, JINTELI-1 MG/5MCG)
  • ESTRADIOL/NORETHINDRONE ACETATE (MIMVEY-1/.05MG, ACTIVELLA-.5/.1 MG, 1/.5 MG)
  • DROSPIRENONE/ESTRADIOL (ANGELIQ-.25/.5, .5/1MG)
  • CEE/MEDROXYPROGESTERONE (PREMPHAISO-625/O 14 DAYS+.625/5 MG14DAYS)
  • CEE/ MEDROXYPROGESTERONE (PREMPRO-.3/1.5, .45/1.5, .625/2.5, .625/5MG)-USED IN WHI TRIAL
  • ESTRADIOL/NORGESTIMATE (PREFEST-1/0 + 1/.09-3 DAYS ESTRADIOL THEN 3 DAYS COMBO)
OTHER HORMONAL OPTIONS AND SERMS

• CEE/BAZEDOXIFEME (DUAVEE-,45/20 MG) VASOMOTOR SYMPTOMS AND OSTEOPOROSIS PREVENTION; PROGESTIN NOT NEEDED BUT WATCH FOR BLEEDING. BAZEDOXIFEME BLOCKS ESTROGEN RECEPTORS IN UTERUS (ANTI-ESTROENIC)

• OSPEMIFEME (OSPHENA-60 MG) DYSPAREUNIA. BINDS TO ESTROGEN RECEPTORS IN VAGINAL EPITHELIUM (AGONIST) AND ENDOMETRIUM (ANTI-ESTROGENIC)

NON-HORMONAL OPTIONS
SUPPLEMENTS

• PHYTOESTROGENS, 
  • SOY ISOFLAVONES 54 MG DAILY. REDUCTION IN HOT FLASHES 
  • USE FOR 6-12 WEEKS FOR FULL EFFECTIVENESS 
  • GENISTEIN AND DAIDZEIN FOUND IN SOY, RED CLOVER 
  • RED CLOVER ISOFLAVONE –IMPROVED VAGINAL CYTOLOGY 

• BLACK COHOSH$_2$ -NO DIRECT EVIDENCE OF BENEFIT 
  • (CONTAINS SALICYLATES-DON’T USE IF ASPIRIN CONTRAINDICATED, POTENTIAL FOR LIVER TOXICITY) 

• STUDIES MIXED ON EFFECTIVENESS; COCHRANE REVIEW SHOWED NO IMPROVED EFICACY WITH ISOFLAVONES WHEN COMPARED TO PLACEBO 

• VITAMIN E$_2$– LIMITED DATA

NON-HORMONAL OPTIONS

- CHINESE HERBS
  - DONG QUAI – COMMON USE; NOT FOUND EFFECTIVE IN ONE RCT
  - DANG GUI BU XUE TANG – MILD VASOMOTOR SYMPTOMS

- ACUPUNCTURE
  - LIMITED DATA ON EFFECTIVENESS

- VAGINAL LUBRICANTS AND MOISTURIZERS
  - REPLENS OTC PLUMPS UP VAGINAL EPITHELIAL CELLS WITHOUT HORMONES
  - SUPPORT FOR SLEEP: TRAZADONE CAN HELP WITH SLEEP AND MAY DECREASE NIGHT SWEATS

SSRI AND SNRI
CLONIDINE AND GABAPENTIN

- PAROXETINE (BRISDELL – 7.5 MG) SSRI – ONLY FDA NON-HORMONAL APPROVED FOR TX OF MODERATE TO SEVERE VASOMOTOR SYMPTOMS

- VENLAFAXINE (EFFEXOR – DISCONTINUED BRAND NAME) SNRI – START WITH LOWEST DOSE AND TITRATE UPWARDS
  - COMMONLY USED WITH BREAST CA TX

- CLONIDINE - ALPHA 2-AGONIST (OFF LABEL) LESS EFFECTIVE THAN HRT BUT ALTERNATIVE PATIENTS WITH HIGH RISK WITH ESTROGEN

- GABAPENTIN - GAMMA AMINOBUTYRIC ACID ANALOGUE (OFF LABEL) REDUCTION IN VASOMOTOR SYMPTOMS. BUT LESS EFFECTIVE THAN HRT

BIOIDENTICAL HORMONE THERAPY

- PLANT-DERIVED HORMONES THAT ARE CHEMICALLY SIMILAR OR STRUCTURALLY IDENTICAL TO THOSE PRODUCED IN THE BODY
  - COMMERCIAL FDA APPROVED DRUGS (ESTRADIOL OR MICRONIZED PROGESTERONE)
  - COMPOUNDED PREPARATIONS USING USP INGREDIENTS ACCORDING TO PROVIDER PRESCRIPTION
    - ESTROGENS (E1) ESTRONE - PRIMARY ESTROGEN AFTER MENOPAUSE, (E2) ESTRADIOL - MOST POTENT ESTROGEN, (E3) ESTRIOL - PRIMARY ESTROGEN IN PREGNANCY
    - PROGESTERONE
    - TESTOSTERONE
    - DHEA
    - PREGNENOLONE (PRE-HORMONE TO ESTROGEN, PROGESTERONE AND OTHER STEROID HORMONES)

COMPounded BIOIDENTICAL HORMONE THERAPY

- IS IT SAFER?
  - NOT REGULATED BY THE FDA. REGULATION COMES UNDER STATE BOARDS OF PHARMACY.
  - LARGE STUDIES LOOKING AT SAFETY FOCUS ON FDA APPROVED DRUGS
  - UNDERDOSAGE AND OVERDOSAGE POSSIBLE DUE TO ABSORPTION AND BIOAVAILABILITY; THIS ALSO OCCURS WITH FDA APPROVED MEDICATIONS (DRUG INTERACTIONS, FOODS, CYTOCHROME P450 ACTIVITY)
  - BOXED WARNINGS NOT REQUIRED ON LABELING
  - USE NOT RECOMMENDED BY ACOG, NAMS OR THE ENDOCRINE SOCIETY

COMPOUNDED BIOIDENTICAL HORMONE THERAPY

• ADVANTAGES
  • DOSAGE AND RATIOS CAN BE ADJUSTED WITH MORE VERSATILITY THAN STANDARD HRT
  • PATIENTS WITH ALLERGIES OR SENSITIVITIES TO FILLERS CAN RECEIVE MEDICATIONS
  • COMBINATIONS OF ESTROGENS, PROGESTERONE AND TESTOSTERONE CAN BE MADE INTO A SINGLE PRODUCT
  • MULTIPLE MODES OF DELIVERY: ORAL, TOPICAL, TROCHE, SUBLINGUAL DROPS, VAGINAL

COMPOUNDED BIOIDENTICAL HORMONE THERAPY

• DISADVANTAGES
  • EXPENSE
  • NOT COVERED BY MOST INSURANCES
  • MEDICOLEGAL LIABILITY IF ADVERSE REACTION
  • VARIABILITY IN QUALITY CAN OCCUR FROM ONE COMPOUNDING PHARMACY TO ANOTHER
  • LACK OF LARGE CONTROLLED STUDIES LOOKING AT SAFETY AND EFFICACY
DO I NEED TO TEST HORMONE LEVELS?

- **SERUM TESTING**
  - Serum testing does not correlate with efficacy or symptom relief.
  - Your patient can tell you if they are getting relief.
  - Start low and increase until effective dose. Keep at lowest effective dose.
  - Testosterone: Easy to overdose. Testing can guide achieving narrow therapeutic window of 50-75 ng/dL. Test for total testosterone.

- **SALIVA TESTING**
  - Not reliable due to variability secondary to diet and time of testing, low concentrations and possible contaminants.

WHEN/HOW TO WEAN OFF

- **Recommendations by NAMS and the Endocrine Society are by age 60; ACOG recommends 60-65.**
- **Strong contraindications such as DVT, stroke, breast cancer, endometrial cancer should discontinue immediately.**
- Wean slowly, decreasing dose gradually.
- Can transition to other modalities such as an SSRI.