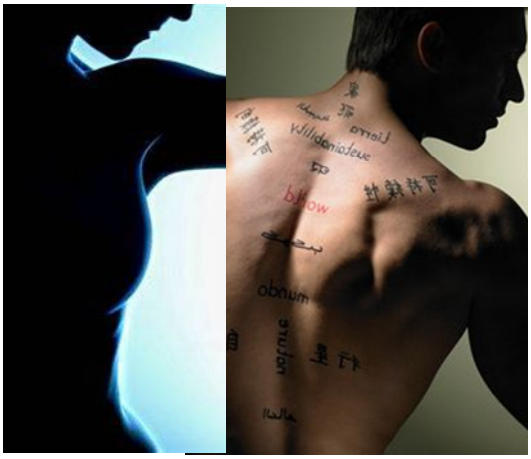
MYERS Medical Pharmacy



Bio-identical Hormone Therapy

Practice Guide

Our thanks to ZRT LABORATORY for contribution to content

Foreword

Hormone therapy has been the subject of a great deal of misinformation and confusion. This section of MYERS Medical Pharmacy's Bioidentical Hormone Therapy Guide is intended to clarify the critical issues and provide you with the most accurate description of the therapies and their benefits. If you've heard any of the following popular myths, you'll appreciate how this guide dispels them with the facts you need to know.

Myth 1: Women who suffer from PMS and hot flashes usually just need depression medication or estrogen supplementation.

Facts: Hormone imbalances can present as a wide variety of symptoms, from PMS to depression, as well as weight gain, headaches, sleeplessness, anxiety, decreased sex drive, fatigue, dry hair or skin, even hair loss. Properly diagnosing and treating hormone imbalance symptoms requires a holistic approach – one that evaluates a broad range of the patient's physical and psychological attributes.

Myth #2: Hormone therapy is risky. It can increase morbidity and mortality from breast cancer, cervical cancer, stroke and cardiovascular disease.

Facts: The Women's Health Initiative (WHI) Study of 1991 caused confusion and widespread panic among patients and practitioners. But it was flawed. It focused on synthetic estrogen-only treatments in (older) postmenopausal women. It failed to consider the inherent weaknesses of synthetic estrogens and that the age of the subjects predisposed them to such risks. In March 2004, that part of the study was also closed down. The press release announced that: "After careful consideration of the data, NIH has concluded that with an average of nearly 7 years of follow-up completed, estrogen alone does not appear to affect (either increase or decrease) heart disease, a key question of the study. It has not increased the risk of breast cancer during the time period of the study."

Myth #3: All hormone supplements are the same.

Facts: Hormone treatments such as Premarin, Prempro and Ceestin are synthetic, i.e. they are **not** true hormones. Molecular differences between synthetic progestins and progesterone result in differences in their pharmacological effects on breast tissue. Some of the pro-carcinogenic effects of synthetic progestins contrast with the anti-carcinogenic properties of progesterone, which result in disparate clinical effects on the risk of breast cancer. In other words, bio-identical hormones are associated with lower risks of breast cancer and cardiovascular disease, and are more efficacious than their synthetic and animal derived counterparts.

Myth #4: If a hormone supplement doesn't appear to resolve symptoms, increase the dosage.

Facts: The symptoms of imbalances among the family of endocrine hormones are subject to significant overlap. An above-normal level of one hormone can present the same symptoms as a below-normal level of another. In many cases, both below- and above-normal levels of the same hormone can present the same symptoms. It is critical to assess and evaluate all of the endocrine hormones to determine which may need adjustment.

Myth #5: Saliva testing is the only acceptable method for measuring hormones.

Facts: Testing is not a "one-size-fits-all" proposition. Saliva, blood spot, serum and urine testing each have their advantages and disadvantages.
The best approach is to evaluate every situation independently, and proceed based upon the patient's symptoms, current treatment regimen, and the hormones being measured.

Contents

Introduction

Thank you for your sincere interest in treating hormone imbalance symptoms, and welcome to the BHRT Practice Guide from MYERS Medical Pharmacy.

We've tried to appreciate the way you think as a practitioner, and anticipate your questions. We are certain you are aware, however, that this is not intended to be, nor can it possibly be considered a complete class or textbook on the subject of treating hormone imbalance symptoms.

We've styled the guide to be practical, informative — easy to read and follow. You'll find information presented somewhat like a slide show, to cut-to-the-chase, present important facts and figures directly, up-front, and to separate fact from fiction. We've included symbols, graphs and color-coding to increase clarity and help you visualize concepts. What you *won't* find is a lot of unnecessary text, clinical jargon, scientific notation, small print or footnotes.

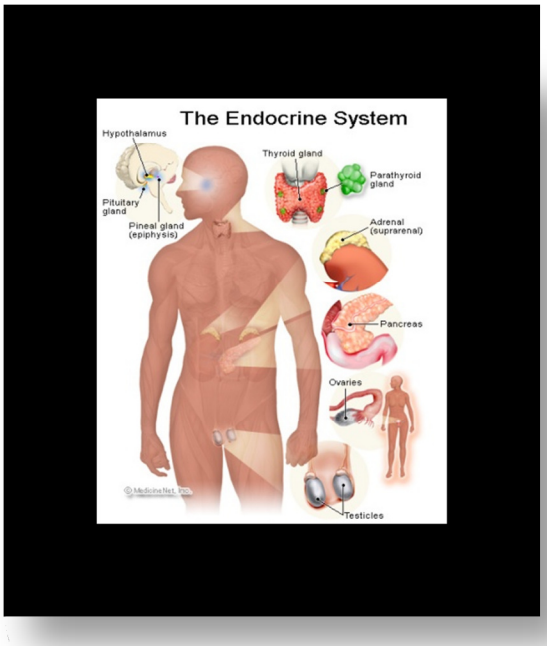
As you go through the material, we ask you to keep in mind that the glands of the human endocrine system and the hormones they produce are extremely complex, interactive and variable. Common themes we emphasize are that no two patients are alike — there are no one-size-fits-all or quick-fix treatments or regimen.

We expect you will have questions along the way, and we encourage you to contact us by phone or email, no matter how small or large the issue. We will be most happy to open a dialogue with you, do our best to answer your questions, and point you to the resources we have used for more information, if needed.

We hope you find this guide a useful tool and welcome your comments and suggestions.

Tim Keffeler, PharmD
Owner and Proprietor
MYERS Medical Pharmacy

Endocrine Hormones

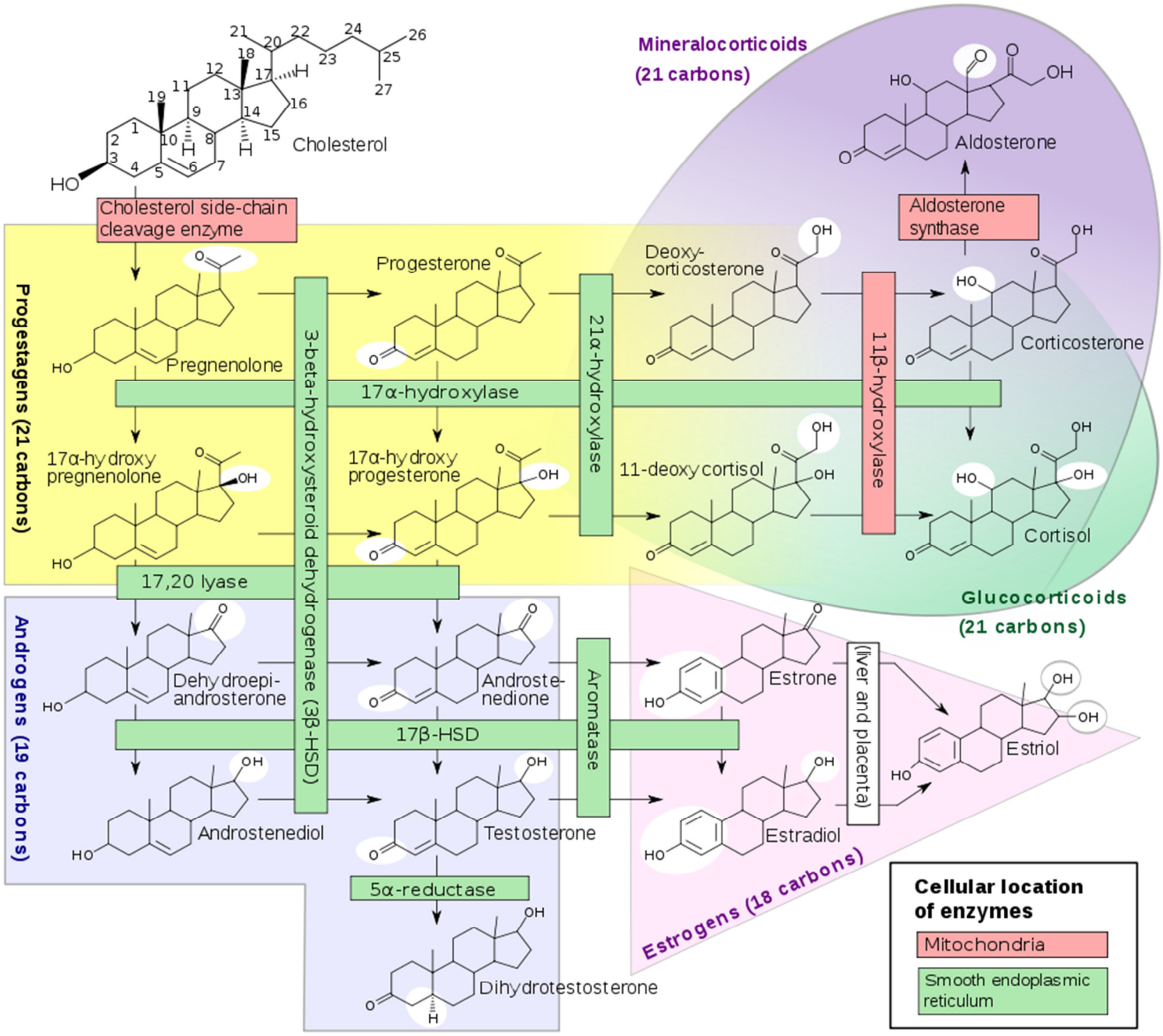


More than just estrogen, the hormones commonly involved in BHRT are produced by the glands of the endocrine system: the hypothalamus, thyroid, pituitary, adrenals, pancreas and ovaries or testes. They include:

- Estrogens
  - Estrone (E1)
    - 50-70% less active than E2
    - produced by oxidation of Estradiol and in peripheral tissues from androstenedione
  - Estradiol (E2)
    - the most potent and active estrogen
      - Binds more tightly to Estrogen receptors
  - Estriol (E3)
    - 10% of the activity of Estradiol
    - produced from hydration of Estrone
    - cannot be converted to Estrone or Estradiol
    - Can impede binding of Estradiol
- Progesterone
- Pregnenolone
- Testosterone
- Cortisol
- DHEA
- Thyroid
  - T3
  - T4

Metabolism & Conversion of Endocrine Hormones

Recognizing the relationships between the common endocrine hormones is imperative to treatment. They are what make resolving hormonal imbalance symptoms so complex. Failure to understand how the endocrine hormones metabolize and convert from one to another can cause adverse reactions and often have the opposite effect of the treatment administered.



Hormone Therapies
Eliminating the Confusion

HRT: Hormone Replacement Therapy
ERT: Estrogen Replacement Therapy
BHRT: Bio-identical Hormone Restoration Therapy

HRT and ERT

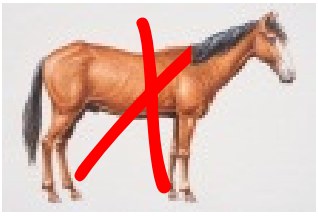
- Generally lumped together
- Supplements to prevent osteoporosis and heart disease
- Do not represent the synthetic agents or doses involved
- "HRT" was halted in 2002
  - 49% of cases involved serious cardiovascular risk
- "Conventional" (synthetic) ERT involves side effects and poses serious possible risks:

- Breast tenderness
- High blood pressure
- Gall stones
- Vaginal bleeding
- Fluid retention
- Blood clots
- Nausea
- Impaired glucose tolerance
- Uterine fibrosis and endometriosis
- Risk of breast and endometrial cancer

Synthetic = Artificial

Natural Is Not *"Natural"*

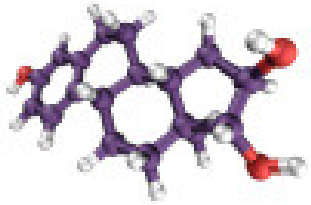
Natural Is Not Bio-identical



Though they claim to be "natural," synthetic hormones are not the same as those found naturally in the human body.

- Synthetic estrogens claim to be *natural* because they are derived from plants such as yams or soy. But these plants only provide "precursors," not hormones
- Pharmaceutical companies call phytoestrogens *natural,* but they are not estrogen. They are *estrogen-like* compounds that suffer from:
  - Very weak estrogen activity
  - Delayed beneficial effects
- Conjugated Equine Estrogen and combinations such as Medroxyprogesterone are not true hormones. They only mimic some hormonal functions
- To establish patents, pharmaceutical companies must add chemical "side chains" to natural substances
  - This creates drugs that lack the full effects of true hormones and cause side effects
- Premarin® is promoted as *natural* because its source – pregnant mare's urine – is found in nature
- Ceestin ® is promoted as *natural* because it comes from a plant source – yet it matches horse estrogens instead of human estrogens

Bio-identical Hormones



bio-identical: the molecular-level chemical structure of the replacement hormone is **identical** to that of the hormone that exists intrinsically in the human body.

The chemical structure must match that of the original hormone in order to replicate all the functions of the hormone throughout the body.

Bioidentical vs. Synthetic Hormones

20 years of physiological data and clinical outcomes demonstrate that bio-identical hormones are associated with lower risks of breast cancer and cardiovascular disease, and are more efficacious than their synthetic and animal derived counterparts.

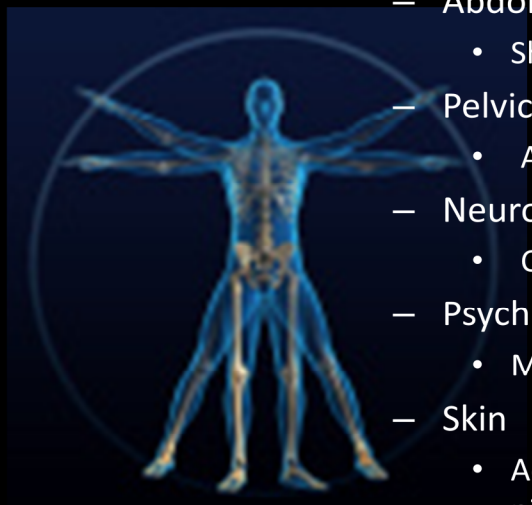
- Molecular differences between synthetic progestins and progesterone result in differences in their pharmacological effects on breast tissue. Some of the procarcinogenic effects of synthetic progestins contrast with the anticarcinogenic properties of progesterone, which result in disparate clinical effects on the risk of breast cancer.
- Progesterone has an antiproliferative, antiestrogenic effect on both the endometrium and breast tissue, while synthetic progestins have antiproliferative, antiestrogenic effects on endometrial tissue, but often have a proliferative estrogenic effect on breast tissue.
- Bioidentical progesterone, compared with MPA, is associated with greater efficacy, patient satisfaction and quality of life.
- Synthetic progestins show increased estrogen-induced breast tissue proliferation and a risk for breast cancer, whereas progesterone inhibits breast tissue proliferation and reduces the risk for breast cancer.
- In cardiovascular disease, synthetic progestins, as opposed to progesterone, negate the beneficial lipid and vascular effects of estrogen.
- Transdermal bioidentical estrogen and progesterone are associated with beneficial cardiovascular and metabolic effects compared with the use of oral estrogens (especially CEE) and synthetic progestins.

Evaluating the Whole Patient

Hormone therapy requires a holistic process that begins with a complete physical, psychological, environmental and behavioral assessment of the patient. Due to the complexity of hormone metabolism and interactions, the therapy must also be seen as an iterative process, where adjustments are made in small increments, perhaps affecting multiple hormones and continually assessing progress. It is neither an exact science nor is there a one-size-fits-all solution. Every patient must be evaluated and treated individually.

Proper evaluation requires in-depth physical exam & assessment

- Vitals
  - BMI
  - Pulse
  - BP
- Waist Circumference
  - Goal: < 35 in.
- Waist/Hip Ratio
  - Goal: < 0.8
- HEENT
  - Scalp, facial hair, eyes, gums, ears
- Neck
  - Presence of goiter



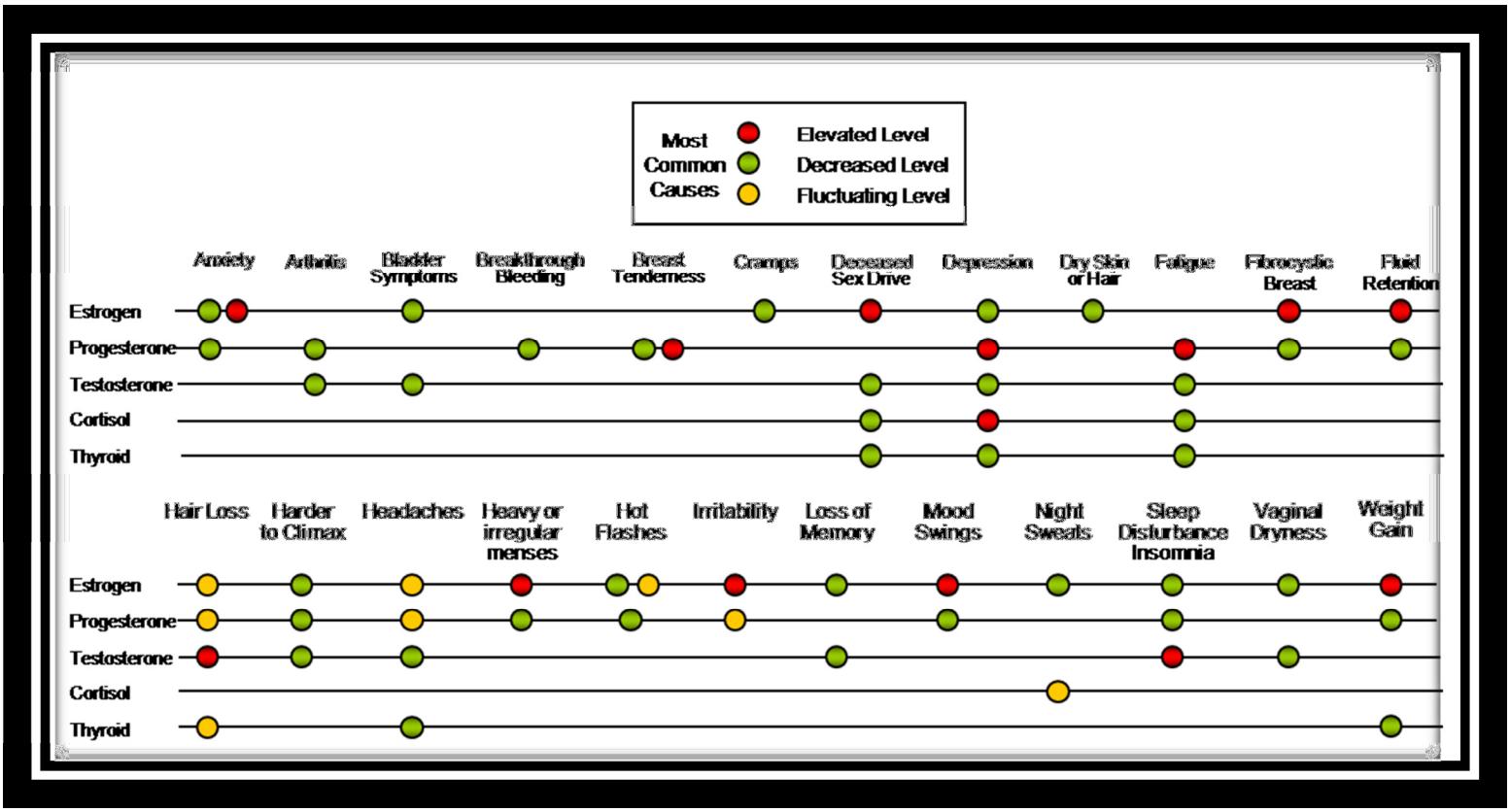
- Breasts
  - Masses, fibrocystic change
- Abdomen
  - Shape, striae
- Pelvic
  - Atrophic changes, fibroids, cysts
- Neurology
  - Cognitive function, deep tendon reflex
- Psychology:
  - Mood, concentration, affect
- Skin
  - Acanthosis, negritans, brittle nails, pigmentation, striae, acne, icthyosis

Physical data and symptoms don't always tell the whole story

- It's important to assess underlying issues that may be responsible for symptoms
  - Diet
  - Exercise
  - Stress
  - Sleep
  - Nutrition
- Know all the possible causes of the symptoms
  - More than one hormone imbalance causes weight gain, hot flashes, fatigue, etc.
- Look at groups of symptoms, and correlate with multiple hormone levels
  - Symptoms of too much of a hormone can closely mimic symptoms of too little
    - Symptoms of excess estrogen or excess progesterone, or high cortisol can mimic symptoms we refer to as "estrogen deficiency"
  - Low thyroid and/or poor nutrition look similar to low testosterone
  - High cortisol symptoms can mimic low testosterone, high estrogen, low progesterone

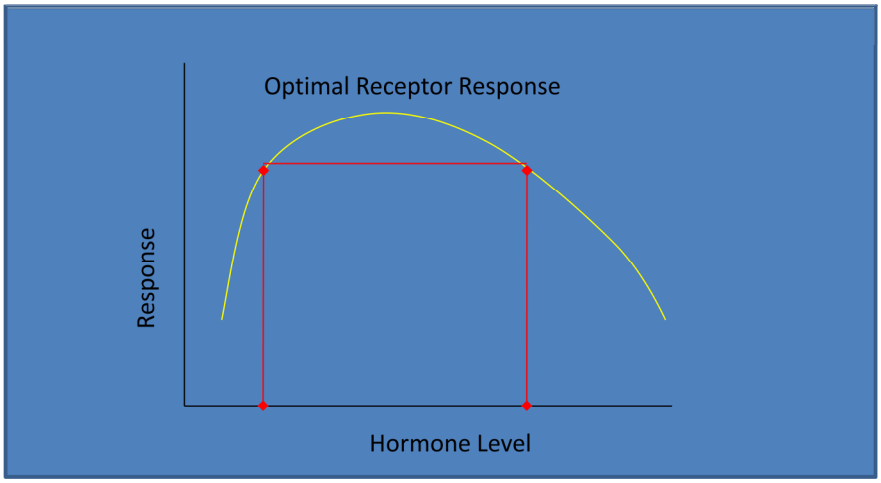
Hormone Imbalance Symptoms

Notice the overlap!



Why Test?

- Symptoms of different imbalances overlap
  - Imbalance of one or more hormones can mimic the effect of other imbalances
- Too much of a hormone can create the same symptoms as too little
  - Too much of a hormone can work to control a symptom, but only temporarily
  - Higher than normal physiologic levels can decrease benefits and create other risks

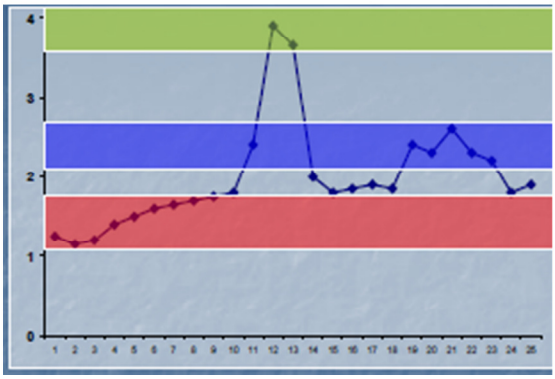


Tests Must Provide Clinical Viability

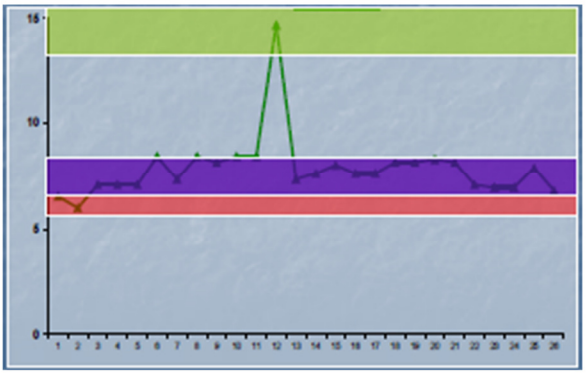
- Validate each hormone independently
- Distinguish follicular, ovulatory and luteal phases of the menstrual cycle
- Adequate sensitivity to differentiate low, normal and high levels as well as variations
- Yield results that correlate with age and symptoms
  - Validate against 20th-80th physiological reference ranges
- Pick a lab that specializes in hormone testing

Detect lower levels of Estradiol

Serum

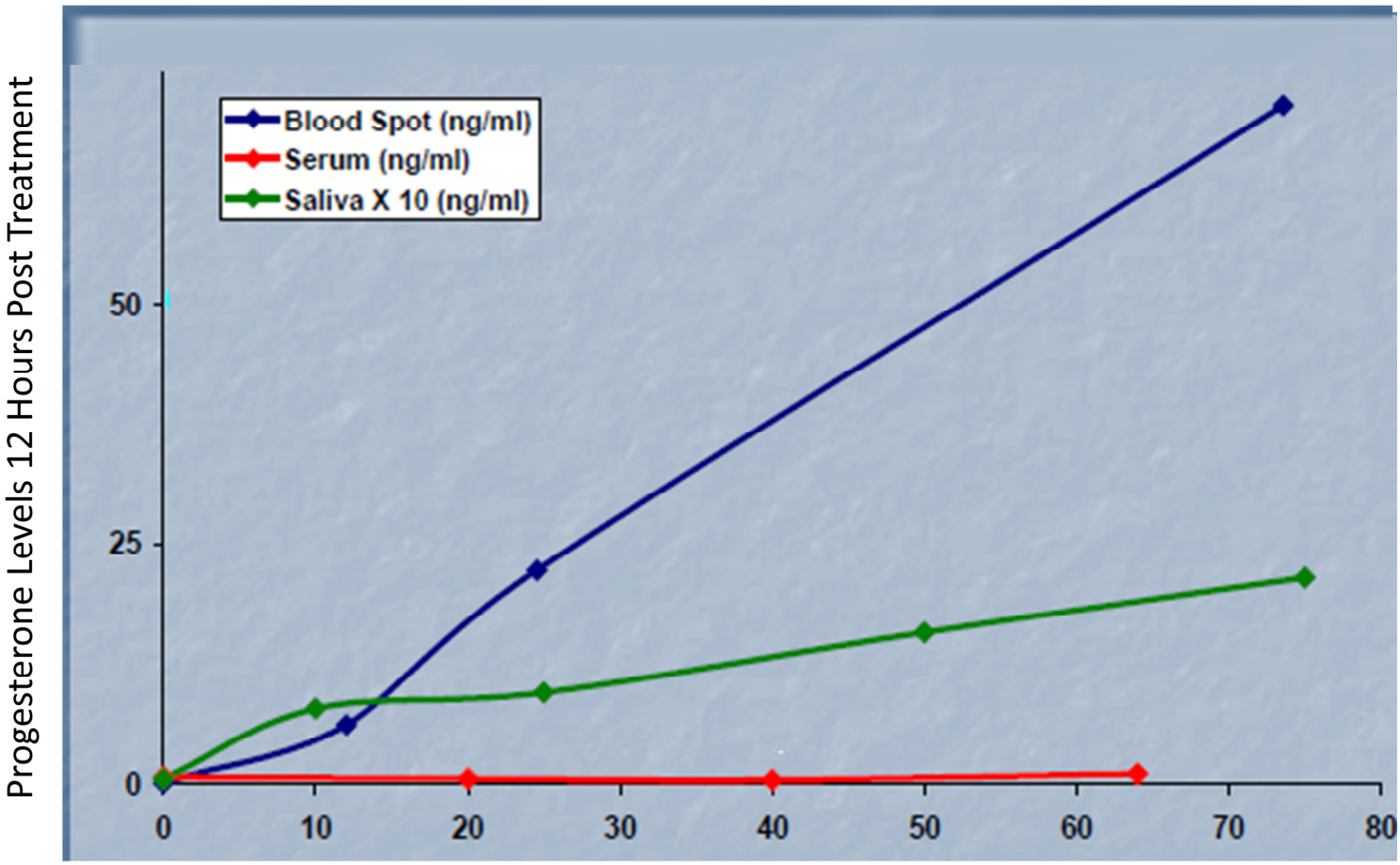


Saliva



Example of Clinical Viability Issue

Progesterone Levels in Different Body Fluids with Topical Supplementation



Testing Is Not a *"One-Size-Fits-All"* Proposition

There is not a single test that is viable for all situations

- Saliva testing is preferred when:
  - Testing for multipoint measurements, e.g. cortisol
  - Patients are using topical supplementation
- Saliva testing works well only if reference ranges are reset for delivery mode
- Saliva testing is subject to contamination from
  - Blood
  - Supplements
- Not everything that can be measured in saliva is clinically viable
  - Vitamin D if blood is present
  - DHT appears to convert to testosterone, but actually cross-reacts with it
- Saliva should never be used within 24 hrs. of taking a troche

- Cortisol testing should use "4-Point" (4X/day) method

- Serum Testing is widely accepted as the norm, but…
  - Subject to overdosing with patients using topical treatment
  - Needs to include binding proteins to assess the level of bioavailable ("free") hormones
  - Some methods inaccurate at low concentrations

- Blood Spot testing
  - Can measure factors that are too large for saliva -- e.g., Thyroid, Vitamin D , Glucose, Insulin, DHEA-S
  - More convenient than serum testing
  - More reflective of tissue uptake for patients on topical supplements
  - Best for evaluating Cardiovascular Metabolic Risk Factors

- Urine Testing can be effective for baseline hormone testing, but…
  - Does not show bioavailable hormone levels
  - Not good for oral estrogens (progesterone)
    - First pass metabolism clouds interpretation
  - Not good when treating with topical progesterone

As the Saying Goes, *"Timing Is Everything"*

- Cycling female
  - Test days 18-21 during luteal phase
- Irregular cycles
  - Test after next menses as above or test now
- Menopausal
  - Test any time
- Patient to take dose of oral hormones 12 hrs. prior to collection, or apply topical 12-24 hours prior to collection

Physiological Reference Ranges

Like Testing, There is No One-Size-Fits-All Patient Profile

As we've tried to convey many times in this guide, endocrine hormone levels vary widely and there are broad relationships among hormones due to their interaction and metabolism patterns. Therefore, similarly, there is no simple, all-purpose chart or table that you can rely upon to determine proper or "normal" hormone levels. The following two tables are intended for general reference. In them, you will notice several key variables to consider: Test Method/Source, Estrus Cycle, Life Stage and time-of-day. Please also pay particular attention to the values' units of measure.

Hormone/Antagonist	Estrus Cycle/ Life Stage	"Normal" Range Serum Test Levels
		0 2 4 6 8 10 15 20 30 50 75 100 200 300 500
Estradiol (pg/mL)	Follicular Phase	50-145
	Midcycle Peak	112-443
	Luteal Phase	50-241
	Postmenopausal	< 59
Progesterone (ng/mL)	Follicular phase	< 1.5
	Mid Luteal Phase	3-20
	Postmenopausal	0-15
Free Testosterone (pg/mL)	20-40 years old	0.6-3.1
	41-60 years old	0.4-2.5
	61-80 years old	0.2-2.0
DHEA-S (µg/dL)	Premenopausal	12-535
	Postmenopausal	30-260
Estrone (pg/mL)	Follicular phase	30-100
	Ovulatory Phase	> 150
	Luteal Phase	90-160
	Postmenopausal	20-40
Estriol (ng/mL)	Non-pregnant	< 2
	30-32 weeks	2-12
	33-35 weeks	3-19
	36-38 weeks	5-27
	39-40 weeks	10-30
Cortisol (µg/mL)	Morning	5-20
	Afternoon	2.5-10
17-Hydroxyprogesterone (ng/mL)	Follicular phase	20-100
	Midcycle Peak	100-250
	Luteal Phase	100-500
	Postmenopausal	< 70
17-Hydroxypregnenolone (ng/mL)	Pubertal	44-235
	Adult	53-357
18-HydroxycortIcosterone(ng/mL)	Recumbent (AM)	22.9-27.7
	Upright (Midday)	43.7-53.5

Physiological Reference Ranges

Saliva Observed Reference Ranges*

	WOMEN		
Estradiol (pg/mL)	Premenopausal		1.3-3.3
	Postmenopausal		0.5-1.7
	Supplement (12-24 Hrs.)	Estradiol Patch	0.8-2
		Hormonal Contraceptives	0.5-2.2
		Oral Estradiol (.5-1.0 mg)	1.2-3.9
		Oral Premarin (0.625 mg)	0.9-3.7
		Topical Bi-est 4:1 (0.6-1.25 mg)	2.4-11.6
		Topical Estradiol (0.5-1.0 mg)	2.9-35.5
Progesterone (pg/mL)	Premenopausal	Luteal	75-270
		Follicular	12-100
	Postmenopausal		12-100
	Supplement (12-24 Hrs.)	Hormonal Contraceptives	10-53
		Oral Progesterone (100 mg)	30-300
		Topical Progesterone	200-3000
Testosterone (pg/mL)		All ages	16-55
		Ages 16-30	18-55
		Age >30	16-47
	Supplement (12-24 Hrs.)	Hormonal Contraceptives	13-45
		Topical Testosterone (0.3-0.5 mg)	22-86
DHEA-S (ng/mL)		All Ages	2-19
		Ages 16-30	6.4-18.6
		Ages 31-45	3.9-11.4
		Ages 46-60	2.7-8
		Ages 61-75	2-6
	Supplement (12-24 Hrs.)	Oral DHEA (5-10 mg)	2.8-8.6
		Topical DHEA (5 mg)	3-8
Estrone (pg/mL)			1.36-5
Estriol (pg/mL)	Premenopausal		<7
	Postmenopausal		<7
	Supplement (12-24 Hrs.)	Oral Estriol	5-20
		Topical Estriol	5-100
	WOMEN & MEN		
Cortisol (ng/mL)	C1	Morning	3-8
	C2	Noon	2-4
	C3	Evening	1-2
	C4	Night	0.5-1.5
	MEN		
Estradiol (pg/mL)			0.8-2.2
Progesterone (pg/mL)	Supplement		15-100
		Topical progesterone (5-10 mg)	42-650
Testosterone (pg/mL)		All Ages	44-148
		Ages 16-30	72-148
		Ages 31-50	58-120
		Ages 51-70	44-94
		Ages > 70	30-77
	Supplement (12-24 Hrs.)	Androgel (25-50 mg)	1300-3700
		Topical testosterone (5-10 mg)	115-800
DHEA-S (ng/mL)		All Ages	2-23
		Ages 16-30	7-23
		Ages 31-45	6-18
		Ages 46-60	4-11.5
		Ages 61-75	2.4-7.5
	Supplement (12-24 Hrs.)	Oral DHEA (25 mg)	6-17
		Topical DHEA (10 mg)	4-15
Estrone (pg/mL)			0-3
Estriol (pg/mL)			0-3

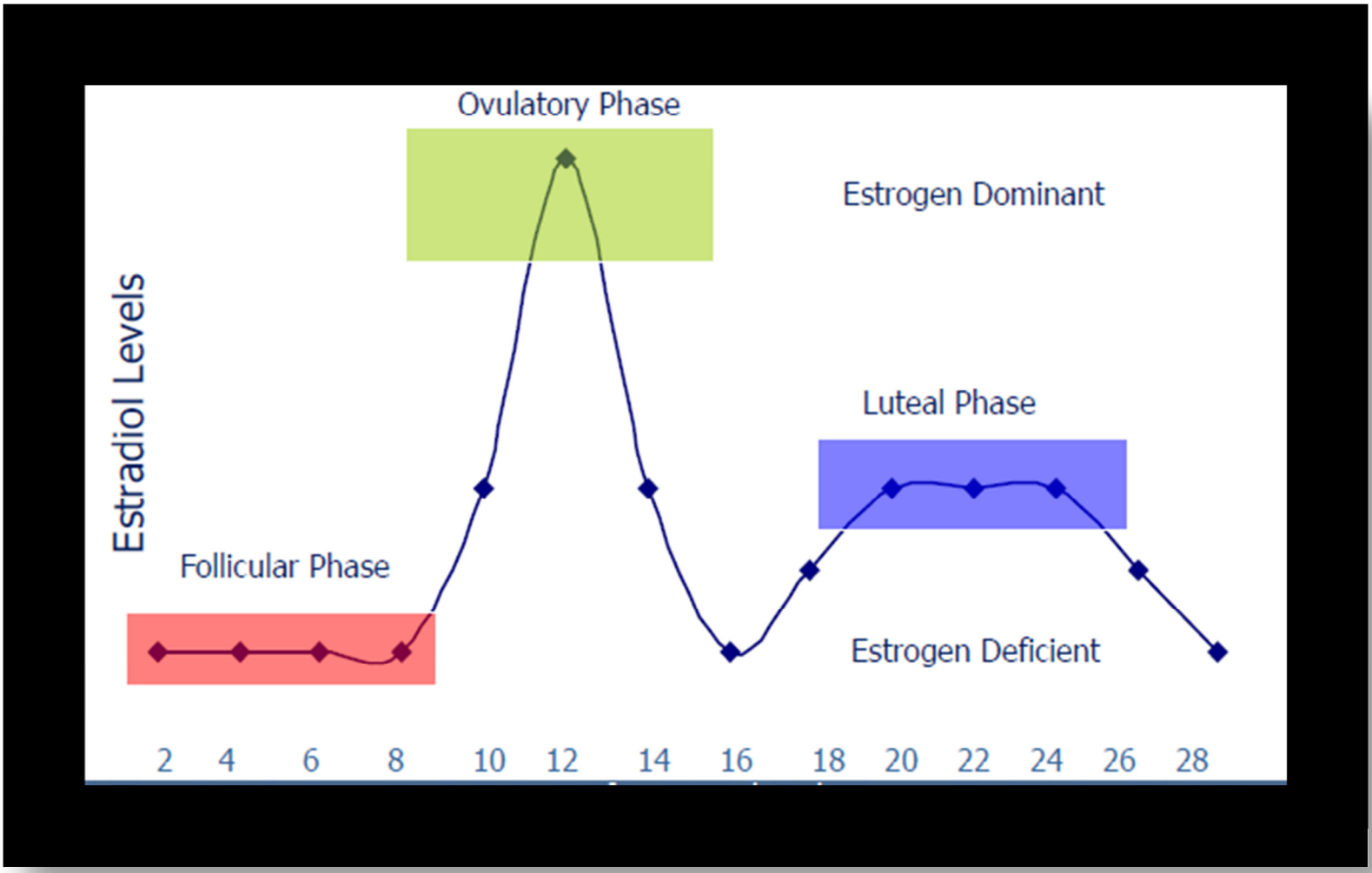
*Note difficulties with wide range of acceptable salivary values, esp. with supplementation

Data provided by ZRT Laboratory, LLC ©2007

Supplement types and dosages are for practitioner information, and are not recommendations for treatment

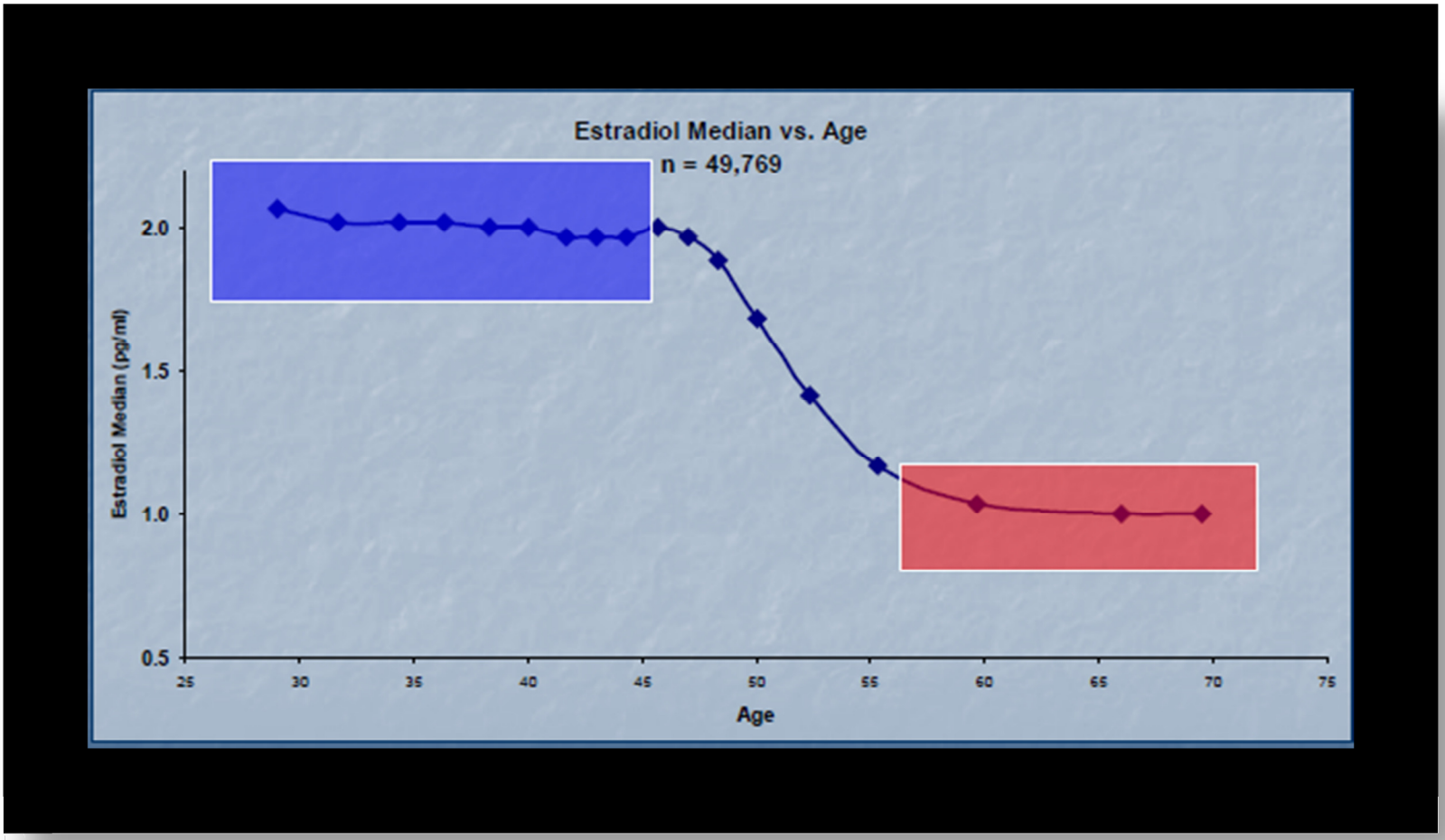
Physiological Reference Ranges

Estradiol Levels in the Menstrual Cycle



Physiological Reference Ranges

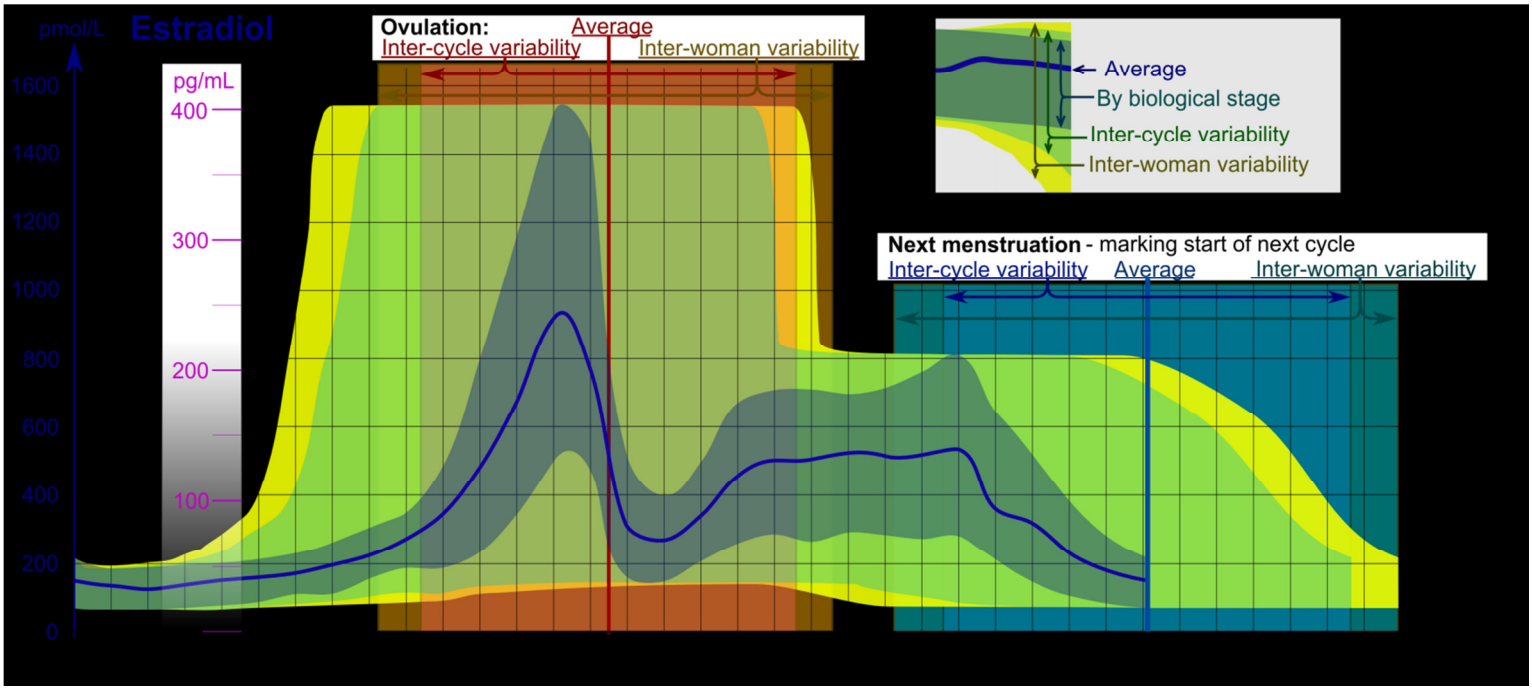
Salivary Estradiol: The Menopausal Transition



Physiological Reference Ranges

Estradiol in Women

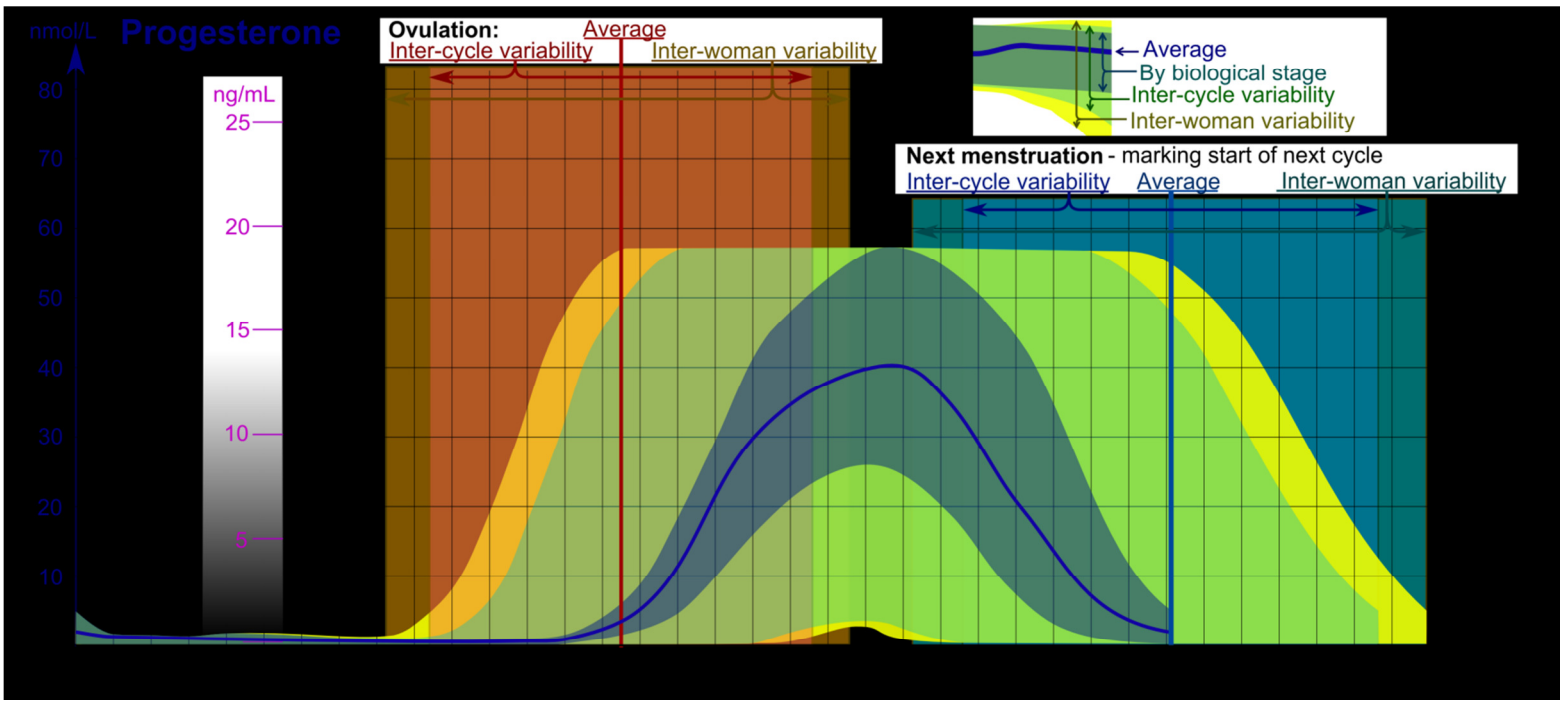
Serum Values During Menses Cycle



Physiological Reference Ranges

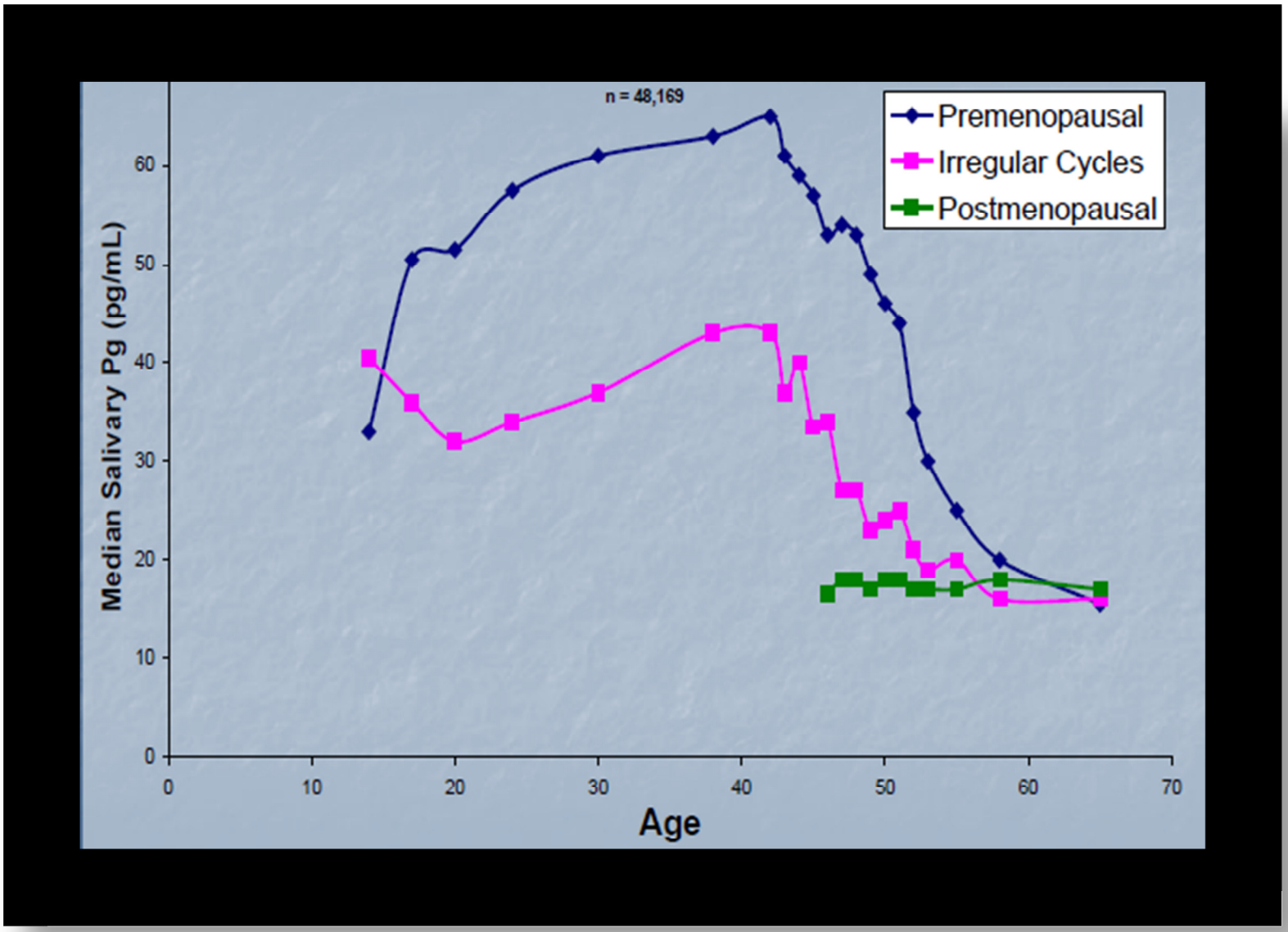
Progesterone in Women

Serum Values During Menses Cycle



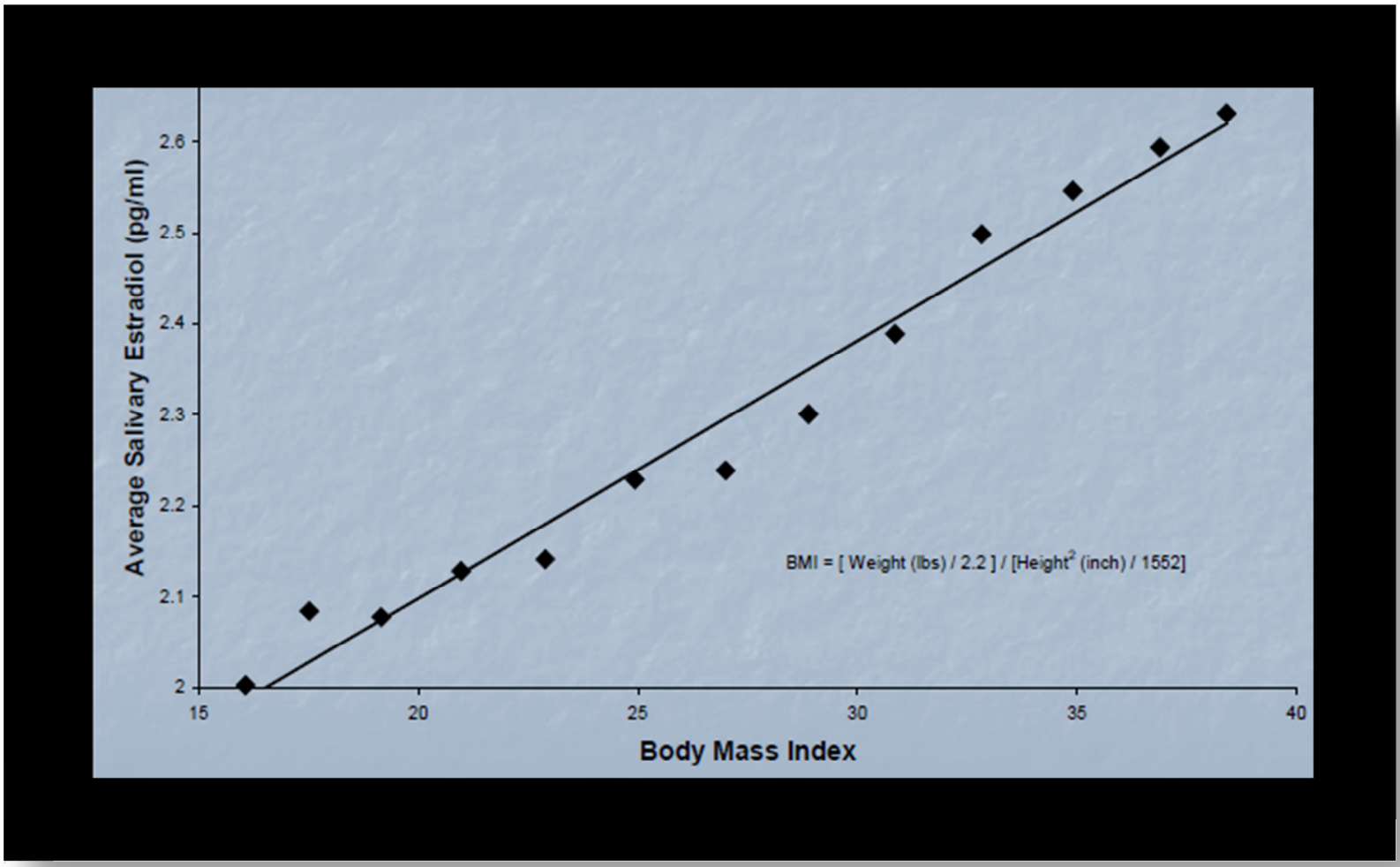
Physiological Reference Ranges

Salivary Progesterone in Women



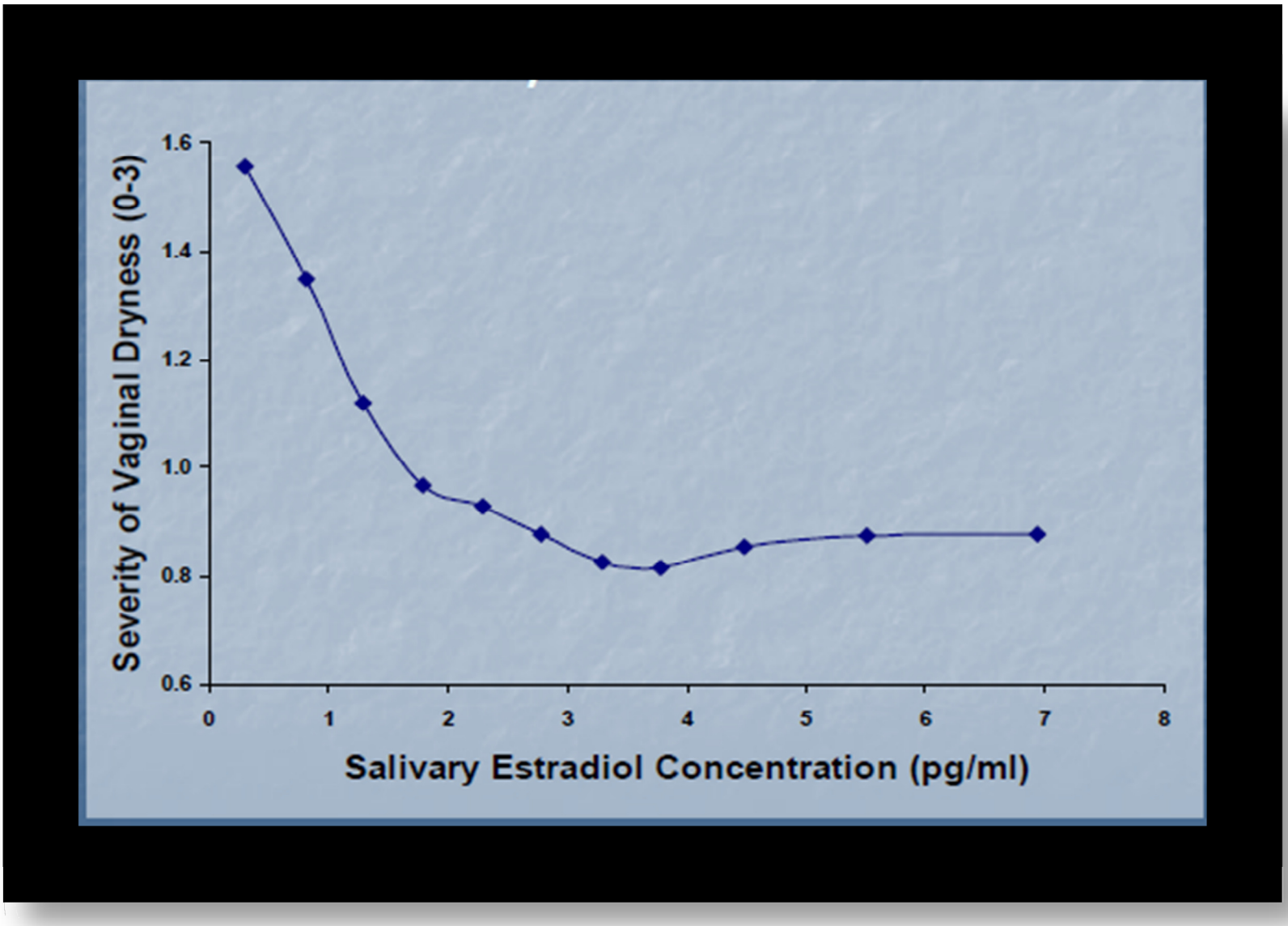
Physiological Reference Ranges

Salivary Estradiol vs. BMI in Perimenopausal Women



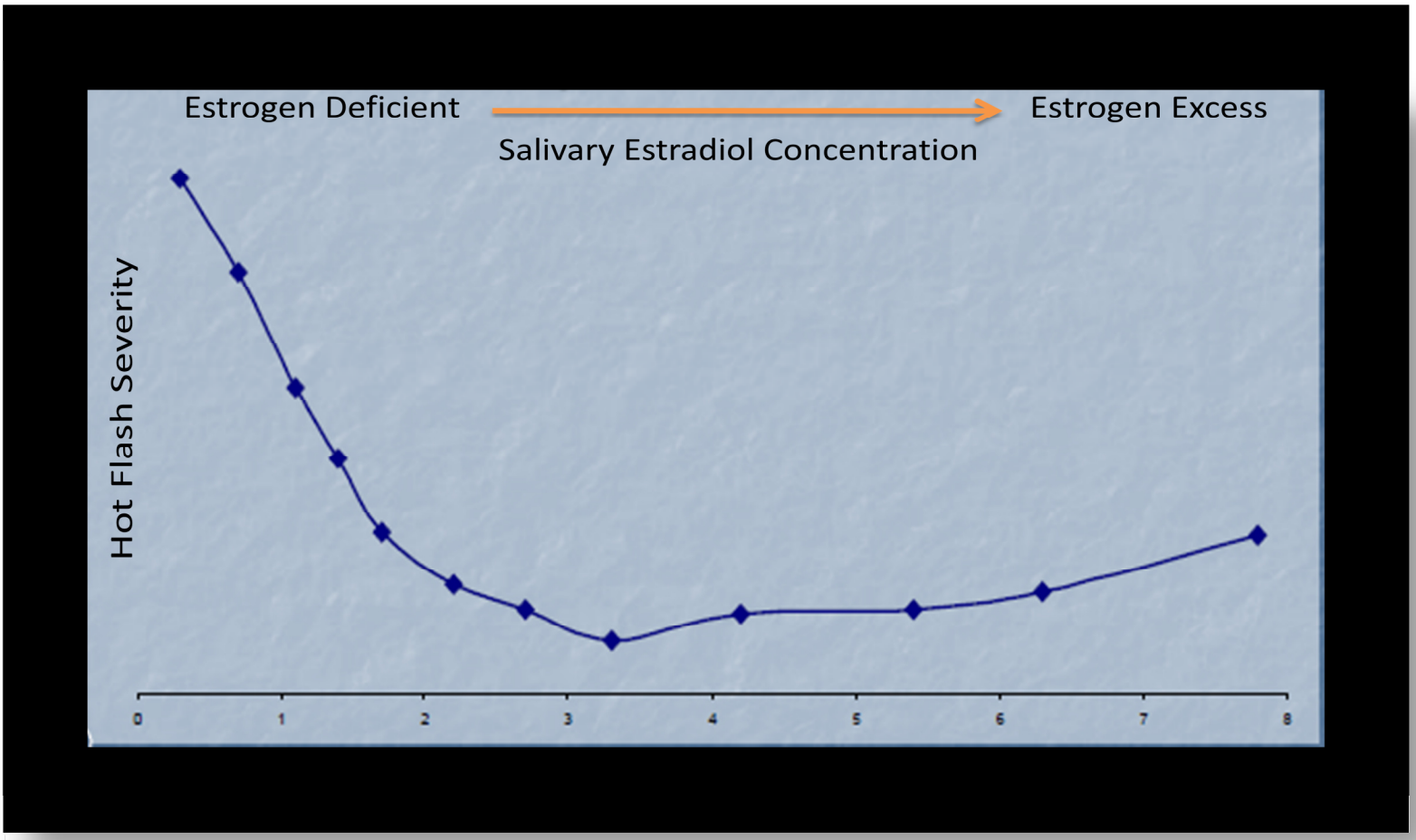
Physiological Reference Ranges

Estrogen Influence on Vaginal Dryness



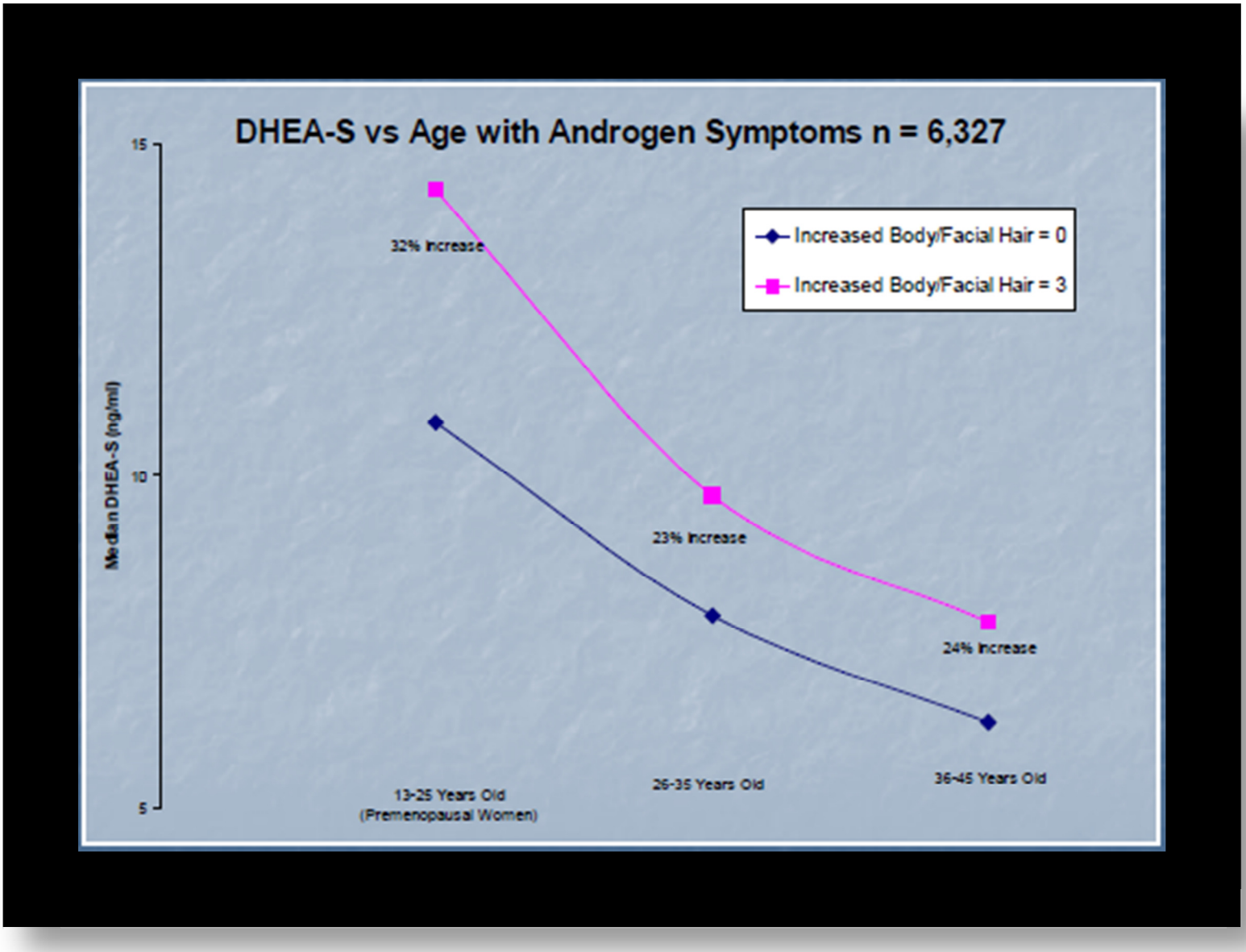
Physiological Reference Ranges

Estrogen Influence on Hot Flashes



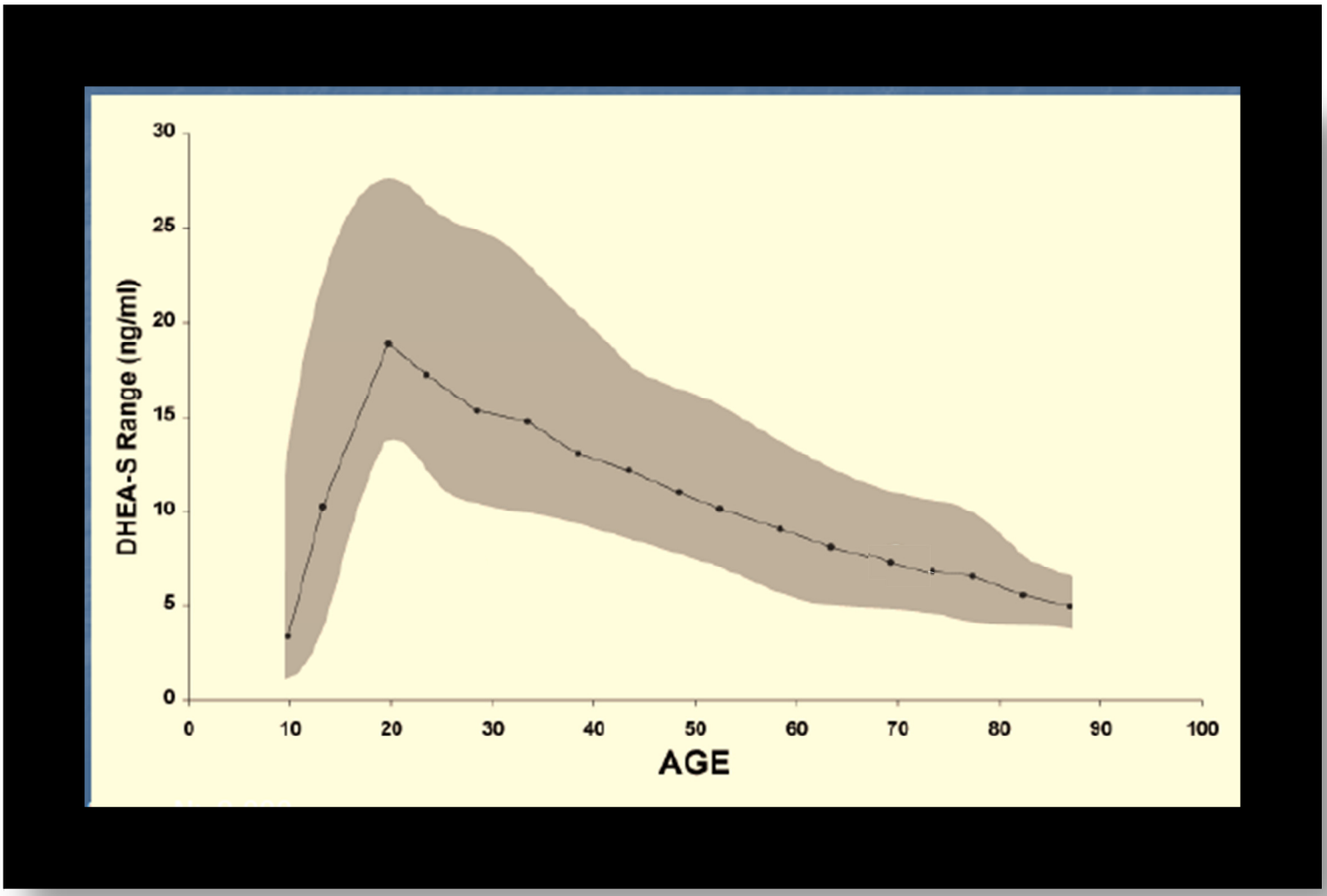
Physiological Reference Ranges

DHEA-S in Women



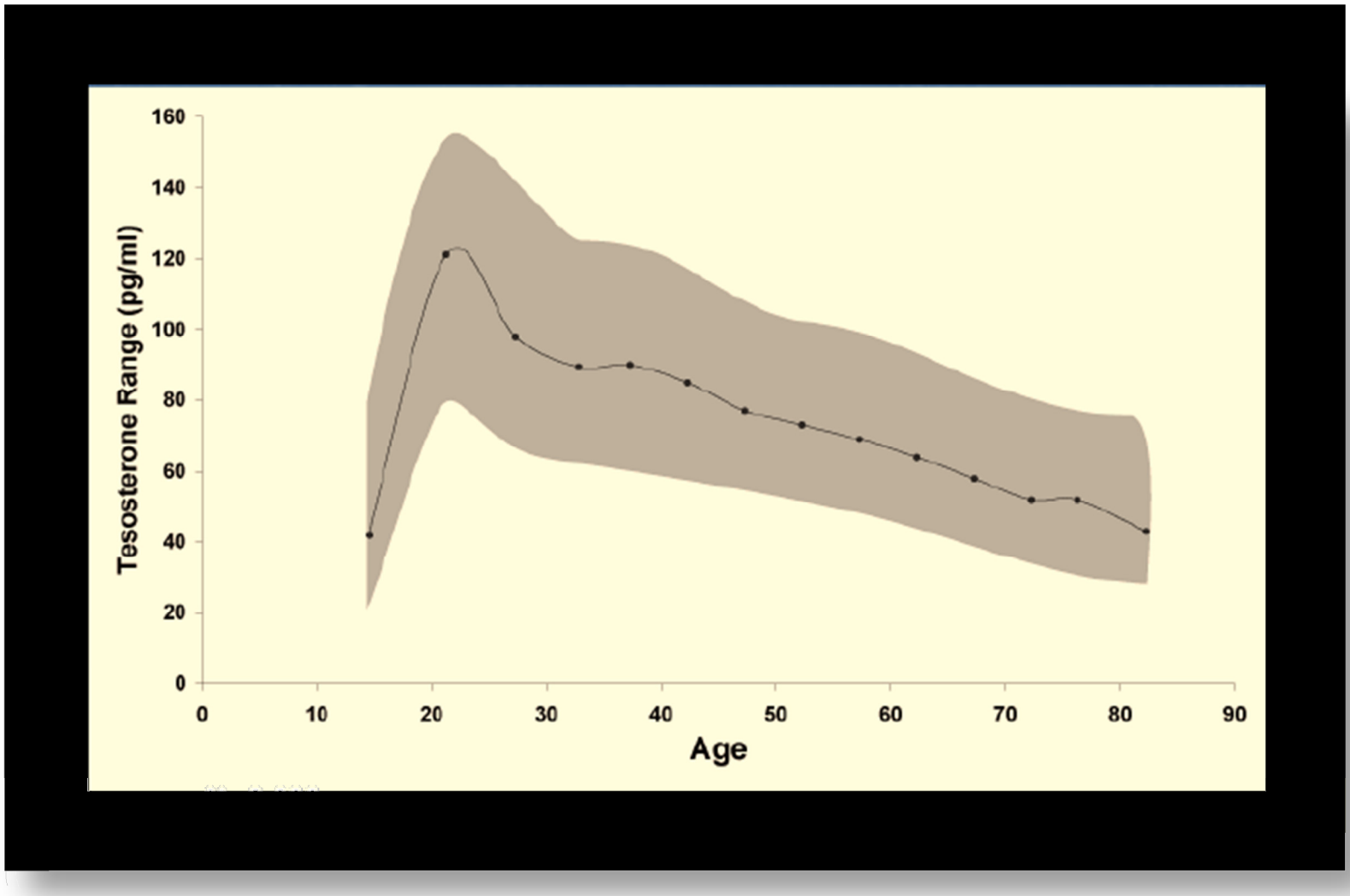
Physiological Reference Ranges

DHEA-S in Men



Physiological Reference Ranges

Testosterone in Men



“Just Tell Me What to Prescribe”

That’s the kind of easy answer many practitioners are looking for. But put quite simply and directly, there just are no easy answers. As you’ve seen, endocrine hormone levels vary widely affected by a variety of variables. There are broad relationships among hormones due to their interaction and metabolism patterns. Symptoms caused by either high, low, or fluctuating levels of various hormones can overlap. And dietary as well as emotional factors also play major roles. That leaves us with the conclusion that treating hormone imbalance must be a holistic and iterative process that varies on a patient-by-patient basis.

Treatment Roadmap

The information provided thus far should help to mitigate what might otherwise lead one to believe that the practice of bioidentical hormone replenishment is no more than a trial-and-error guessing game.

In the following pages of this section you’ll find general guidelines you can follow. However, at the end of the day, continued testing, careful evaluation and gradual treatment modification must be your guideposts along the way.

Treatment: General Guidelines

Goal: Restore hormone levels to the normal physiological levels of a younger individual, to provide the protective benefits of the hormones to the entire system.

- Replenish only the hormones that are necessary
- Correct cortisol, thyroid and progesterone first
- Use the lowest amount required to alleviate symptoms and achieve the desired physiologic effect
- Start bio-identical estrogen dosage at mid-range
  - Never use unopposed Estrogen
- Start low and adjust slowly
  - Efficacy can be improved by changing timing, application , and/or delivery route
- Monitor symptoms
  - If not resolved consider other hormonal and behavioral causes
- Re-test levels
  - To see if normal physiologic levels have been reached

Dosage Forms

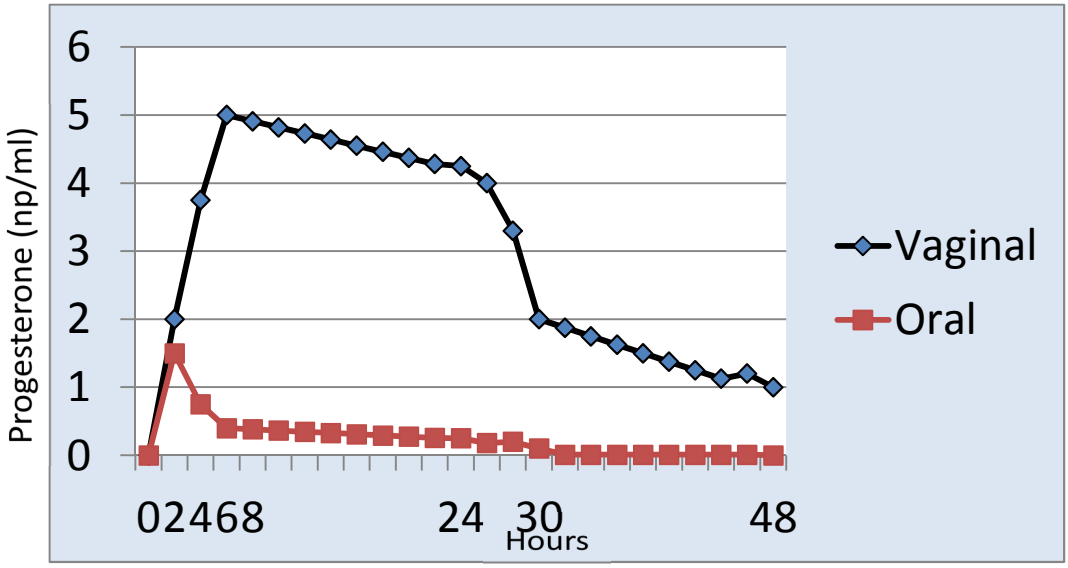
Most <u>synthetic</u> hormones are delivered orally

- Not well absorbed by the body
- Limits to the amounts that can be taken
  - Patients may be taking more to get less or may be unable to take the amount really needed
  - Injections can be expensive, inconvenient, and painful
  - Many of the gels available have unpleasant scents

Compounded BHRT Forms Allow You to Tailor Dosage to Patients' Desires & Lifestyles

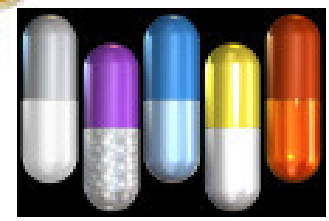
- Vaginal delivery forms provide excellent systemic absorption

  - Suppositories
  - Creams and Gels
    - Non-irritating bases are hypoallergenic and petrolatum-free
- Vaginal delivery of estrogens & progesterone is vastly superior



Compounded BHRT Dosage Forms

(continued)



- Troches (lozenges) provide fast dissolution and rapid onset and avoid destruction in upper GI
  - May require more frequent dosing – up to 3X/day
  - Saliva testing considerations

- Sustained Release Capsules with micronized, dye-free ingredients provide higher production of metabolytes and more level response than commercially-produced pills
  - Can be dispensed in controlled release over 10-12 hrs.
  - Requires only 1-2 X per day

Converting from Synthetics

Goal: Balance Estrogen and Progesterone

- Add Progesterone first
  - Taper-down estrogen dosage first 1-2 months
  - Increase ratio of Estradiol
  - Prescribe Milk Thistle to detox the liver
    30 days from last synthetic dose 250 mg bid-tid
- Converting from Premarin or Prempro
  - Decrease dosage by 50% daily for 2 weeks
  - Then every other day for 2 weeks
    - May take up to 6 weeks to avoid hot flashes
  - Then discontinue synthetics

BHRT Dosing Guidelines for Women

See Reference Notes at end of this section

Source: PCCA

PMS

Progesterone — Oral

300 mg XR

½ tablet at bedtime on Days 1-10; then 1 tablet BID-QID on Day 11 until start of menstruation[42]

Progesterone — Topical

30-40 mg Transdermal[39]

20-40 mg cream — Start using once a day on Day 12 until 2 weeks prior to period; then BID=TID during week prior to period[43]

Premenopausal

Bi-est — Topical

(80:20) 0.375 mg/mL plus progesterone cream 40 mg/mL — Apply 1 mL to thin-skinned area daily at bedtime[42]

Progesterone — Oral

200 mg/day[22, 23]

Progesterone — Vaginal

400 mg vaginal pessary/suppository[22]

300-600 mg/day over 2-3 doses[23]

45-0- mg/day sustained release[23]

30-40 mg/mL — Apply 0.5 mL to thin-skinned area on Days 1-10; then 1 mL QD on a different thin-skinned site Days 11-28[42]

Testosterone — Oral

4 mg in oil — One capsule QD[42]

Testosterone — Topical

150 or 300 mcg/day transdermal[30]

Perimenopausal

DHEA Oral

50 mg/day[34]

BHRT Dosing Guidelines for Women

(Cont'd.)

Postmenopausal

Estradiol — Oral

2 mg/day micronized estradiol[1, 4, 5, 6, 7, 8, 41]
1 mg/day micronized Estradiol in 1st-25th day of each month[3, 41]
50 mg every 3 months[31]
0.7-1.05 mg/day[36]
0.5 mg/day[38]

Estradiol — Topical

0.05 mg/day continuous transdermal Estradiol (surgical menopause)[2]
1.5 mg transdermal[5]
1 g transdermal gel[6]
1 mg twice weekly transdermal[7]
0.5-2.5 mg/day gel once a day in the morning on the 1st-25th day of each month[41, 44]

Estradiol — Vaginal

0.125 mg and 0.5 mg daily[28]

Estriol — Oral

2-8 mg/day[9, 10, 11, 12, 13, 14, 15, 16, 17, 18]
0.5-5.0 mg/day[40]

Estriol — Vaginal

0.5 mg vaginal cream once each night for 2 weeks[19, 44]
1 mg vaginal suppository — Insert 1 suppository vaginally daily at bedtime for 3 days; then twice weekly at bedtime[42]

Bi-est (80:20) or (90:10) — Oral

1.25, 2.5, or 5 mg on 1st-25th day of each month[40, 41, 42]

Bi-est — Transdermal

(50:50) 0.5-3 mg/day in the morning on the 1st-25th day of each month[41]
(80:20) 0.1-1.2 mg/day in the morning on the 1st-25th day of each month[41]

Tri-est (80:10:10)— Oral

1.25, 2.5, or 5 mg[40]
1.25, 2.5, or 5 mg on 1st-25th day of each month[41]

Tri-est (80:10:10)— Vaginal

0.1-0.6 mg/day at bedtime on 1st-25th day of each month[41]

BHRT Dosing Guidelines for Women

(Cont'd.)

Postmenopausal (Cont'd.)

Progesterone — Oral

300 mg/day at bedtime 10 days/month (for regular monthly bleeding) [20, 36]
200 mg/day 14 days/month (to remain amenorrheic) [20, 21, 36]
100 mg/day 25 days/month (to remain amenorrheic) [20]
100 mg/day for 1st-23rd day of each month[25]
50-200 mg/day micronized progesterone 1st-25th day of each month[26, 41]
400 mg/day micronized progesterone[27, 42]
100-200 mg QD-BID for at least 2 weeks/month[44]

Progesterone — Topical

20 mg/day cream — apply 20 mg to thin-skinned area daily at bedtime[24, 40, 42]
20-40 mg cream QD-BID on days 12-26 to thin-skinned area[43, 44]
100 mg micronized progesterone applied vaginally[38]
100-400 mg/day on 1st-25th day of each month[41]
¼ - ½ tsp 2% progesterone cream[44]

Progesterone — Vaginal

25 mg and 50 mg daily[28]

Testosterone — Topical

150 or 300 mcg/day transdermal[29, 37]
50 mg implants every 3 months[31]
2.5-10 mg/day liposomal gel[41]

Testosterone — Vaginal

1-2 mg natural testosterone in cream base 2-3 times/week[44]
0.25 mg and 0.5 mg daily[28]

DHEA — Oral

25-50 mg/day[33]
100 mg/day[35]
5-30 mg/day[41, 44]

DHEA — Topical

10% cream (3-5g) once daily in the morning[32, 41]

DHEA — Vaginal

1.25 mg and 50 mg daily[28]

Pregnenalone — Oral

25-200 mg QD[44]

BHRT Guidelines for Women

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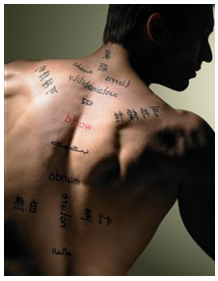
Commonly Requested BHRT Compounds for Women

- Progesterone 5% Topical Cream
- Progesterone 100 mg Troche
- Progesterone 200 mg Troche
- Progesterone 8% Vaginal Gel
- Progesterone 100 mg Suppository
- Progesterone 100 mg Sublingual Suspension
- Progesterone 100 mg Slow-Release Capsules
- Testosterone 0.1% / Estriol 0.05% Topical Foam
- Testosterone 0.25 mg/0.25 mL Topical Cream
- Bi-Est (50/50) 0.1 mg /0.25 mL Topical Cream (Estriol/Estradiol [50/50])
- Bi-Est (50/50) 0.25 mg /0.25 mL Topical Cream (Estriol/Estradiol [50/50])
- Bi-Est (50/50) 0.5 mg /0.25 mL Topical Cream (Estriol/Estradiol [50/50])
- Bi-Est (50/50) 0.5 mg Slow-Release Capsules (Estriol/Estradiol [50/50])
- Bi-Est (50/50) 1 mg Slow-Release Capsules (Estriol/Estradiol [50/50])
- Bi-Est (80/20) 0.5 mg Slow-Release Capsules (Estriol/Estradiol [80/20])
- Bi-Est (80/20) 1 mg Slow-Release Capsules (Estriol/Estradiol 80/20])
- Bi-Est 1.25 mg/Progesterone 50 mg Slow-Release Capsules (Estriol/Estradiol 80/20])
- Estriol 3 mg/mL Vaginal Cream
- Estriol 5 mg/mL Vaginal Cream
- Tri-Est 1.25 mg/mL Topical Cream
- Tri-Est 0.625 mg Slow Release Capsules (Estriol/Estradiol/Estrone [80/10/10])
- Tri-Est 1. 25 mg/Progesterone 50 mg Slow-Release Capsules (Estriol/Estradiol/Estrone [80/10/10])
- Tri-Est 0.625 mg/0.25 mL or 5 mg/mL Sublingual Suspension (Estriol/Estradiol/Estrone [80/10/10])
- Dehydroepiandrosterone 5 mg Slow-Release Capsules
- DHEA 10 mg/mL Slow Release Drops

Commonly Requested BHRT Compounds for Men



- Testosterone 2.5% Topical Gel
- Testosterone 5% Topical Gel
- Testosterone 10% Topical Gel
- Testosterone 30 mg/mL Topical Cream
- Testosterone 5%/Chrysin 5% Topical Cream
- Testosterone 2.5% /Isopropyl Myristate 5% Topical Gel
- Testosterone 5% /Isopropyl Myristate 5% Topical Gel
- Testosterone 10% /Isopropyl Myristate 5% Topical Gel
- Testosterone 1% Topical VanPen Cream
- Testosterone 5 mg Troche
- Testosterone 10 mg Troche
- Testosterone 25 mg Troche
- Testosterone 10 mg/mL Sublingual Suspension
- Pregnenalone Slow-Release Capsules

Clinical Observations

Case Study 1: "Menopause" — Basic Study Model

Patient Profile

55 year old business woman, normal body weight, irregular exercise

Last Physical – 2 years ago

No breast cancer history

Key Symptoms

- Hot flashes
- Night Sweats
- Foggy thinking
- Fatigue
- Urinary incontinence
- Vaginal dryness
- Low libido

Test Results

HORMONE TEST	IN RANGE	OUT OF RANGE	UNITS	RANGE
E2 (Estradiol)	1.0		pg/ml	1.0-1.5
Pg (Progesterone)		20 L	pg/ml	25-100
Pg/E2 Ratio		20 L		50-100
Testosterone		15 L	pg/ml	20-50
DHEA-s	4.5		ng/ml	3-10
AM Cortisol		10 H	ng/ml	3-8

Analysis

- Low normal Estradiol contributes to hot flashes, night sweats, memory lapses, vaginal dryness and urinary incontinence
- Progesterone is low. It is needed for Estrogen receptor response and helps stabilize vasomotor symptoms
- Low Testosterone contributes to vaginal dryness, memory loss and low libido
- Low-normal DHEA-S contributes to low testosterone.
  - DHEA from the adrenals often converts to T in women
- High AM Cortisols, low testosterone and E2 contribute to bone loss
  - Indication of adrenal dysregulation
  - Restore balance if adrenal function is not in balance

Treatment

- Start bioidentical Estradiol at low dose and increase only as clinically required
- Dose bioidentical Progesterone to achieve balance for uterine protection
- Sig: BHRT daily for a woman who is not cycling
  - — Allow a 2-3 day monthly "hormone holiday" to allow cell receptors to reset
- Correct vaginal dryness and relieve urinary incontinence with Estriol vaginal cream, applied locally and massaged into tissues.

Clinical Observations

Case Study 2: "Perimenopause"

Patient Profile

48 year old business woman, history of endometriosis, depression, fibromyalgia

Meds: Paxil®, Ambien®, acetaminophen, calcium

Works part-time in family business, volunteers 4 hrs./wk., family includes spouse, 2 children, conflict w. in-laws, increased alcohol consumption due to PMS

Key Symptoms

- Mid-body weight gain
- Headaches
- PMS
- Body aches and pains
- Poor sleep
- Cognitive changes
- Bloating
- Fatigue

Exam Results

VALUE	UNITS	MEASURED	STATUS	NORMAL SALIVARY RANGE
E2 (Estradiol)	pg/ml	4.5	High	1.3-3.3
Pg (Progesterone)	pg/ml	132	OK	75-270
Pg/E2 Ratio		29	Low	22-200
Testosterone	pg/ml	33	Norm	16-47
DHES-s	ng/ml	7.1	Norm	2.7-8
AM Cortisol	ng/ml	6.8	Norm	3-8
Noon Cortisol	ng/ml	2.1	Norm	2-4
Evening Cortisol	ng/ml	0.6	Low	1-2
PM Cortisol	ng/ml	7.1	High	0.5-1.5
BMI		28	OK	19-35
Waist	In.	35	Normal	35
Waist/Hip		0.81	OK	< 0.8

Analysis

- PMS with features of emotional turmoil account for symptoms of depression, anger, feeling overwhelmed, out of control, decreased self esteem, anxiety and mood swings.
- Emotional arousal likely responsible for increased food intake, cravings for certain foods.
- Absolute serum values for estrogen and progesterone are only slightly outside the normal range for women reporting PMS. However, changes in ratios of hormones or their rate of conversion to active metabolites may contribute to PMS symptoms.

Case Study #2: "Perimenopause" (Cont'd.)

Treatment

- Rx: BHRT topical progesterone 80 mg/ml — 0.5 ml to skin daily, days 1-10, then 0.5 mg to skin bid, days 11 until menses
- Nutrition: modify meals to Mediterranean diet and decrease fast food intake
- Exercise: Yoga 1-3 times weekly

Follow-up

VALUE	UNITS	MEASURED	STATUS	NORMAL SALAVARY RANGE
E2 (Estradiol)	pg/ml	4.0	OK	2.9-35.5
Pg (Progesterone)	pg/ml	2890	OK	200-3000
Pg/E2 Ratio		772	OK	5.6-1000
Testosterone	pg/ml	36	Normal	16-47
DHES-s	ng/ml	5.4	Normal	2.7-8
AM Cortisol	ng/ml	5.4	Normal	3-8
Noon Cortisol	ng/ml	2.0	OK	2-4
Evening Cortisol	ng/ml	3.0	Normal	1-2
PM Cortisol	ng/ml	1.3	OK	0.5-1.5
BMI		24	OK	19-35
Waist	In.	32	Normal	35
Waist/Hip		0.75	Normal	< 0.8

- Patient reports significant reduction in pain and that some days she is "completely pain free." Palpitations have markedly decreased, and stamina has increased. Patient feels less dependent on foods to modulate energy level and moods. Patient is doing yoga 3 times weekly. Patient notes PMS symptoms are better but escalate week prior to menses.
- Continue topical progesterone. At day 1 of next menses, add oral BHRT progesterone 300 mg in MBK base, p.o. bid-tid for late luteal PMS flare-ups. Begin to taper off psychotropics.

Clinical Observations

Case Study 3: "Stress & Hyperthyroidism"

Patient Profile

48 year old woman, Allergenic rhinitis, Hypertension, Restless Leg Syndrome, Gallstones, Dyslimpidemia, Depression, Anxiety

Meds: Maxzide® 75/50 1 p.o. daily, Glucosamine Chondroitin 750mg daily, Cardizem® 300 mg daily, Calcium 600 mg daily, Vytorin® 10/20 daily, Prilosec ®20 mg daily, Singulair® 10 mg daily, ASA 81 mg daily

Lives with adopted son, renter, 4 dogs. Caregiver for parents with heart disease, sister with substance abuse.

Pt. works one full-time and one part-time job, volunteers 3 hrs./wk.
No exercise. High soda intake, snacking at work

Key Symptoms

- Fatigue
- Dysphoric mood
- Disturbed sleep
- Food cravings
- Weight gain
- Cognitive changes
- Bloating
- Cold intolerance
- Dry hair/skin
- Thinning hair

Exam Results

VALUE	UNITS	MEASURED	STATUS	NORMAL SALIVARY RANGE
E2 (Estradiol)	pg/ml	0.5	Low	1.3-3.3
Pg (Progesterone)	pg/ml	12	Low	75-270
Pg/E2 Ratio		24	Low	5.6-1,000
Testosterone	pg/ml	16	Norm	16-47
DHES-s	ng/ml	1.0	Low	2.7-8
AM Cortisol	ng/ml	10.1	High	3-8
Noon Cortisol	ng/ml	4.6	High	2-4
Evening Cortisol	ng/ml	1.8	Norm	1-2
PM Cortisol	ng/ml	6.1	High	0.5-1.5
BMI		39.5	High	19-35
Waist	In.	44	High	35
Waist/Hip		0.89	High	<0.8

Analysis

- "Aha! Discovery" — Additional testing reveals TSH=2.5-10 mlU/L w. normal FT4 level
- Subclinical hyperthyroidism — associated symptoms: dyslimpidemia, endothelial dysfunction, neurocognitive disorders, increased BMI. Presents risks for CV disease, cancer dementia with elevated liver function
- Strain = Emotional demands v. potential for control

- Support: How many people can you rely on to help with children, pets, household, transportation?

Case Study #3: "Stress & Hyperthyroidism" (Cont'd.)

Treatment

- Rx: BHRT Topical Bi-Est 80% Estriol + 20% Estradiol 0.375 mg. + Progesterone 40 mg/mL + DHEA 1.5 mg/mL to skin daily. Compounded D3 50,000 IU to skin once weekly. Armour Thyroid® 15 mg p.o. daily. Idoral daily. Co-enzyme Q 10 100 mg daily
- Nutrition: Take meals, snacks to work. Taper off sodas
- Lifestyle: Increase support, self-care

Fo

VALUE	UNITS	MEASURED	STATUS	NORMAL SALIVARY RANGE
E2 (Estradiol)	pg/ml	1.5	Low	2.4-11.6
Pg (Progesterone)	pg/ml	1004	OK	200-3,000
Pg/E2 Ratio		669	OK	17-1,250
Testosterone	pg/ml	22	Normal	16-47
DHES-s	ng/ml	4.0	Normal	2.7-8
AM Cortisol	ng/ml	14.4	Normal	3-8
Noon Cortisol	ng/ml	2.8	OK	2-4
Evening Cortisol	ng/ml	1.2	Normal	1-2
PM Cortisol	ng/ml	0.7	OK	0.5-1.5
BMI		35	OK	19-35
Waist	In.	35	Normal	35
Waist/Hip		0.79	Normal	<0.8

- Patient reports improvement in skin, nails, hair, energy, stamina and sleep. Mood less irritable and less tearful. Weight decreased 6 lbs.
- Increase Armour Thyroid® to 30 mg daily
- Begin yoga exercise program
- Take on a handwork project

Clinical Observations

Case Study 4: "CV Risks"

Patient Profile

50 year old woman complaining of headaches, vaginal dryness, tearfulness; palpitations and chest pain with negative cardiology work-up; night sweats;; fatigue, aches and pains; dry hair and skin. Mid-body weight gain, food cravings for sugar; cognitive changes. Unhappy with psychotropics. Last menses 2 years ago.

Meds: Excedrin PM®, Multivitamin, B-Complex, Vitamin C

Lives alone after 2 marriages. Divorced for 6 yrs. Moved frequently during childhood. 2 cats and horses..

Pt. works full-time job with high stress. One glass of wine daily. "Too tired to exercise." Watches TV 14 hrs. per week. Four sodas per day.

Key Symptoms

- Fatigue
- Dull complexion
- Obese abdomen
- Tension headaches
- Migraine headaches
- Thinning hair
- Crepitance of knees

Exam Results

VALUE	UNITS	MEASURED	STATUS	NORMAL SALIVARY RANGE
E2 (Estradiol)	pg/ml	0.5	Low	1.3-3.3
Pg (Progesterone)	pg/ml	15	Low	75-270
Pg/E2 Ratio		30	Low	22-200
Testosterone	pg/ml	39	Norm	16-47
DHES-s	ng/ml	4.1	Low	2.7-8
AM Cortisol	ng/ml	12.9	High	3-8
Noon Cortisol	ng/ml	1.4	Low	2-4
Evening Cortisol	ng/ml	1.0	OK	1-2
PM Cortisol	ng/ml	0.3	Low	0.5-1.5
BMI		30	OK	19-35
Waist	In.	35	Normal	35
Waist/Hip		0.8	Normal	<0.8

Analysis

- Coronary hyperactivity

Case Study #4: "CV Risks"
(Cont'd.)

Treatment

- Rx: BHRT Topical Bi-Est 80% Estriol + 20% + Progesterone 20 mg/mL to skin daily.
- Nutrition: Eat breakfast. Take lunch, snacks to work. Decrease soda consumption
- Exercise: Yoga

Follow-up

VALUE	UNITS	MEASURED	STATUS	NORMAL SALIVARY RANGE
E2 (Estradiol)	pg/ml	3.2	OK	2.4-11.6
Pg (Progesterone)	pg/ml	690	OK	200-3,000
Pg/E2 Ratio		216	OK	17-1,250
Testosterone	pg/ml	31	Normal	16-47
DHES-s	ng/ml	2.3	OK	2.7-8
AM Cortisol	ng/ml	8.5	OK	3-8
Noon Cortisol	ng/ml	6.8	High	2-4
Evening Cortisol	ng/ml	2.2	High	1-2
PM Cortisol	ng/ml	1.5	OK	0.5-1.5
BMI		27	OK	19-35
Waist	In.	32	Normal	35
Waist/Hip		0.74	Normal	<0.8

After 2nd follow-up — 12 months after 1st visit

- After beginning with exercise class, patient reports exercising with walking, swimming, kick boxing class; improving self-care regimen with limits on time/emotional exp. Eating under control. "Overall feeling better than I've felt in years." Contemplating a sabbatical.
- Increase Progesterone to 40 mg daily
- Nutrition: Mediterranean diet
- Encourage exercise

Clinical Observations

Case Study 5: "Never Too Old"

Patient Profile

70 year old woman previously on Estradiol tablet and OTC progesterone cream, but stopped. Pt. complains of hot flashes, aches and pains, cognitive changes and fatigue

Meds: Excedrin, Levothyroxine, Retin A, acetaminophen pm

College degree. Lives with spouse. Volunteers 10 hrs./wk.; exercises 5 hrs./wk.; 5 glasses of wine/wk. smokes ½ pk./day.

Pt. exhibits healthy outlook, emotional resilience and insight — says she "wants respect, answers and real numbers.

Exam Results

VALUE	UNITS	MEASURED	STATUS	NORMAL SALIVARY RANGE
E2 (Estradiol)	pg/ml	0.5	Low	0.5-1.7
Pg (Progesterone)	pg/ml	15	Low	12-100
Pg/E2 Ratio		30	OK	7-200
Testosterone	pg/ml	187	High	16-47
DHES-s	ng/ml	3.7	Normal	2-6
AM Cortisol	ng/ml	7.0	Normal	3-8
Noon Cortisol	ng/ml	3.7	Normal	2-4
Evening Cortisol	ng/ml	1.1	Normal	1-2
PM Cortisol	ng/ml	0.4	Low	0.5-1.5
BMI		30		19-35
Waist	In.	41	High	35
Waist/Hip		0.85	OK	<0.8

Analysis

- Cortisol/DHEA ratios normally elevate with aging, depression and dimentia
- If pt. responds to BHRT, there is no upper age limit — no reason not to continue treatment
- Repeat Testosterone was 57 pg/mL

Case Study #5: "Never Too Old "
(Cont'd.)

Treatment

- Rx: BHRT Topical 0.375 mg 80% Estriol/20% + Progesterone 20 mg/mL to skin daily.
- Armour® Thyroid 90 mg daily
- Co-enzyme Q 10, Omega 3 fatty acids

Follow-up

VALUE	UNITS	MEASURED	STATUS	NORMAL SALIVARY RANGE
E2 (Estradiol)	pg/ml	3.2	OK	2.4-11.6
Pg (Progesterone)	pg/ml	630	OK	200-3000
Pg/E2 Ratio		196	OK	17-1,250
Testosterone	pg/ml	29	Normal	16-47
DHES-s	ng/ml	4.2	Normal	2-6
AM Cortisol	ng/ml	8.5	OK	3-8
BMI		29	OK	19-35
Waist	In.	38	High	35
Waist/Hip		0.83	OK	<0.8

After 2nd follow-up — 12 months after 1st visit

- Pt. reports, "I don't know anybody my age that feels as good as I do

Further saliva test-based case study analyses are available from ZRT Laboratory's web site:

http://www.zrtlab.com/information-and-research/case-studies.html

End