

Case Studies in Management of the Menopausal Patient

Pamela W. Smith, M.D., MPH, MS

May 25, 2016





Michael Chapman, ND Medical Education Specialist - Asheville





Pamela W. Smith, M.D., MPH, MS





Please type any technical issue or clinical question into either the "Chat" or "Questions" boxes, making sure to send them to "Organizer" at any time during the webinar.

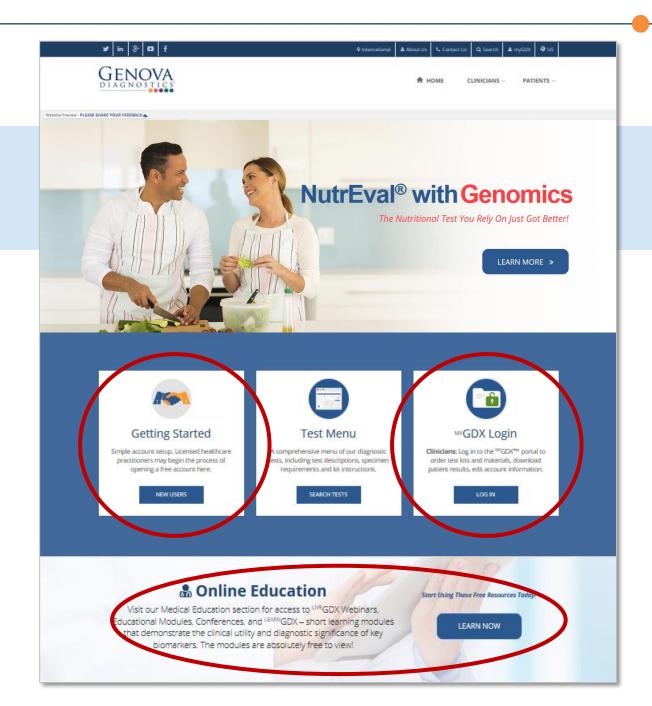
We will be compiling your clinical questions and answering as many as we can the final 15 minutes of the webinar.



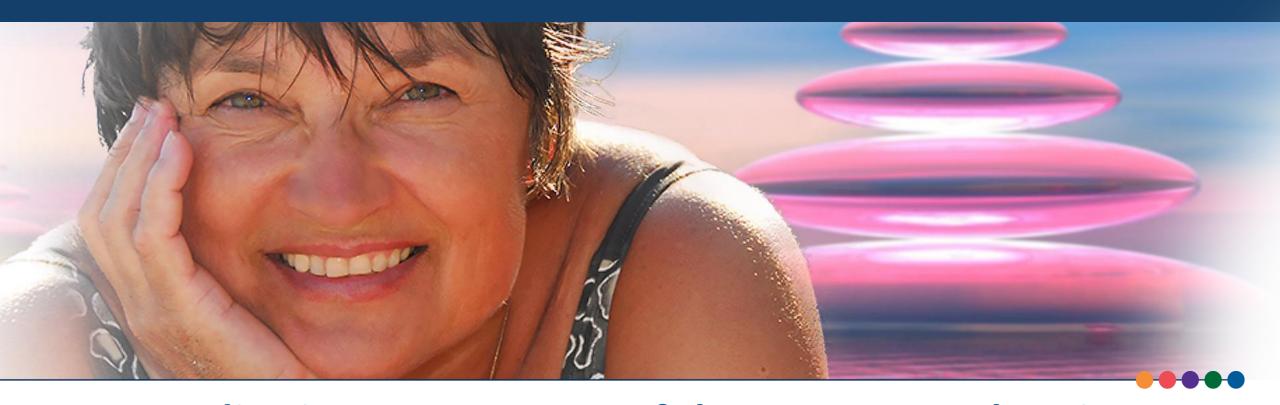


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Case Studies in Management of the Menopausal Patient

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Disclaimer

- The suggested dosages are for educational purposes only.
- They are suggestions for patients with normal renal and hepatic function.
- They are based upon my research and my personal and professional experiences after reviewing 20,000 saliva tests.
- They are not intended as a substitute for a personalized approach to each patient but are designed instead to be a guideline.
- Genova Diagnostics and Pamela W. Smith, M.D., MPH, MS are not responsible for any adverse effects or consequences resulting from the use of any of these suggestions or preparations in this seminar.



Overview

- Health Considerations for the Menopausal Patient
 - Common Menopausal Symptoms
 - Primary Medical Concerns
- Core Diagnostics for the Management of the Menopausal Woman
 - Salivary Hormones + Genova's Therapeutic Cohort Results Cover Page
- Hormone Replacement Therapy and Breast Cancer Risk
- Core Therapeutics for the Management of the Menopausal Woman
- Case Studies





Symptoms of Menopause

- Hot flashes
- Night sweats
- Vaginal dryness
- Anxiety
- Mood swings
- Irritability
- Insomnia
- Depression
- Migraine headaches
- Memory lapses
- Weight gain

- Loss of sexual interest
- Hair growth on face
- Painful intercourse
- Panic attacks
- Weird dreams
- Urinary tract infections
- Vaginal itching
- Lower back pain
- Bloating
- Dizzy spells
- Panic attacks
- Skin feeling crawly

- Flatulence
- Indigestion
- Osteoporosis
- Aching ankles, knees, wrists, shoulders, heels
- Hair loss
- Frequent urination
- Snoring
- Sore breasts
- Palpitations
- Varicose veins
- Urinary leakage





Cardiovascular Health

- Estrogen is cardioprotective.
- After menopause → HDL down, LDL up, total cholesterol up

Bone Health

 Declining levels of estrogen in menopause pose the greatest threat to bone health in post-menopausal women





- Genova Diagnostics'
 Therapeutic Cohort Results Cover Page
- Salivary Sex Hormone Profiles



Genova's Therapeutic Ranges Cover Page

Genova Diagnostics includes a Therapeutic Ranges Cover Page on four of our salivary sex hormone profiles:









- This cover page provides Therapeutic Ranges for sex hormones based on a select cohort of supplemented peri/menopausal women and enables clinicians to compare their patient's results to this treated group of individuals.
- These profiles also include Genova's standard Reference Ranges which provide comparison of patient results to other relevant healthy cohorts of patients.

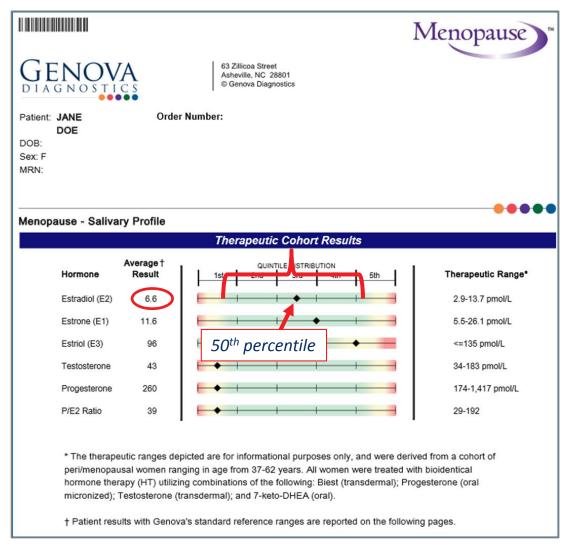




- Genova Diagnostics' Therapeutic Range specifically refers to the range of results that were established from a cohort of patients receiving therapeutic hormone treatment
- Because the therapeutic cohort comprises women who are being treated with hormone therapy due to symptoms or health problems, the therapeutic range does not indicate whether a specific individual's test results are "normal" or "abnormal"
 - A detailed explanation of the Therapeutic Range Cover Page can be found on Genova's website at the Endocrine University

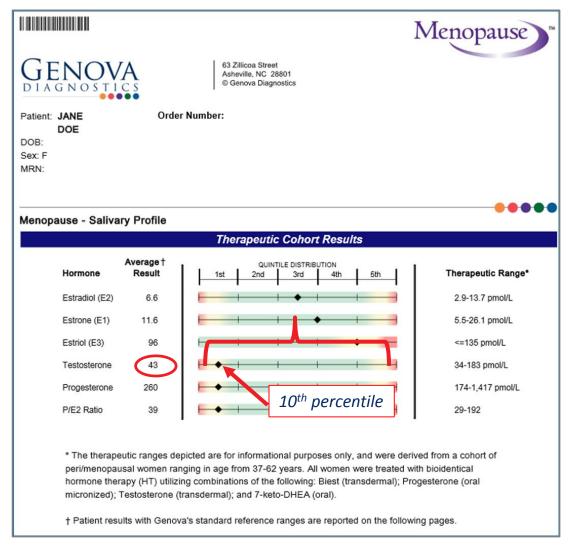














Core Therapeutics for the Management of the Menopausal Woman



Core Therapeutics: Biodentical Hormone Replacement Therapy

Prescribing Hormones

 Before prescribing hormones it is very important to know how much of each hormone that the body makes in a day!





Twenty-Four-Hour Production Rates of Sex Steroids in Women At Different Stages of the Menstrual Cycle

Sex Steroids	Early Follicular	Preovulatory	Midluteal
Progesterone (mg)	1.0	4.0	25.0
17-hydroxy-progesterone (mg)	0.5	4.0	4.0
Dehydroepi-androsterone (mg)	7.0	7.0	7.0
Androstenedione (mg)	2.6	4.7	3.4
Testosterone (mcg)	144.0	171.0	126
Estrone (mcg)	50.0	350.0	250.0
Estradiol (mcg)	36.0	380.0	250.0











Do Not Give Estrogen by Mouth for HRT







- Increase blood pressure
- Increase triglycerides
- Increase estrone
- Cause gallstones
- Elevate liver enzymes
- Increase SHBG (decreases testosterone)
- Interrupt tyrptophan metabolism and consequently serotonin metabolism

- Lower growth hormone
- Increase prothrombic effects
- Increase CRP
- Increase carbohydrate cravings





- Can put in syringe: best to use 1 mL so that the hormone is dispensed over a wider area for better absorption. Use a 10 mL syringe
 - Larger syringes are hard for the patient to use and see the dosages
- Best not to dispense in less than 0.5 mL
- Can instead put in MegaPump. This pump comes in 30 mL, 75 mL, and 150 mL sizes
- The 30 mL and 75 mL dispenses 0.5 mL
- The 150 mL size dispenses 1.0 mL



HRT: Disease Risk Including Breast Cancer Risk





HRT: Disease Risk

In a 2013 study: researchers estimated that over the past decade between 18,600 to 91,600 postmenopausal women, ages 50-59 years old, who had had a hysterectomy may have died prematurely because they did not take estrogen

Sarrel, P., et al., "The mortality toll of estrogen avoidance: An analysis of excess deaths among hysterectomized women aged 50 to 59 years,"
 Amer Jour Public Health 2013; July 18





Another study which was a meta-analysis from 27 published studies showed a 28% reduction in mortality in menopausal women under age 60 who used hormone replacement therapy and the participants also had improved quality of life

 Salpeter, S., et al., "Bayesian meta-analysis of hormone therapy and mortality in younger postmenopausal women," Amer Jour Med 2009; 22(11):1016-22





Studies have shown that progesterone does NOT induce estrogen-stimulated breast cell proliferation

- Murkes, D., et al., "Effects of percutaneous estradiol-oral progesterone versus oral conjugated equine estrogensmedroxyprogesterone acetate on breast cell proliferation and bel-2 protein in healthy women," Fertil Steril 2011; 95(3):1188-91
- Wood, C., et al., "Transcriptional profiles of progesterone effects in the postmenopausal breast," Breast Cancer Res Treat 2009; 114(2):233-42





- Neubauer, H., et al., "Overexpression of progesterone receptor membrane component 1: possible mechanism for increased breast cancer risk with norethisterone in hormone therapy," Menopause 2013; 20(5):504-10
- Murkes, D., et al., "Percutaneous estradiol/oral micronized progesterone has less-adverse effects and different gene regulations than oral conjugated equine estrogens/medroxyprogesterone acetate in the breast of healthy women in vivo," Gynecol Endocrinol 2012; 28(Suppl 2):12-5





- Chang, K., et al., "Influences of percutaneous administration of estradiol and progesterone on human breast epithelial cell cycle in vivo," Fertil Steril 1995; 63(4):785-91
- Foidart, J., et al., "Estradiol and progesterone regulate the proliferation of human breast epithelial cells," Fertil Steril 1998; 69(5):963-69
- Mueck, A., et al., "Comparison of the proliferative effects of estradiol and conjugated equine estrogens on human breast cancer cells and impact of continuous combined progestogen addiction," Climacteric 2003; 6(3):221-27





- Natural progesterone has been shown to decrease the risk of developing breast cancer
- A study looked at 80,000 postmenopausal women for 8 years using different kinds of HRT
 - It found that women who used estrogen in combination with synthetic progestin had a 69% increased risk of developing breast cancer when compared to women who never took HRT
 - Women who used progesterone in combination with estrogen had no increased risk in developing breast cancer compared to women that did not use HRT and also had a decreased risk in developing breast cancer compared to the women that used progestin





Reference

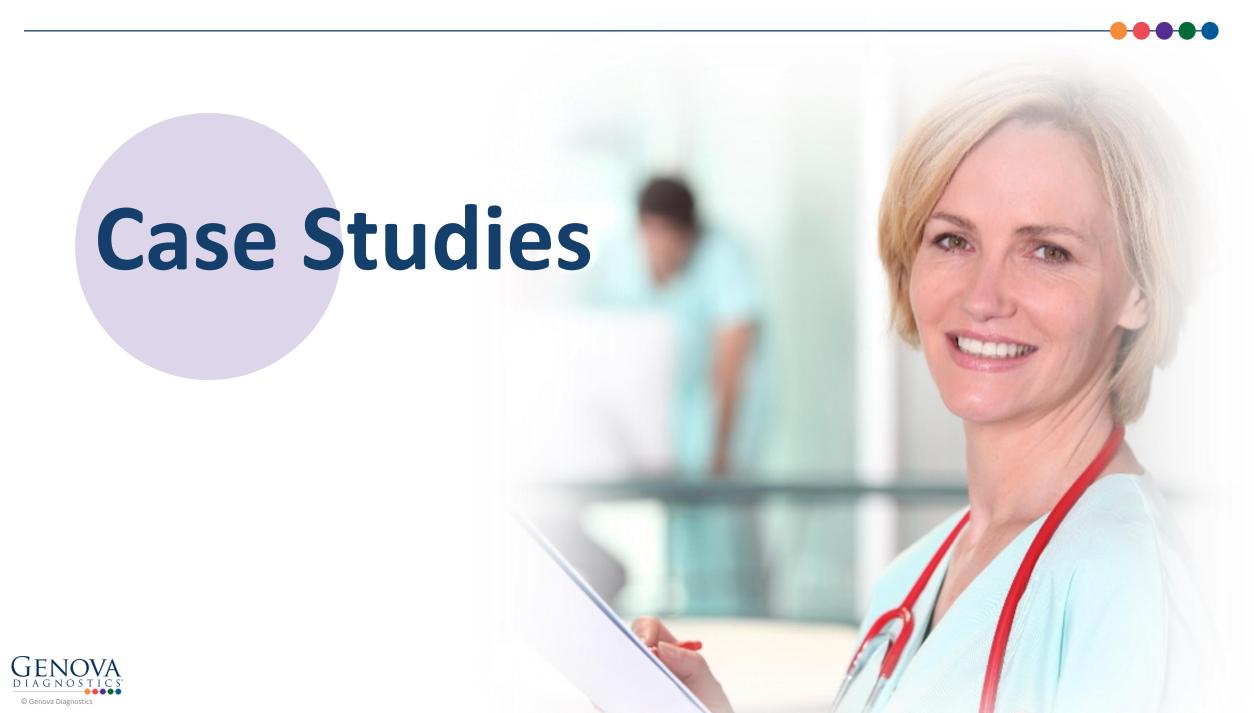
 Fournier, A., et al., "Unequal risks for breast cancer associated with different hormone replacement therapies: results from the E3N cohort study," Breast Cancer Res Treat 2008; 107(1):103-11

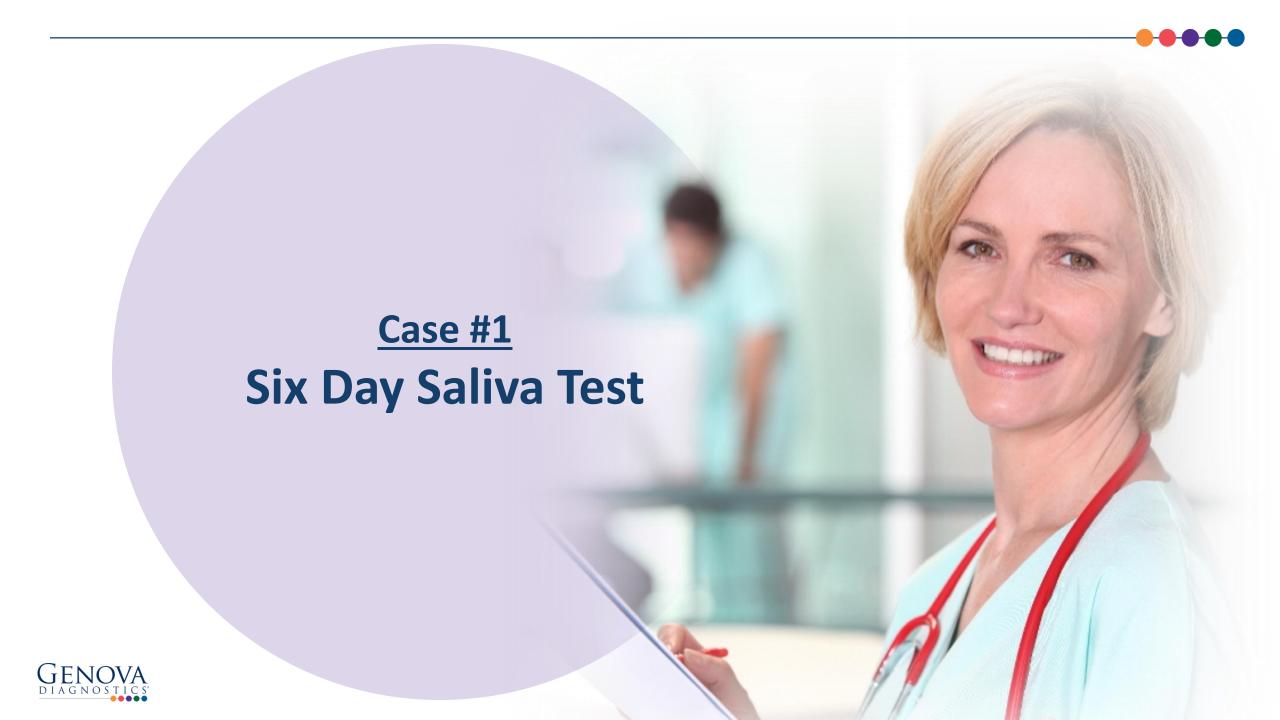




- Another study done by the same researchers found a 40% increased risk of developing breast cancer in women who used estrogen with progestin
- In women who used estrogen combined with progesterone there
 was a trend toward a decreased risk of developing breast cancer
 - Fournier, A., et al., "Breast cancer risk in relation to different types of hormone replacement therapy in the E3N-EPIC cohort," Int Jour Cancer 2005; 114(3):448-54

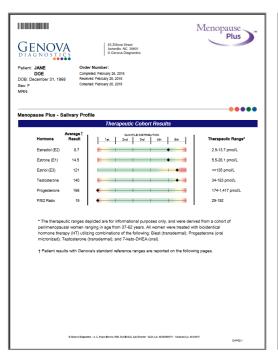


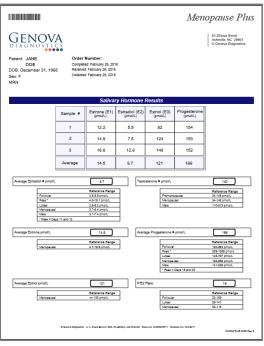


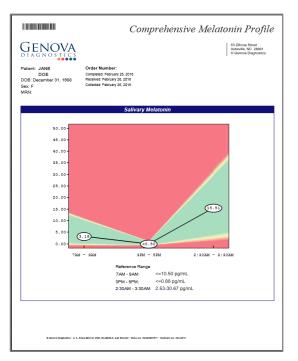


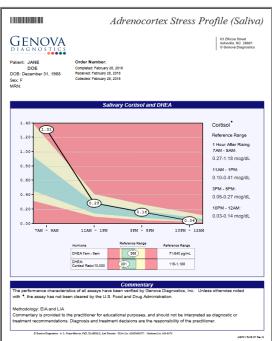


A 6-day saliva test is very beneficial to do for peri-menopausal women since their hormones may change over time if they do not want to do a 28-day test















- You start the test on day 16 of their cycle
- If you are going to do a one day test then day 20 or 21 of their cycle is best
- If the patient really needs to do a 28-day test but will not do one for one reason or another then have them do a one day test on day 4 of their cycle and another one day test on day 21 of their cycle
 - For younger women a 28-day always gives you more information



Case #1: Six Day Test







63 Zillicoa Street Asheville, NC 28801 © Genova Diagnostics

Patient: JANE DOE Order Number:

DOB: Sex: F MRN:

Menopause - Salivary Profile

Therapeutic Cohort Results

	Average †	. QUINTILE DISTRIBUTION	
Hormone	Result	1st 2nd 3rd 4th 5th	Therapeutic Range*
Estradiol (E2)	6.6	+ + + +	2.9-13.7 pmol/L
Estrone (E1)	11.6	+ + +	5.5-26.1 pmol/L
Estriol (E3)	96	⊢	<=135 pmol/L
Testosterone	43	• • • • • • • • • • • • • • • • • • •	34-183 pmol/L
Progesterone	260	• • • • • • • • • • • • • • • • • • •	174-1,417 pmol/L
P/E2 Ratio	39	→ + + + + + + + + + + + + + + + + + + +	29-192

† Patient results with Genova's standard reference ranges are reported on the following pages.



^{*} The therapeutic ranges depicted are for informational purposes only, and were derived from a cohort of peri/menopausal women ranging in age from 37-62 years. All women were treated with bioidentical hormone therapy (HT) utilizing combinations of the following: Biest (transdermal); Progesterone (oral micronized); Testosterone (transdermal); and 7-keto-DHEA (oral).

Case #1: Six Day Test

Salivary Hormone Results

Sample #	Estrone (E1) (pmol/L)	Estradiol (E2) (pmol/L)	Estriol (E3) (pmol/L)	Progesterone (pmol/L)
1	11.9	6.4	<70	282
2	10.6	6.8	102	215
3	12.2	6.6	89	284
Average	11.6	6.6	96	260

Average Estradiol ◆ pmol/L 6.6 Testosterone ◆ pmol/L 43 Reference Range Reference Range Follicular 2.8-8.8 pmol/L Premenopausal 34-148 pmol/L Peak * 4.5-19.1 pmol/L Menopausal 34-148 pmol/L 2.8-8.2 pmol/L Male 110-513 pmol/L Menopausal 3.7-9.4 pmol/L 3.1-7.4 pmol/L * Peak = Days 11 and 12 Average Estrone pmol/L Average Progesterone ◆ pmol/L 260 11.6 Reference Range Reference Range 4.7-18.9 pmol/L 120-593 pmol/L Menopausal Follicular Peak * 328-1385 pmol/L Luteal 145-797 pmol/L 163-669 pmol/L Menopausal 141-529 pmol/L * Peak = Days 18 and 20

Average Estriol pmol/L 96

Reference Range

<= 133 pmol/L

Menopausal

P/E2 Ratio 39

	Reference Range
Follicular	23-159
Luteal	25-141
Menopausal	33-116



Norms for Estrogens on 6-Day Test

- Estradiol
 - Follicular: 2.8-8.8 pmol/L
 - Peak: 4.5-19.1 pmol/L
 - Luteal: 2.8-8.2 pmol/L
 - Menopausal: 3.7-9.4
- Estrone
 - 4.7-18.9 pmol/L
- Estriol
 - <133 pmol/L





- Cycling women very rarely need estrogen replacement
- The exception to this is menstrual migraines at peri-menopause
- If the patient develops menstrual migraines or if they become more common or much more severe peri-menopausally then start:
 - Biest Cream 0.10 mg as 1mL in Versabase
 - Sig: apply qd to thigh or buttock. Rub in for two minutes. Rotate sites





Peri-Menopause

- Oral administration of E4M capsules (if issues with insomnia and better breast protection)
 - Progesterone 25 to 200 mg days 14-25
 - May need to give low dose days 4-13
- Topical administration
 - Progesterone
 - 10-30 mg days 14-25
 - May need to give low dose on days 4-13





Follicular: 120-593 pmol/L

Peak: 328-1385 pmol/L

Luteal: 145-797 pmol/L

Menopausal: 163-669 pmol/L

- Can be given transdermally, PO, or transvaginally
 - Doses are for transdermal and PO





Case #2: Patient on HRT





63 Zillicoa Street Asheville, NC 28801 © Genova Diagnostics

Order Number:



Patient: JANE

DOE

DOB: Sex: F MRN:

One Day Hormone Check - Salivary Profile

Therapeutic Cohort Results

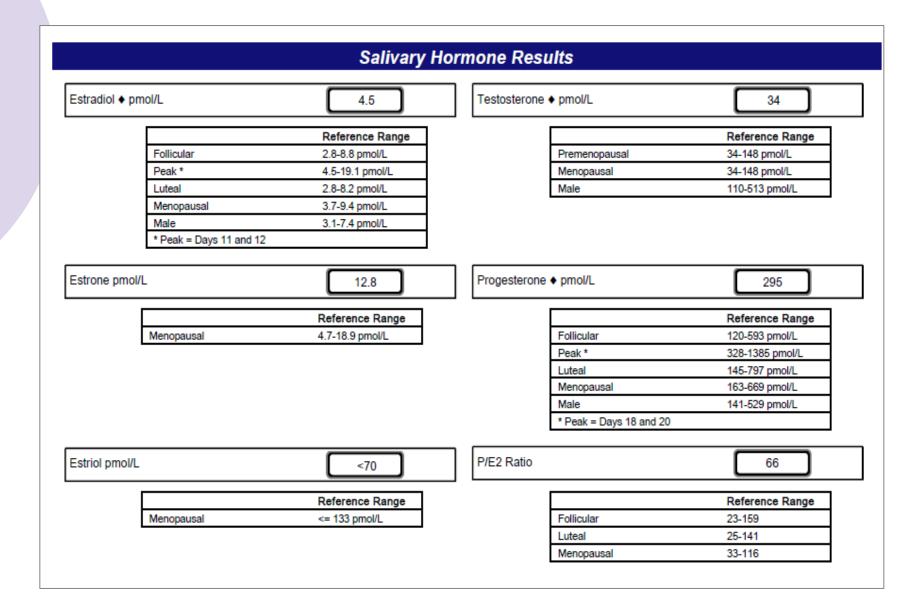
Harmana	Result †	QUINTILE DISTRIBUTION	Therapeutic Range*
Hormone	Result	1st 2nd 3rd 4th 5th	
Estradiol (E2)	4.5	→	2.9-13.7 pmol/L
Estrone (E1)	12.8	<u> </u>	5.5-26.1 pmol/L
Estriol (E3)	<70	• + + + - +	<=135 pmol/L
Testosterone	34	→ + + + + + + + + + + + + + + + + + + +	34-183 pmol/L
Progesterone	295	• • • • • • • • • • • • • • • • • • •	174-1,417 pmol/L
P/E2 Ratio	66	→ + + + + + + + + + + + + + + + + + + +	29-192



^{*} The therapeutic ranges depicted are for informational purposes only, and were derived from a cohort of peri/menopausal women ranging in age from 37-62 years. All women were treated with bioidentical hormone therapy (HT) utilizing combinations of the following: Biest (transdermal); Progesterone (oral micronized); Testosterone (transdermal); and 7-keto-DHEA (oral).

[†] Patient results with Genova's standard reference ranges are reported on the following pages.

Case #2: Patient on HRT

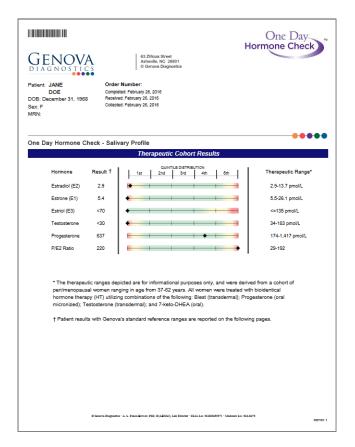


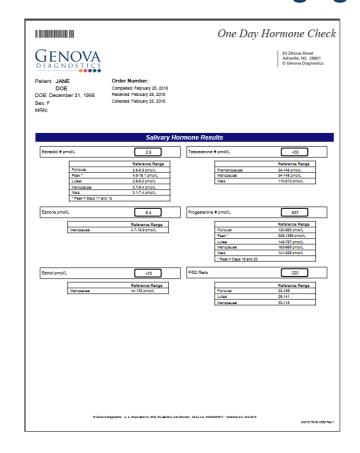


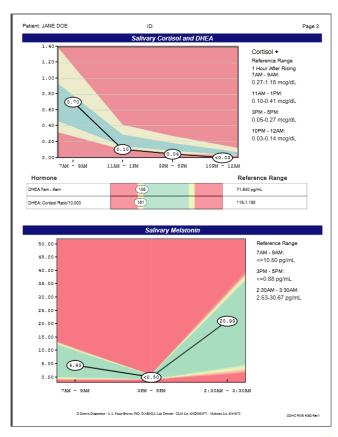




For menopausal women a one day saliva test is perfect since her hormones are now stable and are not changing

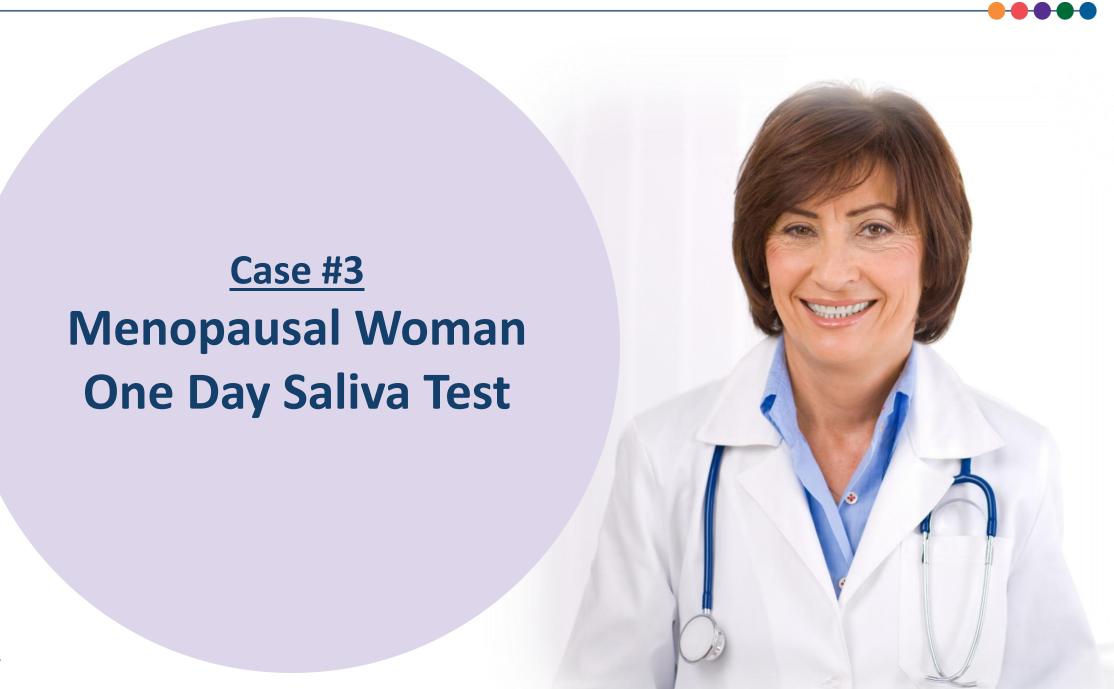










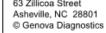








63 Zillicoa Street





Order Number:

DOB: Sex: F MRN:



One Day Hormone Check

One Day Hormone Check - Salivary Profile

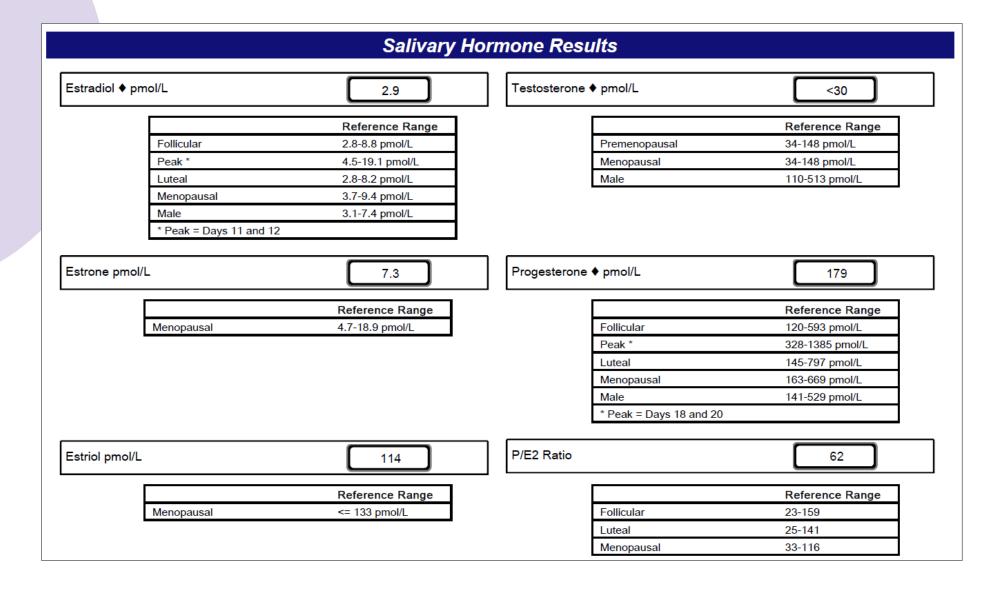
Therapeutic Cohort Results

Uarmana	Decult +	QUINTILE DISTRIBUTION	Therapeutic Range*
Hormone	Result †	1st 2nd 3rd 4th 5th	
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Estrone (E1)	7.3	•	5.5-26.1 pmol/L
Estriol (E3)	114	├	<=135 pmol/L
Testosterone	<30	•	34-183 pmol/L
Progesterone	179	• • • • • • • • • • • • • • • • • • •	174-1,417 pmol/L
P/E2 Ratio	62	▶ 	29-192

† Patient results with Genova's standard reference ranges are reported on the following pages.



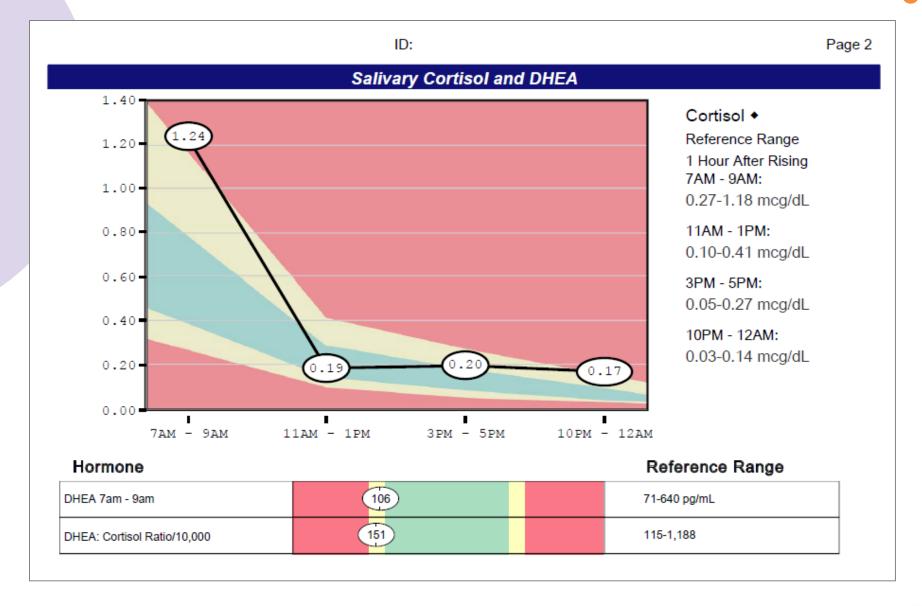
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- DHEA should be in the middle of the green section for optimal health
- Normal DHEA: 71-640 pg/mL
- Women are much more sensitive to DHEA than men, so start with low dosages
- In younger women you may not need to replace DHEA since the cause of low DHEA is usually due to stress.
 Balance cortisol and the DHEA level will rise



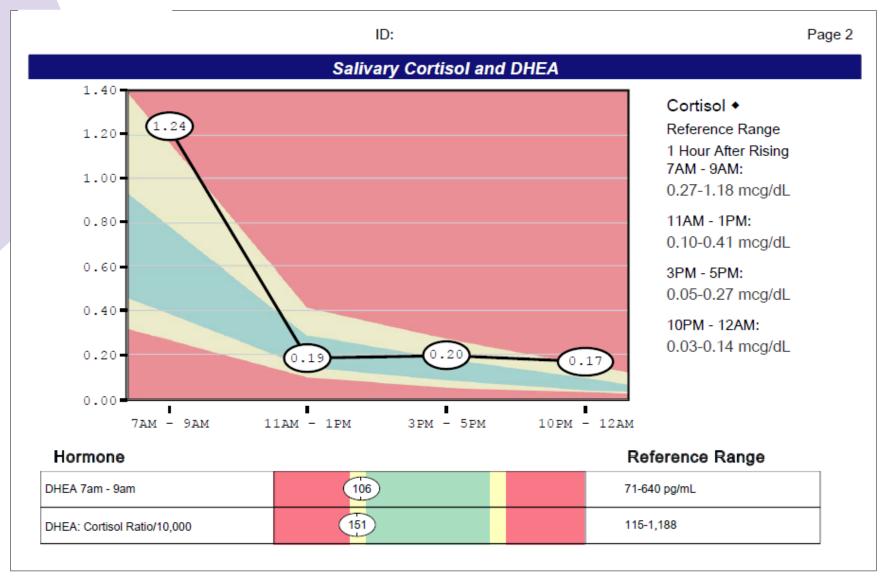


- DHEA balances cortisol
- If cortisol levels are abnormal then treat, do not just give
 DHEA hoping that cortisol levels will come up
- If cortisol is abnormal and you just give DHEA without working on the abnormal cortisol levels then the next time that you measure DHEA, the levels will be even lower













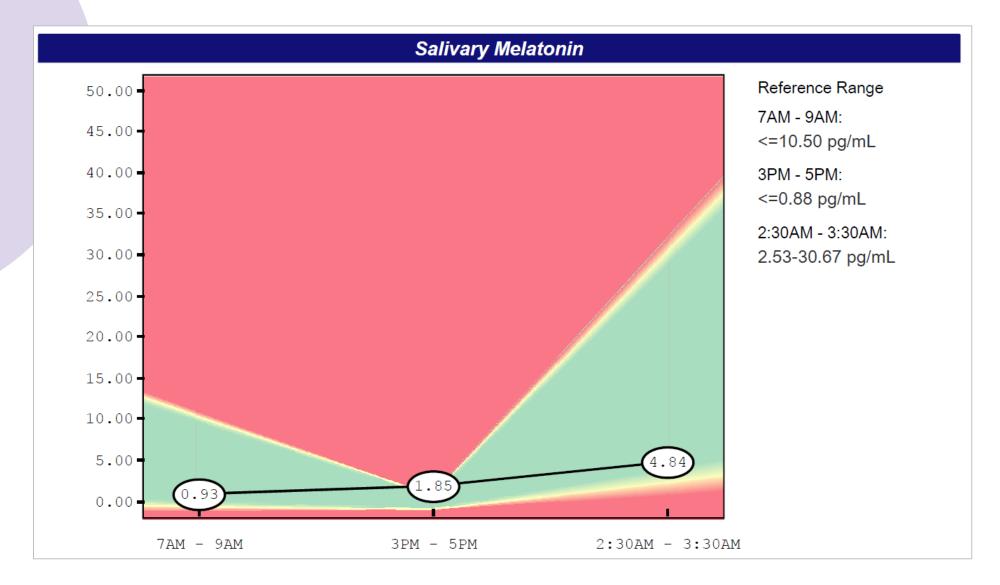


- Replacement of DHEA with adrenal support
- Adaptogenic herbs
- Essential Nutrients
- Calming herbs
- Stress reduction techniques
- If cortisol is high in the evening then add phosphatidylserine
 300 mg which may be taken any time of the day



Melatonin











- High levels of melatonin in the morning usually mean that cortisol levels were too low in the am
- If melatonin levels are to high any time of the day or night then serotonin levels may go down
- Middle of the night level is done with the lights off otherwise the reading will not be accurate





Moderator:
Michael Chapman, ND



Presenter: Pamela W. Smith, M.D., MPH, MS

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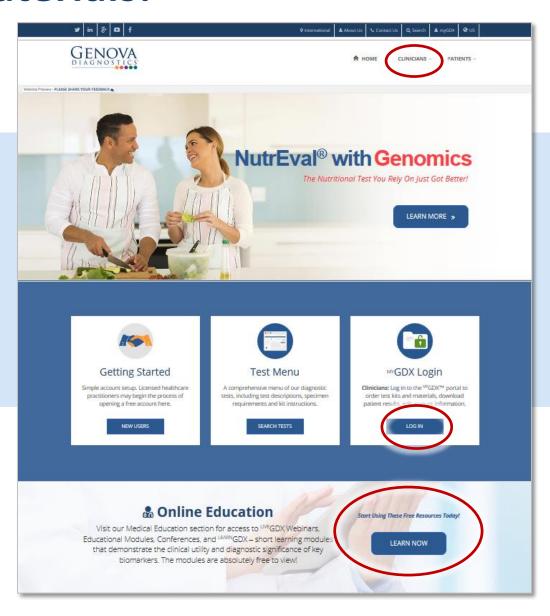
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- One-day event on June 11th, 2016
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LearnGDX Seminar Series

MANAGING THE (PERI)MENOPAUSAL PATIENT: DIAGNOSTICS AND THERAPEUTICS

Saturday, June 11, 2016

Fort Lauderdale, Florida



An educational workshop focusing on the comprehensive clinical management of the (peri)menopausal patient including: salivary hormone assessment, related functional lab testing, disease risk, and personalized therapy protocols.

Although a time of natural transition, the "change of life" can cause shifting hormone levels associated with a continuum of physiologic and metabolic changes that can produce troubling symptoms and risk for more serious health conditions. Specialized laboratory diagnostics provide insight into these changes and offer guidelines for personalized clinical support. Identification of imbalances and their treatment with customized hormone therapy, targeted nutritional supplementation, and dietary/lifestyle changes can help improve symptoms, reduce disease risk, and enhance guality of life.

Join us for a day of expert discussion on clinical strategies to effectively support patients as they transition to a "new normal".

SPEAKERS INCLUDE:



Pamela W. Smith, MD, MPH, MS Teacher, author, and recognized Anti-Aging/Metabolic Medicine specialist



Andrea Girman, MD, MPH Director of Medical Education Genova Diagnostics

EVENT SCHEDULE

8:30-9:00:	Introduction/Event Overview
9:00-10:30:	A Comprehensive Assessment of the (Peri)Menopausal Patient (Pamela W. Smith)
10:30-10:45:	Snack / Break
10:45-12:00:	Menopause Plus™ Report & Therapeutic Range Cover Page Review (Andrea Girman)
12:00-1:00:	LUNCH (Provided)
1:00-3:15:	Therapeutic Protocol and Interactive Case Study Review (Pamela W. Smith)
3:15-3:30:	Break
3:30-4:30:	Strategies for Incorporating Specialty Diagnostics into Clinical Practice (Pamela W. Smith, Genova Diagnostics Team)

EVENT LOCATION:

Fort Lauderdale Marriott North 6650 N. Andrews Ave. Fort Lauderdale, FL 33309 (954) 771-0440



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Please schedule a complimentary appointment with one of our Medical Education Specialists for questions related to:

- Diagnostic profiles featured in this webinar
- How Genova's profiles might support patients in your clinical practice
- Review a profile that has already been completed on one of your patients

We look forward to hearing from you!





June 2016

- The Steroidogenic Pathway: Understanding What Influences Each Step
 - Ellen Antoine, DO

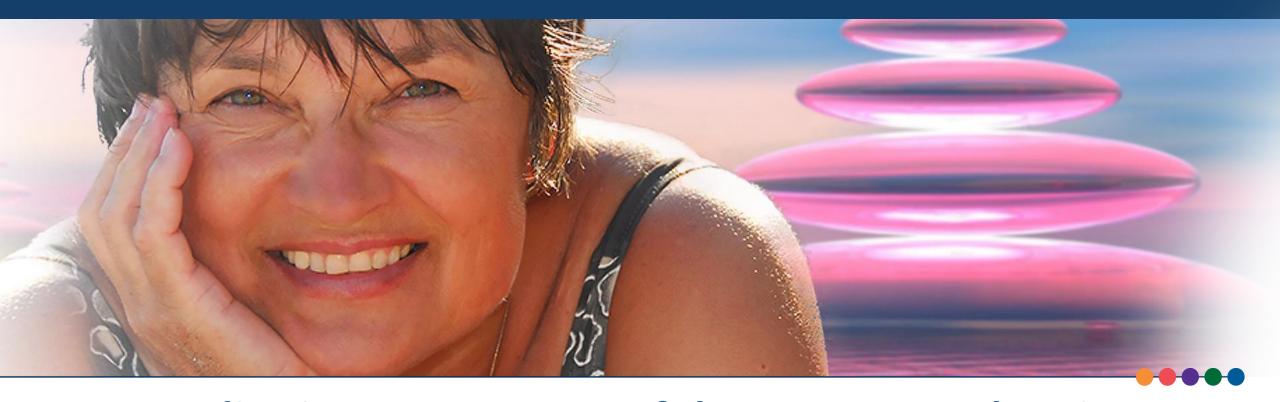
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