

Hormone Dosing

A Pharmacist's Perspective

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Objectives

- 1. Dispensing devices for compounded BHRT**
- 2. BHRT and Evidence base studies**
- 3. Quality and Safety of BHRT**
- 4. Pearls & Nuggets**
- 5. Case studies**

Dispensing Devices

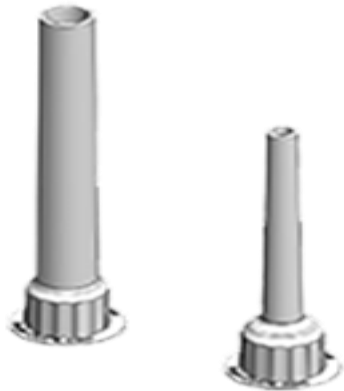
- ▶ **Oral syringes**
Dispenses 0.1-0.2ml



Dispensing devices

EMP jars

Dispenses 1-1.25ml



Dispensing devices

Mega Pumps
Dispense 0.5-1ml



Dispensing devices

Topi-Click Dispenses 0.23ml



Turn the base to dispense the number of clicks specified on label.



When rotating base, watch the Visual Indicators

Indicator Node on Body is fixed at the Click Point



Indicator Column moves with Base. This shows Node in line with column.

LEAVE IN THIS POSITION
AFTER EVERY CLICK
(The Home Position)

Dispensing devices

Tickers

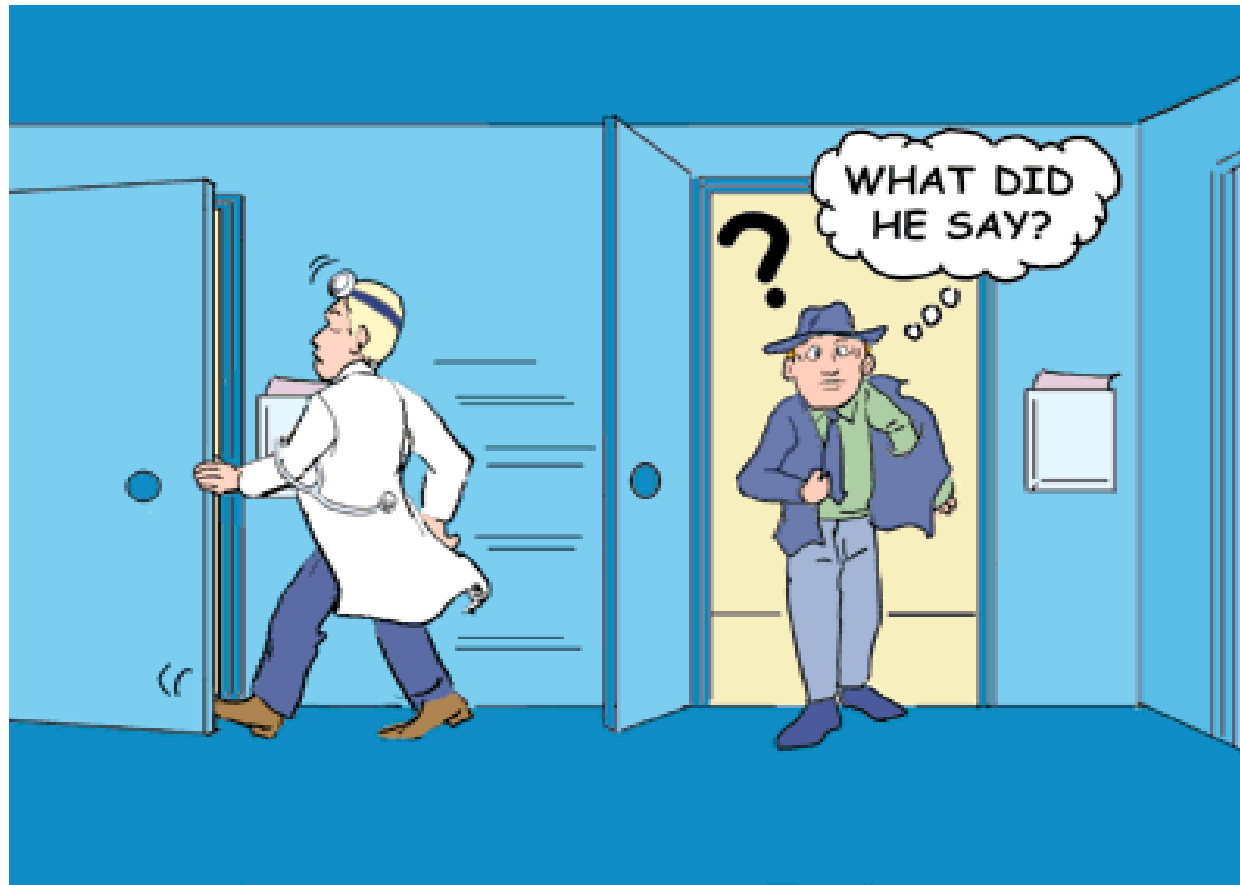
Dispenses 0.05ml increment



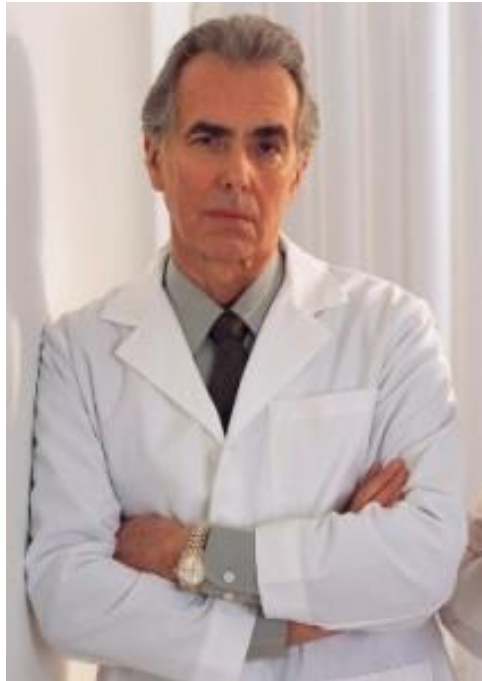
Dispensing devices For vaginal products



Studies



Studies



Studies

KEEPS Study

Hormone Therapy has many favorable effects in newly menopausal women

http://www.keepstudy.org/news/pr_100312_a.cfm

Studies KEEPS Study

For symptomatic menopausal women who are **under 60 years of age or within 10 years of menopause**, the benefits of MHT generally outweigh the risks. Systemic MHT initiated early in menopause appears to **slow the progression of atherosclerotic disease, thereby reducing the risk of cardiovascular disease and mortality**. During this window of opportunity, **MHT might also provide protection against cognitive decline**. In older women and women more than 10 years past menopause, the risk-benefit balance of MHT is less favorable, particularly with regard to cardiovascular risk and cognitive impairment. For women entering menopause prematurely (<40 years), MHT ameliorates the risk of cardiovascular disease, osteoporosis, and cognitive decline.

Keeps Study Cont'd

- ▶ **Nonoral administration of estrogen offers advantages due to the lack of first-pass hepatic metabolism, which in turn avoids the increased hepatic synthesis of clotting proteins, C-reactive protein, triglycerides, and sex hormone-binding globulin.** The duration of combined MHT use is ideally limited to less than 5 years because of the known increase in breast cancer risk after 3-5 years of use. Limitations to use of estrogen only MHT are less clear, since breast cancer risk does not appear to increase with use of estrogen alone. For women under the age of 60 years, or within 10 years of onset of natural menopause, MHT for the treatment of bothersome menopausal symptoms poses low risk and is an acceptable option, particularly when nonhormonal management approaches fail.

- ▶ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3897322/>
<https://www.menopause.org/annual-meetings/2012-meeting/keeps-report>

Studies

ESTHER Study [Int J Gen Med. 2014; 7: 433-440.](#)

Conclusion: “Oral but not transdermal estrogen is associated with an increased VTE, stroke, myocardial infarction risk”

Therefore, bioidentical hormone therapy via the transdermal route seems to be the safest opportunity for hormone replacement therapy

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4155999/>

Studies

Stanczyk FZ, Paulson RJ, Roy S. Menopause.
2005 Mar;12(2):232-7.

“.. anti-proliferative effects on the endometrium have been demonstrated with progesterone creams when circulating levels of progesterone are low. Despite the low serum progesterone levels achieved with the creams, salivary progesterone levels are very high, indicating that progesterone levels in serum do not necessarily reflect those in tissues

Studies

Vashisht A, Wadsworth F, Carey A, Carey B, Studd J. *Gynecological Endocrinology*, 2005;21(2):101-5

“..PE40mg/ E2 “1mg” cream, highly significant reduction in symptoms of anxiety, depression, vasomotor symptoms and libido issues when compared with baseline after 12/24/48 weeks..”

Studies

Holtorf K. Postgrad Med. 2009 Jan;121(1):73-85

Conclusion: “..Physiological data and clinical outcomes demonstrate that **BHRT** are associated with lower risks, including the risk of breast cancer and cardiovascular disease, and more effecaious than their synthetic and animal derived counterparts”

Studies

Andres D Ruiz, et al. BMC Women's Health 2011, 11:27

The most common compounded BHRT dosage forms utilized is topical 71%. The study **demonstrates that compounded BHRT improves mood symptoms. Women experienced a 25% decrease in emotional lability ($p < 0.01$), a 25% decrease in irritability ($p < 0.01$), and a 22% reduction in night sweats ($p = 0.09$) and a 6% reduction in hot flashes ($p = 0.50$).**

Studies

2015 Jun;1(3):296-305. doi: 10.1001/jamaoncol.2015.0494.
**Breast Cancer After Use of Estrogen Plus Progestin and Estrogen Alone:
Analyses of Data From 2 Women's Health Initiative Randomized Clinical
Trials**

**In the estrogen alone trial, the lower breast cancer risk seen during
intervention was sustained in the early postintervention phase but was not
evident during the late postintervention follow-up**

<https://www.ncbi.nlm.nih.gov/pubmed/26181174>

Studies

▶ 2010 Jun;26(6):404-12. doi: 10.3109/09513591003632258.

▶ **Low-dose vaginal estrogens or vaginal moisturizer in breast cancer survivors with urogenital atrophy: a preliminary study.**

▶ [Biglia N¹](#), [Peano E](#), [Sgandurra P](#), [Moggio G](#), [Panuccio E](#), [Migliardi M](#), [Ravarino N](#), [Ponzone R](#), [Sismondi P](#).

▶ [Author information](#)

▶ **Abstract**

▶ The study aim is to evaluate the efficacy and safety of two low-dose vaginal estrogen treatments (ETs) in postmenopausal breast cancer survivors with urogenital atrophy. Eighteen patients receiving **estriol cream 0.25 mg** (n = 10) or estradiol tablets 12.5 microg (n = 8) twice/week for 12 weeks were evaluated and compared with eight patients treated with polycarbophil-based moisturizer 2.5 g twice/week. Severity of vaginal atrophy was assessed using subjective [Vaginal Symptoms Score (VSS), Profile of Female Sexual Function (PFSF)] and objective [Vaginal Health Index (VHI), Karyopycnotic Index (KI)] evaluations, while safety by measuring endometrial thickness and serum sex hormones levels. After 4 weeks, VSS and VHI were significantly improved by both vaginal ETs, with further improvement after 12 weeks. PFSF improved significantly only in estriol group (p = 0.02). **Safety measurements did not significantly change. Vaginal moisturizer improved** VSS at week 4 (p = 0.01), but score returned to pre-treatment values at week 12; no significant modification of VHI, KI, PFSF was recorded. Both low-dose vaginal ET are effective for relieving urogenital atrophy, while non-hormonal moisturizer only provides transient benefit. **The increase of serum estrogens levels during treatment with vaginal estrogen at these dosages is minimal.**

▶ PMID: 20196634 DOI: [10.3109/09513591003632258](#)

Visit your Compounding Pharmacy, Ask the right questions:

1. Do they have the right **equipment**?
2. Do they have the right **sourcing for chemicals**?
3. Do they have the right **SOP**?
4. Are they updated in their knowledge
(**training / certificates**)?

Equipment

1. Containment hood



2. Ointment mill

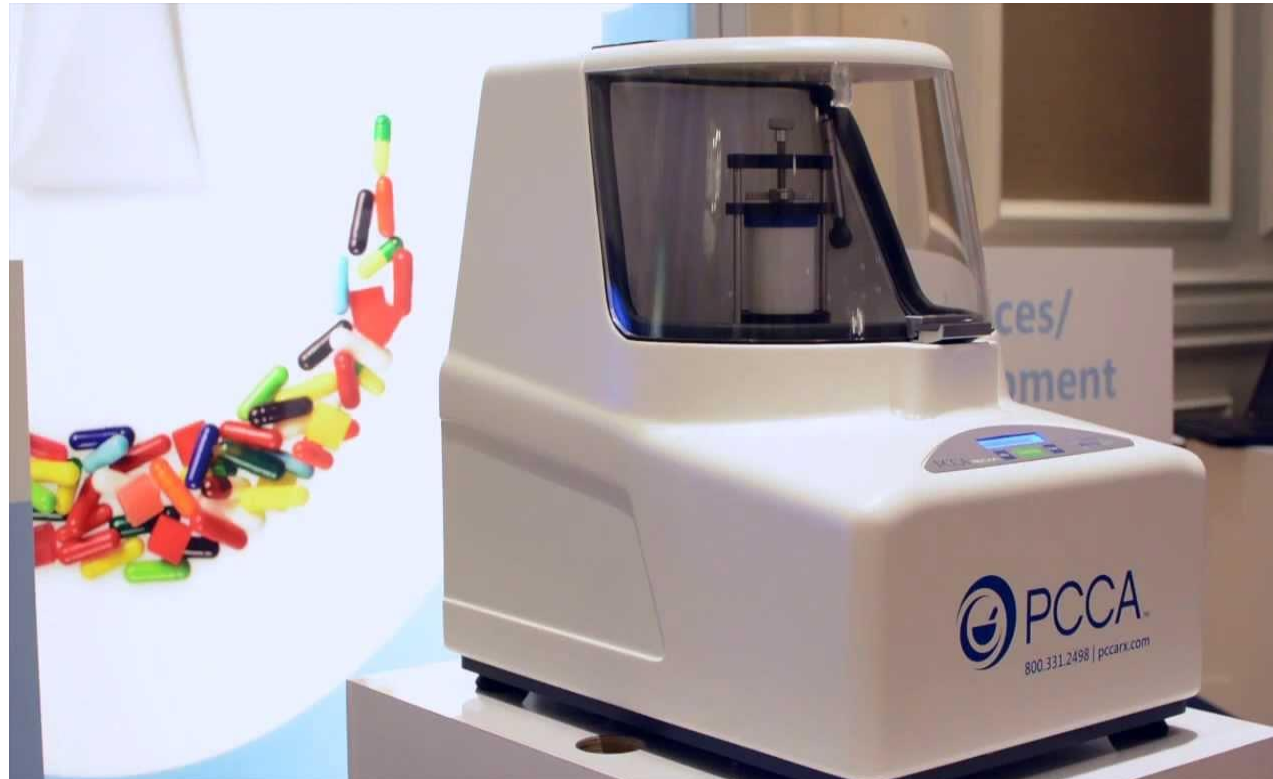


3. Unguator mixer



4. RAM Mixer

Resonance Acoustic Mixer



Sourcing API

We source all of our hormones
from **PCCA-Professional Compounding
Centers of America**

Sourcing API

1. Are chemicals tested for potency and contamination?
2. Are hormones in their micronized forms?

Bases

Does the **topical** cream base have the ability to **transport** hormones deep into the dermis?

Bases

Does the vaginal cream base have the ability to bond to mucosal membranes for increased contact time?

Continuing Education

USP <800> and NAPRA guidelines
What's next?

Clinical pearls & Nuggets

Estriol, is the least potent of physiological hormones, and it acts as an agonist and antagonist at the receptor site and in essence balance the Estradiol

Bi-est ratio, 80:20 or 50:50?

Clinical Pearls

Estradiol deficiency may have a role in developing Alzheimer's disease

Helps maintain memory

increases cerebral blood flow

Influences neurotransmitter systems

Lumsden MA, Benefits of treatment: local and general menopause symptoms. Chapter 53, IN: Fraser IS, Jansen RPS Lobo RA, Whitehead MI eds. Estrogens and Progesterones in Clinical Practice London UK: Churchill Livingstone 2000

Clinical Pearls & Nuggets

Phytoestrogens (Black cohosh, soy containing products, Flaxseed, Chaste berry, Red Clover) can be helpful with symptoms of menopause, specifically hot flashes.

A patient that has a diet that is rich in phytoestrogen like soy or tofu, will have a higher estrogen burden, and should be counseled about this effect. This also should be considered when dosing BHRT.

<https://naturalmedicines.therapeuticresearch.com>

Clinical Pearls & Nuggets

Continued vasomotor symptoms such as **hot flashes** and **night sweats**;

1. Increase the estrogen
2. Make sure the patient is applying the hormones properly
3. Monitor hormonal levels

Clinical Pearls & Nuggets

Breakthrough bleeding or Heavy menses;

1. May need to increase progesterone or decrease estrogen specially if estrogen dominance symptoms are present
2. If persistent, comprehensive management requires a pelvic ultrasound to evaluate the endometrial lining

Clinical Pearls & Nuggets

Weight gain

1. It is not unusual, just like other hormone replacement to see some fluid retention with the addition of BHRT. It is usually **transient**.
2. Be sure exercise, diet, supplements are in place in life style, along with adequate sleep.
3. Reassessment of **thyroid** may be required.
4. **Reassurance** that this is all will improve as hormones are optimized; energy will return, motivation will improve and weight will come off.

Pearls and Nuggets

Estrogen depletes Vitamin B12

Testing

BHRT:

Progesterone

Estrogen

Testosterone

Adrenals :

Cortisol

DHEA

Thyroid:

TSH

T3 free

RT3

T4 free

TPO

Progesterone/Estrogen Ratio



How is the ratio calculated?

Optimal ratio of 100-500

1. Only when E2 is within a normal luteal phase range;
(1.3-3.3 pg/mL in saliva, and 43-180 pg/mL in blood spot.
2. The ratio is calculated from the Pg value in pg/mL divided by the E2 value in pg/mL.

Saliva test example: a patient has E2 = 1.5 pg/mL and Pg = 300 pg/mL. The units are the same (pg/mL), so the ratio is 300 divided by 1.5: ratio is 200

Blood spot or serum example: a patient has E2 = 100 pg/mL and Pg = 20 ng/mL. The Pg units are first converted to pg/mL before calculating the ratio: 1 ng/mL is equivalent to 1000 pg/mL. Therefore, the ratio is 20 ng/mL x 1000 = 20,000 pg/mL Pg, divided by 100 pg/mL E2, ratio is pg:E2 = 200

Both of these examples represent normal endogenous luteal phase levels of E2 and Pg.

Is the ratio relevant in women using hormone therapy?

With some types of hormone therapy such as topical progesterone, Pg levels in saliva are much higher than endogenous luteal phase levels, ranging from 200-3000 pg/mL at 12-24 hours after dosing, and so the ratio can appear high. However, because symptoms of both estrogen dominance and progesterone dominance can look the same, testing and assessing the ratio along with clinical symptoms can help determine the next step for treatment.

Clinical Case #1

Mary complains of hot flashes and night sweats. She's a 50-year-old, newly postmenopausal woman who has never been on hormones. Her BMI is normal and she has no other health issues. A saliva test finds an **E2 of 1.1 pg/mL (reported as "OK")**, but a **Pg level of 15 pg/mL (also "OK" for a postmenopausal woman)**, giving a ratio of **13.6** which is low.

- ▶ Based on her symptoms and a low ratio you start her on **topical progesterone**, which immediately helps the patient symptomatically. A few months later, you test her hormone levels again in saliva. Her E2 is 1.3 pg/mL and her Pg level is now 2500 pg/mL (within range for topical treatment). Her ratio is now **1923, reported as “high”**. What do you do? The patient has no symptoms, feels great and her E2 and Pg levels are within appropriate ranges - **no adjustments in treatment are needed.**

A year later Mary comes back reporting hot flashes and night sweats. She was doing well until about 3 months ago. She had done a detox diet and had lost about 5 lbs. A saliva test shows that her E2 has dropped to 0.5 pg/mL: still “OK”, but much lower than last year; her Pg is still within the supplementation range at 2350 pg/mL. Her ratio is now 4700, which is still high. Unlike the last visit, however, Mary is now symptomatic.

- ▶ You have 3 choices: add estrogen therapy, reduce progesterone therapy, or both. Why is her higher Pg making things worse?
- ▶ Excessive Pg when E2 is low can down-regulate estrogen receptors and worsen estrogen deficiency symptoms. If Mary chose not to start estrogen therapy, just reducing the progesterone dosage would likely normalize her symptoms.

Case Study #2

Patient who had a partial hysterectomy 14 years ago and was left with 1 ovary. Patient is menopausal.

- ▶ She has a child with special needs and is chronically stressed.
- ▶ She was gaining abdominal weight and generally felt 'off'
- ▶ Severely fatigued in the morning and in the evening
- ▶ Patient is not on any hormone replacement therapy

DOB: 1963/01/15
Gender: Female

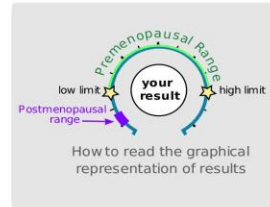
Provider:

Accession #

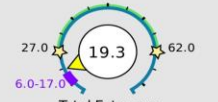
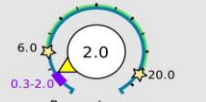
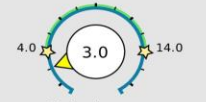
Collection Times:
 2016-11-10 08:45AM
 2016-11-10 05:00PM
 2016-11-10 10:50PM
 2016-11-11 07:00AM

Hormone Testing Summary

All units are given in ng/mg creatinine

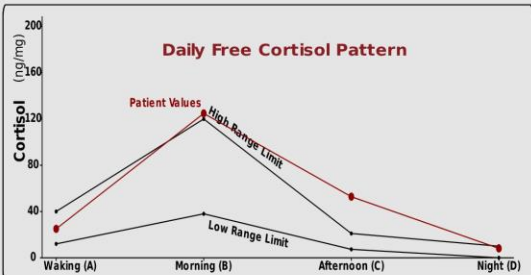


Sex Hormones See Pages 2 and 3 for a thorough breakdown of sex hormone metabolites

 <p>Total Estrogen (Sum of 8 Estrogen Metabolites)</p>	 <p>Progesterone (Serum Equivalent, ng/mL)</p>	 <p>Testosterone</p>
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Progesterone Serum Equivalent is a calculated value based on urine pregnanediol.


Adrenal Hormones See pages 4 and 5 for a more complete breakdown of adrenal hormones




Free cortisol best reflects tissue levels. Metabolized cortisol best reflects total cortisol production.

Total DHEA Production

Age	Range
20-40	800-2500
40-60	530-1550
>60	400-1350




Total DHEA Production
(DHEAS + Etiocholanolone + Androsterone)



24hr Free Cortisol
(A+B+C+D)

→ cortisol metabolism →



Metabolized Cortisol (THF+THE)
(Total Cortisol Production)

Patient reports regular menstrual cycles
 Last Menstrual Period -

Thank you for testing with us!

=====

Please be sure to always read below for any specific lab comments. More detailed comments can be found on page 7.

- The patient shows significantly higher free cortisol compared to metabolized cortisol. It may be advisable to check thyroid hormones if you have not. See comments in the notes for more details.

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Your DUTCH Complete report will include a summary (page 1), a list of all of the hormones tested and their ranges (pages 2,4) as well as a graphical representation of the results (pages 3,5). You will also see a steroid pathway for your reference (page 6) and provider notes. This report is not intended to treat, cure or diagnose any specific diseases. There is a series of videos in our video library at dutchttest.com that you may find useful in understanding the report. The following videos (which can also be found on the website under the listed names) may be particularly helpful in aiding your understanding:

[DUTCH Complete Overview \(quick overview\)](#)
[Estrogen Tutorial](#); [Androgen Tutorial](#); [Cortisol Tutorial](#)

Treatment Protocol

- ▶ Bi-Est (80:20) 0.25mg cream

Once daily (Monday to Saturday, Sunday off)

- ▶ Progesterone 15mg cream

Once daily at bedtime (Monday to Saturday,
Sunday off)

- ▶ Vitamin B-complex
- ▶ Vitamin C 1gm
- ▶ Adrenal support formula
- ▶ To increase her Testosterone levels, add (Magnesium 300mg / Zinc 25mg/ Ginseng 250-500mg/ exercise)
- ▶ Further testing: Thyroid panel (TSH, T3 free, T4 free, TPO, rT3)
- ▶ Monitor: in 6 weeks

Clinical case #3

- ▶ She is a menopausal woman who went through a terrible last year looking after her aging mother, who has subsequently passed away. She is fully aware she did not look after herself and is now doing an amazing job of taking control of her health. Her diet has been great, her exercise has been good, her stress levels are moderate and her mental health is awesome.
- ▶ She is on the medications and supplements listed below. We have been gradually increasing her (ERFA) thyroid, and she is now taking 30mg daily and her body temperatures are still 34-35 C.
- ▶ She is hypochlorhydric, but otherwise she does not complain of any GI symptoms

Patient:
 Age: 61 years Gender: F
 Date of Birth: Dec 27 1954
 HC #: ██████████
 Patient's Phone: (████) ██████████

Lab No: 2016-██████████
 Reference #:
 Patient ID:
 Referring Site ID:
 Date of Service: Sep 15 2016 13:19
 Reported on: Sep 16 2016 10:27



Address: 100 International Blvd.
 Toronto, Ontario
 Canada M9W 6J6
 Telephone: (877) 849-3637
 Toll Free: (877) 849-3637
 Fax: (905) 795-9891

Ordered by: ██████████
 Copy To:

Test	Flag	Result	Reference Range - Units	Lab Lic. #
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General Comments

Reference Interval Note:

Please note change in methodologies for routine chemistry, immunochemistry and infectious disease (hepatitis and rubella) serology tests. Reference intervals for some tests have been changed, as appropriate.
 For a complete list of tests which have been changed, please visit <https://www.lifelabs.com>

#5687

Biochemical Investigation of Anemias

Vitamin B12	HI	>1476	138-652	pmol/L
Ferritin		29	5-272	ug/L

Thyroid Function

Thyroid Stimulating Hormone [TSH]		4.0	0.60-4.00	mIU/L
Thyroxine Free [Free T4]		11	9-19	pmol/L
Triiodothyronine Free [Free T3]		4.4	3.1-6.2	pmol/L
Thyroperoxidase Antibody	HI	167	< 35	kIU/L

Anti-Thyroid peroxidase antibody values up to 250 kIU/L may be seen in 5-10% of the normal population without demonstrable thyroid disease. This incidence increases with age.

Patient currently takes;

- ▶ Multivitamin
- ▶ Krill oil 1g/d
- ▶ B-complex 500mg
- ▶ Vit D 1000IU
- ▶ Melatonin
- ▶ Probiotics 1/d
- ▶ Magnesium 1 tsp hs
- ▶ Adrenal SAP 2 bid
- ▶ Thyroid balance tea 2c/d
- ▶ Digestive enzymes SAP 2 tid
- ▶ OsteoSAP 2 tid
- ▶ Turmeric tea 2caps dy

Treatment protocol;

- ▶ Patient has Hashimoto's
- ▶ Selenomethaionin 200mcg, increase to 400mcg daily
- ▶ Betaine capsules
- ▶ Increase her Erfa Thyroid to 60mg in the morning (counsel on how she takes it)
- ▶ Gluten free / Dairy free and sugar free diet
- ▶ Further testing: Iodine testing
- ▶ Monitoring: 6-8 weeks

Converting Patients from Synthetic to Bioidentical Hormones

- . What dose is the patient on?
- . Counsel the patient that the transition may occur over weeks to months and symptoms could worsen
- . Tapering the synthetic therapy

(provide a calendar with the tapering protocol clearly outlined, along with beginning date of new therapy and days to use it with taper protocol)

Tapering protocol

High dose usage of oral CEE

1. Decrease the commercial oral dose by 1 daily pill, every 2 weeks
2. Start progesterone therapy upon initiation of the CEE taper
3. Start milk thistle or DIM, 250mg 2-3 times daily throughout protocol.
4. Print out calendar with doses / days marked

Tapering protocol

Low dose of oral CEE

1. Decrease commercial dose by 50% (1/2 tablet), give daily for 2 weeks
2. Discontinue medroxyprogesterone and add progesterone special micronized topical cream daily
3. On the days not using oral CEE, apply Bi-Est topical cream, Apply to genital tissue

Dose Queues

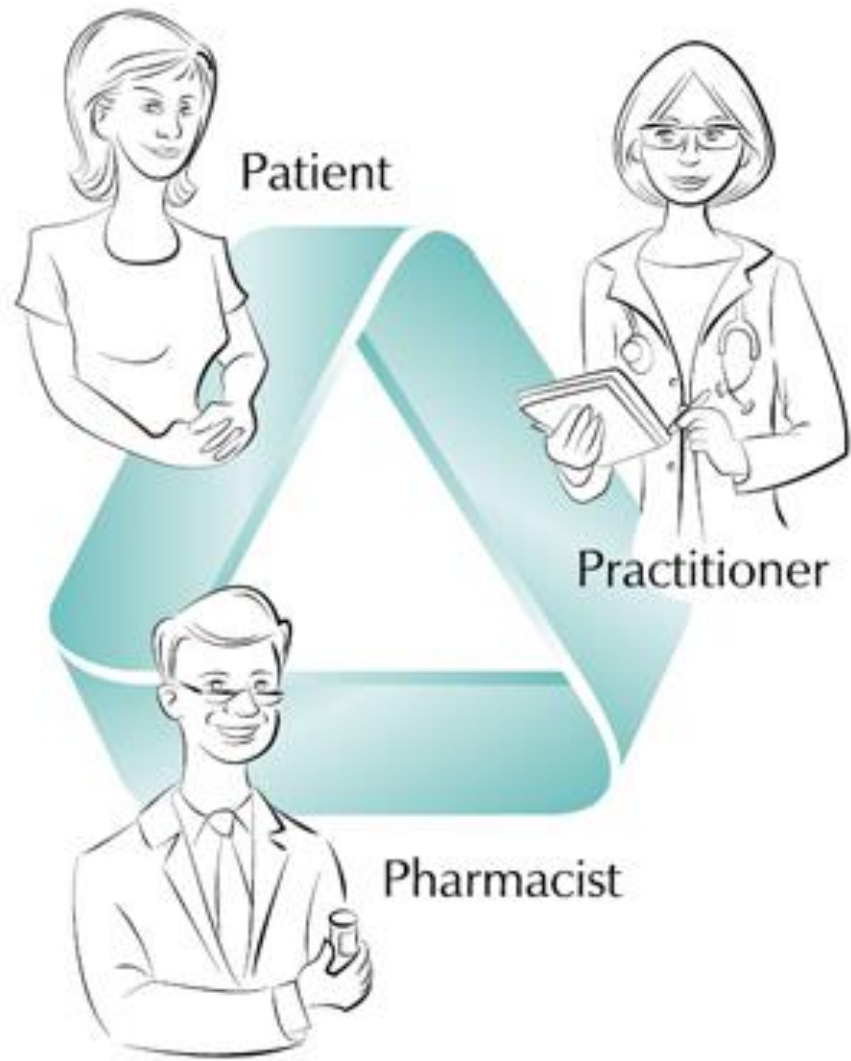
Immediate results are not usually seen, however, some symptoms like hot flashes, may resolve faster than others such as libido and vaginal issues

Dose adjustment

Adjustment and addition are common after the first 2-3 visits, and it is better to be done in person, to ensure that the patient is using the hormones as prescribed in a manner that optimizes the hormone dose

Dose adjustment

- Should be relatively small and should be monitored for another 6-8 weeks prior to next adjustment
- Use a follow up assessment form



Navigating the Pharmacy: How it all works

- ▶ **First:** You fax in the patient's prescription to the pharmacy (email is not secure and not PHIPPA compliant)
- ▶ **Second:** Pharmacy calls the patient to confirm that the patient would like it to be made, provide pricing, get credit card info and confirm address for shipping (free shipping)

- ▶ **Third:** Prescription is made and shipped out
- ▶ **Fourth:** Pharmacist **Counsels** patient on how to use the prescription, in person or on the phone. A usage guide is also sent out in the delivery with details on application areas, storage and use of dispensers
- ▶ **Fifth:** **Receipt is provided to the patient**, which they can submit to their insurance. Most insurance companies cover BHRT prescriptions

Refills

- ▶ If you have not indicated refills on the prescription, and the patient requests a refill, we will fax your office to get authorization.
- ▶ If you do not want the patient to have more until testing or follow up appointment, You can indicate that on the fax and send back. We will let the patient know that they need to connect directly with your office.



Questions?

Thank You

Please feel free to contact me with any
further questions

ehab@peopleschoicepharmacy.ca