PART IV - 2016

Mastering the Protocols for Optimization of Hormone Replacement Therapy

Joint Providers—The Foundation For Care Management And WorldLink Medical

Featuring world renown expert and successful author, Neal Rouzier, M.D.

21 AMA PRA Category 1 Credits™
21 Nursing Contact Hours (21 Pharmacologic Hours)
21 Contact Hours Pharmacy Credit *(knowledge based)

December 2-4, 2016
Salt Lake City, UT

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THE ACADEMY OF PREVENTIVE & INNOVATIVE MEDICINE

PART IV – ADVANCED CASES

2016 Medical Seminar Series

PART IV OF THE SEMINAR SERIES

21 AMA PRA Category 1 Credits ™, 21 Nursing Contact Hours (21 Pharmacologic Hours), 21 Contact Hours Pharmacy Credit *(knowledge based)

Complexities of Hormone Replacement Therapy: An Evidence Based Protocol Review

December 2-4, 2016 – Salt Lake City, UT

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Disclosure Statements

Dr. Rouzier is a Speaker for BioTE.

Carolyn Rouzier has no significant financial interest in any of the products or manufacturers mentioned.

Planning Committee:
Neal Rouzier, MD, Content Expert is a Speaker for BioTE. Jeanette M. Dunn, RN, EdD, Lead Nurse Planner, Rachelle Meenach-Ligrano, MSN, FNP-C, Nurse Planner, have no significant financial interest in any of the products or manufacturers mentioned.

Objectives:

Upon completion of this workshop, the healthcare professional will be able to:

1) Recognize the benefit of MR-guided trans-rectal prostate biopsy and subsequent state of the art focal laser ablation of prostate cancer in comparison with other more problematic standard treatment modalities.
2) Implement into your practice the Dynamic contrast Enhanced MRI with real time temperature mapping and tracer washout for accurate diagnosis and location of prostate CA.
3) Review prognosis and complications for radical prostatectomy, proton gun radiation therapy, brachytherapy, cryotherapy, HIFU, laser ablation, as well as costs.

4) Review management strategies and importance of testosterone utilization in prostate cancer survivors as well as literature support. How to be your patient's advocate as no one else where explain all the ins and outs of the various available treatments.
5) Evaluate the association of testosterone and estradiol levels and the risk of developing prostate cancer. Should be raise, block, or administer estrogen based on the literature?
6) Recognize that based on the recent medical literature, physicians should be freed of any antiquated and unscientific restrictions that inhibit optimal treatment of their patients with testosterone, whether it is before or after prostate cancer diagnosis.
7) Recognize that optimal thyroid levels are best as recent studies determine that high TSH levels are associated with increased arterial stiffness and plaque thereby increasing CVD risk.
8) Review the recent NAMS position statements that further distinguish the emerging differences in the therapeutic benefit-risk ratio between ERT & HRT at various ages and time intervals from onset of menopause.
9) Recognize high testosterone levels in women are associated with an increased risk of breast cancer. Also understand that studies show testosterone administration is protective against breast cancer and is apoptotic to cancer cells. This demonstrates that association does not prove causation and one should not extrapolate them to be the same.
10) Recognize high estrogen levels in men are associated with increased cardiovascular risk. However estrogen administration in men protects against heart disease and prostate cancer. This demonstrates another example where association does not imply causation.
11) Evaluate and discuss my 50 most difficult management cases involving HRT.
12) Identify current approaches to manage vaginal bleeding, DUB, and endometrial hyperplasia.
13) Discuss the recent medical evidence that seems to counter everything that you have learned in regards to preventing prostate cancer.
14) Review medical studies demonstrating the various mechanisms of estrogen's ability to stop prostate cancer growth.
15) Recognize androgen deprivation therapy in men results in higher cardiovascular mortality and metabolic complications and this can be prevented by simply administering estrogen.
16) Identify how Traumatic Brain Injury affects quality of life by pituitary dysfunction: When and how to test and not miss it.
17) Evaluate recent literature demonstrating the mechanism by which synthetic progestins increase breast cancer development through the production of the RANKL protein.
18) Utilize dual intravaginal therapy to maximize the effect on atrophic vaginitis, chronic UTI, incontinence, and sexual dysfunction.
19) Review the historical perspective that pieces together the studies to understand the complexities in the NAMS recommendation for HRT.
20) Review a fun and entertaining article that puts in perspective the often distorted, oversimplified, over-exaggerated, and simply wrong conclusions from the WHI investigators.
21) Evaluate abnormal lab tests and various symptoms in complex and confusing cases.
22) Evaluate exactly when to use estrogen in premenopausal women and when not to use it: Anovulation vs. amenorrhea.
23) Identify different types of estrogen and progesterone and when to prescribe each.
24) Review various scenarios that dictate when to switch to alternate forms of HRT, based on history, BMI, risks, and compliance.
25) Discuss Hair loss in women: Current approach to reverse hair loss.
26) Describe various alternatives in testosterone administration in women.
27) Review when to switch from oral to transdermal estrogen; when to switch from transdermal to oral estrogen.
28) Discuss the current approach to preventing CVD in women with Syndrome W (X).
29) Discuss how to treat the vagina with pills, patches, rings, and things.
30) Review of management strategies for progesterone intolerance.
31) Discuss HRT review, myths, updates, alternatives when the usual routine doesn't work.
32) Update on diagnosis, treatment, and prevention of prostate cancer. Should we be prescribing estrogen to men instead of blocking it.
33) Review management strategies for estrogen intolerance.
34) Evaluate the best prevention and treatment for incontinence and UTI, from wet to dry and dry to wet. Prevention is the key before use of drugs or surgery.
35) Identify current recommendations from NAMS for HRT and ERT and how they differ from past recommendations. Oh how the pendulum swings.
36) Review the history as to why the world believes testosterone causes prostate cancer.
37) Review further data demonstrating that E2 is the best estrogen but not the safest.
38) Review the work up for elevated PSA and that doesn't mean biopsy and what to do when the biopsy is negative.
39) Discuss how to design a study of T3 to make sure that it fails.
40) Review literature of spironolactone and its BBW.

41) Discuss the most recent FDA BBW for testosterone as it pertains to MI, CVA, and DVT.
42) Review dosing and administration of tranexamic acid to stop your patients from bleeding.

ACCREDITATION STATEMENTS

AMA PRA Category 1 Statement

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PART IV: COURSE DESCRIPTION

One would think that 3 courses on HRT would be all that is needed to adequately practice BHRT. However attendees have requested that they want more, but with more complexity and problem solving as opposed to didactic. Hence Part IV.

Although there are new articles, research, updates, literature critiques, and sarcasm (of course), the majority of this course will be problem solving, case management, mistakes to avoid, and tricks of the trade. The audience will consist of those with significant experience, questions, and issues that make for an excellent experience for both me and participants as we all learn from patients and ourselves. Extensive literature review in Parts I, II, & III have not allowed me to present all the interesting and complicated cases and situations that I have encountered in the last 15 years of practice. I have included 60 of my most complex and problematic cases from the last 15 years but it will require you to have masterful understanding of Parts I, II, and III in order to understand the reasoning behind the treatment and management of these problematic cases.

First we will review the latest NAMS recommendations. It is a step in the right direction. However I will use the medical literature to, of course, prove to them what they should have said and done as opposed to their sole reliance on the WHI trial. It should be the summation of all available data that should dictate our treatment, not just one study. We will then review the evolution from testosterone causes prostate cancer to maybe it protects against cancer to now where we prescribe it to men with active cancer. Although commonly (incorrectly) thought to cause prostate cancer, estrogen has been a mainstay to treat and protect against prostate cancer. In fact it may be through aromatization that testosterone can protect against prostate cancer. We will also review at what level of estradiol results in a flip of the lipids that then become cardio-protective. Although it has been customary and fashionable to utilize aromatase inhibitors to block aromatization of testosterone to estrogen, the most recent study demonstrates using an AI increases gynecomastia, visceral and subq fat, cholesterol, and sexual dysfunction.

Please read the agenda and course outline for a more complete synopsis of topics and objectives. So bring your tough cases, comments, thoughts and ideas and have another fun weekend with your talented peers. This will be a collection of the most talented and experienced physicians in this industry. Caution: Part IV will be thought provoking, intense, and very complex. And just maybe you'll be able to pass that Certification Exam. Enjoy.
Neal

PART IV: OUTLINE & AGENDA

Friday
7:00 – 8:00 am
Registration

8:00-9:00 a.m.
Section 1: 35 Q & A

- Risks of PCOS and treatment to prevent complications.
- Relative risks of P4 and clotting.
- Effects of oral P4 on estradiol levels and effects of SL P4 on weight.
- Relative risks of estradiol levels and prostate CA.

9:00-10:00 a.m.
Section A

- Appreciate a literature review of which type of estrogen to use in which circumstances and why. Oral vs transdermal, risks vs. benefits, and recent NIH studies.
- Evaluate the most important literature summary chapter on estrogen and progesterone that you will ever read proving the harm of estrogen deprivation and the benefit of replacement = a must for everyone's library.
- Review all the long-term studies demonstrating the effect of estrogen on morbidity and mortality and the pathophysiology behind it all.
- Determine how to assess studies of association that do not prove causation in contrast to RCT's that prove causation through interventional study.
- Do not extrapolate to prove a theory as one must intervene to prove causality.

10:00 Break

10:15 -11:15 a.m.
Section 2: 39 Q & A:
Estrogen in men for CVD protection and that cause CVD.

- Understand the risks of estrogen deprivation in men and importance of SHBG.
- Learn the importance of fatty acid esters in CVD protection and how to increase them.
- All hormones provide CVD protection in the correct form.

11:15 - 12:15 p.m.
Section B
Estrogen in men: Good, bad, or indifferent?

- Review the studies demonstrating estrogen is associated with an increased risk of heart disease and cancer in women as well as heart disease in men = an association.
- Review the extensive literature on the beneficial effect of estrogen in men in the treatment and prevention of prostate cancer and heart disease = proves benefit= causation.
- Understand the various methods for raising estrogen in men and consequences of each.
- Evaluating the literature and understanding the difference between cause and effect and how it pertains to hormones.
- Discuss how association does not prove causation and to prove this requires the need for RCT's to differentiate.
- Practice HRT according to the EBM and not confabulation = don't lower estrogen.

- Learn how to increase visceral fat, decrease libido, increase lipids, and increase dementia through aromatase inhibitors as per NEJM.

12:15 - 1:15 p.m. Lunch

1:15 - 2:15 p.m.
Section 3: 43 Q & A:

- Methods to increase risk of depression and how to avoid it.
- Amenorrhea vs. anovulation, work-up, diagnosis & treatment.
- Breast proliferation markers and how to reduce them with HRT.
- Treatment of endometrial proliferation. Easy Treatment made easy for "no man's land." Evaluating the various effects of SHBG in HRT.

2:15-3:15 p.m.
Section C:
Review the historical perspective of testosterone causing prostate CA or how easily we can be lead astray.

- Understand how Huggins was correct in his assumption but also very wrong in his conclusion. Huggins led us astray with just one patient!
- What level of testosterone is conducive to the growth of prostate cancer?
- What level of testosterone is safest to maintain for prostate cancer protection?
- Is it possible or safe to utilize testosterone in prostate cancer survivors and at what point in time?
- Using testosterone in men with active cancer? What does the literature support and under what circumstances.
- Understand the complexity of the saturation model that is demonstrated in the world's literature.
- Does testosterone cause prostate cancer or does it not? Well it depends. Yes it does but treatment does not, rather endogenous does but exogenous does not.
- Review of the meta-analysis and world's expert opinions.

3:15 – 3:30 Break

3:30 - 4:30 p.m.
Section 4: 23 Q & A:
Treatment for high TSH and high Free T3. Really, what is estrogen dominance and is it really IR in disguise?

- Hair loss in men vs. hair loss in women.
- Blood donation with use of HGH, testosterone, finasteride.
- When to use estrogen in premenopausal women and when not to.
- When to measure it and when not to.

4:30 - 5:30 pm
Section D
Review the new NAMS recommendations for HRT with comparison of past recommendations- understanding why the change in attitude.

- Evaluate whether they utilize all current literature on which to base their recommendations or are they still stuck on the WHI? My critique and commentary follows.

- Discuss the pathophysiology of estrogen deprivation and biology of estrogen replacement.
- Describe the nonsensical use of long-term of estrogen blockade in women.

5:30 - 6:30 pm
Section 5: 31 Q & A
40 case scenarios requiring alternate types of hormones.

- Which vaginal estrogen to use, when, and why.
- TOC for vaginal atrophy and UTI. Work-up and treatment for vaginal bleeding. Alternative treatment for excessive, non-pathological vaginal bleeding (DUB).
- Vaginal estrogen troche, pills, patches, rings and things to protect the vagina.

Saturday
Registration
8:00 - 9:00 a.m.
Section E
Look at the advanced treatment of the vagina and how to make it work better with estrogen, DHEA, and Oxytocin.

- Review of the literature of further treatment of sexual dysfunction, both for women and men using Oxytocin.

Section F
Review the diagnosis and treatment of prostate cancer-state of the art with MRI-S and laser ablation.

- Discuss treatment centers, procedures, side effects, and costs of ablation vs HIFU.
- Other treatment modalities for prostate cancer vs. newer treatments not covered by insurance.
- Relative Risks of HRT in comparison with standard drug regimens for other illnesses- HRT is really quite safe in comparison with commonly prescribed medicines.
- Review the detriments of estrogen blockade and benefits of testosterone and estrogen replacement in men.
- Case presentation of before and after MRI laser ablation with lab review. What values to shoot for when treating with estrogen. A virtual reality of lab values when treating with estrogen.

9:00 - 10:00 a.m.
Section 6: 27 Q & A
Interesting HRT cases and how to solve the mysteries.

- Serum sickness from testosterone, diagnosis, treatment, avoidance.
- Treatment of young men with hormones can be life-saving also.
- Alternative testosterone treatments for women and how to reduce side effects and improve compliance.
- Lab review with case management for problems with lab values and how to manage the complicated and confusing cases.

10:00 Break

10:15-11:15 a.m.
Section G:
Discuss new insights into thyroid hormone replacement.

- Discuss use of T3 alone and what it does to lab values.
- Review the studies demonstrating genetics (DIO2 gene) predict response to T3 that explains the wide range of responsiveness.
- Discuss the plethora of data from pharmaceutical studies that prove that T3 is worthless and not needed.
- Explain how to design a study to prove that T3 does not work.
- Discuss why athyreotic patients don't do well on T4.
- Thyroid for ED?
- Review the recent Medco advisory to stop Armour thyroid.

11:15 - 12:15 p.m.
Section 7: 74 Q & A:
Optimal levels of estrogen and progesterone in men.

- Alternative methods of testosterone administration in men.
- The ins and outs of PCOS, harm, prevention.
- HRT cycling?
- HRT and fertility, what to advise.
- Function of inhibin and treatment of loss.
- HGH and mitosis vs. apoptosis.
- Side effects of estrogen and treatment. Use of metabolites and DIM.
- Treatment of erythrocytosis for pre-surgery clearance.

12:15 – 1:15 Lunch

1:15 – 2:15 pm
Section H:
An entertaining review of HRT literature and the use of statistics to change outcomes or what the investigators should not have done with the numbers.

- HRT-Real Concerns and False Alarms: Understanding statistics of the WHI and how they make no sense on re-evaluation.
- Traumatic Brain Injury and pituitary insufficiency that everyone misses.

2:15 - 3:15 p.m.
Section I:

- Review the treatment for common side effects/complications of HRT.
- Evaluate different treatment options for heavy menstrual bleeding (dysfunctional uterine bleed or DUB) in pre-menopausal women.
- Discuss work-up and various treatment modalities including tranexamic acid (Lysteda) to decrease fibrinolysis.
- Evaluation and management with laboratory work-up to assist in the diagnosis of postmenopausal vaginal bleed.
- Review complex estrogen lab levels, that don't make sense and why, and various treatment options.

- Understand the treatment of a man with prostate cancer, both active and cured.

3:15 – 3:30 pm
Break

3:30 - 5:30 pm
Section J:
How high can one go with estrogen therapy to treat sub-therapeutic levels? Why do you fear it? A lab review with various doses and corresponding estradiol levels.

- Review the latest NAMS article deciphering the safety and efficacy of HRT in comparison with other commonly used medications.
- Understand the difference in mortality when comparing estrogen vs. statins vs. ASA for cardiovascular protection.
- Review which medicines reverse plaque and which ones don't.
- Evaluate the various studies showing increased breast cancer with statins in comparison with HRT/ERT.
- Review which hormone/med provides the best protection against CVD mortality as well as all-cause mortality and which hormone/med increase mortality.
- Update and evaluate breast markers and MPA vs. OMP.
- Study the mechanism behind Provera and Depo-provera in stimulating the RANKYL protein and the subsequent increase in breast cancer risk.
- Review why and how to block RANKYL with Denosumab.

Sunday
7:30 – 8:00 a.m.
Registration

8:00 - 9:00 a.m.
Section K:
Final review of the testosterone studies demonstrating testosterone causes an increase in MI. Letters to patients and doctors.

- How to CYA when prescribing testosterone and what to add to your consent forms.

9:00 a.m.
Break

9:15 - 11:00 a.m.
Section 8
50 complex cases, treatment and management.

11:00-12:00 Noon
Section L: Q & A
Questions and answers with case reviews from articles from Part IV:

- What is the course of action to take when women report weight gain after starting HRT?
- What is the course of action to take when women report progesterone intolerance?
- A patient with an elevated PSA has a (-) TRUS biopsy. So now what?

- So what makes you the prostate cancer expert?
- Your BHRT patient of 15 years suffers an MI which results in her cardiologist taking her off HRT. Should she be off HRT or on HRT? What the PMD won't understand and doesn't know.
- At what point can hormones be resumed after a diagnosis of CA prostate, breast, uterus, and ovary?
- What is the appropriate treatment to block progesterone in a patient with a progesterone receptor site (+) breast cancer who is a normally menstruating 45 y/o female on Tamoxifen? What if the chemo resulted in loss of menstruation and ovulation and she developed endometrial proliferation from Tamoxifen?
- Review cases demonstrating when and when not to use oral E2.
- Which E2 does one use in older men with heart disease that also have prostate cancer and are very symptomatic on Casodex and Lupron?
- When to transition from oral estrogen to transdermal and vice versa and whether it differs in men or women?
- Why use oral E2, P4, and testosterone for Syndrome X and not transdermal? Think SHBG, weight gain, and hirsutism respectively.
- Why use oral P4 and oral testosterone in older women? Think about saliva and compliance.
- What is the appropriate treatment for endometrial hyperplasia in postmenopausal women on Tamoxifen?

12 pm: Adjourn

- Discussion of Part V.

Table of Contents
Seminar Series Part IV
December 2-4, 2016, SLC, UT

Section 1

- **Vitamin D is a hormone**
  - **True**
- **Toxic levels are typically > 300**

  True
- **Toxic symptoms are weakness and hypercalcemia**
  - **True**
- **Cholecalciferal is D3, ergocalciferal is D2**
  - **True**

PCOS increases risk of:

- Endometrial Cancer
- Breast Cancer
- Infertility
- Anovulation
- CAD
- CVD
  - Answer ALL

PCOS

- **Lean women with PCOS are not necessarily insulin resistant, yet they still respond to metformin.**

  True, as insulin levels can be normal with PCOS

- **Young women may need dipeptidyl peptidase-4 inhibitors or glucagon-like peptide-1 agonists instead of metformin if they can't tolerate metformin.**

  True

- **Over 50% of women with PCOS will miscarry.**

  True, that can be prevented by progesterone and metformin and thyroid.

- **Adrenal hyperplasia mimics PCOS. Dx by elevation of 17α-hydroxyprogesterone.**

  True, r/o tumor or hyperplasia

- **IR increases aldosterone production which increases systemic inflammation and CAD.**

  True, therefore treat older PCOS women with spironolactone regardless of skin issues in order to lower LH and aldosterone.

PCOS

- **Any woman with PCOS symptoms and elevated testosterone level can be diagnosed by the flipped FSH/LH ratio. However if the FSH/LH ratio is normal, then the only other blood test needed to R/O ovarian tumor or any virilizing adrenal tumor is?**

  17α-hydroxyprogesterone

- **If this test is (-), is MRI/CT indicated?**

  No, if blood test is normal, then w/u is finished.

PCOS

- **Measuring insulin levels is important for making the diagnosis of PCOS.**

  False as levels can be normal.

- **PCOS commonly occurs in thin women**

  True

- **What % of thin women with PCOS have a fatty liver?**

  40%, still treat with metformin to ↓ IR

Am J Med 2006,163:1519-30

- **T3 at 50 ug/day resulted in more remissions of depression than lithium.**

  True

- **IGFBP-3 protects against cancer.**

  True = apoptotic

- **New evidence proves tumor initiation by IGF-1**

  False, but IGF-1 can be mitotic, so don't use it alone.

HGH is a controlled substance, schedule III.

False

JCEM 2001,76(7):2929-2933

- **According to Melmed, IGF-1 levels should be titrated to upper levels of normal for maximal health benefits.**

  True

- **In a large, multi-center analysis of acromegaly, no increased cancer incidence was found.**

  True

- **Over 15,000 patient years with acromegaly revealed a cancer incidence of 0.76.**

  True

- **Recent analysis of several studies demonstrated an 8 fold increased risk of DVT with use of progestins.**

  True

- **Oral progesterone increases clotting risk by first pass production of pregnanediol.**

  False, no effect on clotting

- **Progesterone caused only a 2 fold increased risk of DVT in at risk patients.**

  False, no risk in any study.

Hormone Interactions

- **Oral progesterone decreases absorption of oral estradiol.**

  True, therefore measure and adjust accordingly.

- **Transdermal (SL) progesterone decreases it even more so.**

  False, no effect whatsoever.

- **Oral estrogen increases CRP, but it also reduces many other inflammatory markers and proteins.**

  True if CEE, false if oral E2 which does not increase CRP.

- **Transdermal estradiol affects lipids & lipoproteins at 90% of oral estrogen.**

False, as some studies demonstrate no benefit on lipids or CVD outcomes.

- **Current data supports no role of estrogen causing prostate cancer.**

True, estrogen doesn't cause cancer but rather is associated with a decreased risk for every 2-fold increase in estradiol level in men.

- **Current data supports an inverse relationship between estradiol and prostate CA.**

True = protection by estrogen.

- **Current data support a 30% lower risk for prostate cancer for a doubling of estradiol levels.**

  True = protective
- **SHBG is inversely associated with prostate cancer.**

  True
- **IR is directly associated with prostate cancer.**

  True

Prostate Cancer

- **Estrogen improves survival in androgen deprivation.**

True, but survival is not improved with LHRH agonists alone.

- **"Raising" serum estradiol levels with estrogen is associated with an increased cardiovascular risk.**

False, yes for oral estrogen (5 mg of DES) but not for raising serum levels of estradiol by testosterone or E2 administration.

It is estrogen deficiency, and not testosterone deficiency, that is responsible for osteoporosis in men.

True

Estrogen in men

- **Oral DES at 5 mg doses increased MI and mortality in men treated for prostate CA.**

  True, but only 5mg dose did; 1mg dose did not.

- **Oral estrogen has an additional direct cytotoxic effect on cancer cells not seen with LHRH agonists.**

  True, which is why estrogen is such a better treatment of prostate cancer that LHRH agonists.

- **Oral estrogen in men = oral estrogen in women as far as benefit of CVD protection.**

  True

SHBG

- **The best method to lower SHBG is by high carbohydrate diet and weight gain.**

  True as it increases IR.

- **The best way to raise SHBG is through low carb diet, exercise, weight loss, and oral estrogen.**

  True

- **The two most important benefits that make oral estrogen the most important hormone (drug) for CAD prevention are the effects on lipids and SHBG.**

  True, and this affect decreases IMT

- **Transdermal estrogen has minimal effect on lipids and no effect on SHBG.**

  True

- **Low physiologic levels of testosterone in menopausal women are inversely related to coronary and carotid atherosclerosis.**

  True

PCOS

- **Femara and metformin have greatly increased pregnancy rates in PCOS patients.**

  True

- **They should be continued through pregnancy to prevent IR and miscarriage.**

  False, as metformin should be continued but Femara is a teratogen.

- **SHBG is a very strong predictor of CAD and CVD.**

  True, also of cancer

Breast CA

- **HGH increases IGF-1 that can be mitogenic.**

  True

- **HGH produces ↑ IGFBP-3 which is apoptotic to cancer cells.**

  True, opposes effect of IGF-1.

- **Recent studies use IGF-1 levels to diagnosis HGH deficiency instead of the ITT test.**

  True, but insurance does not recognize it.

- **One benefit of transdermal estrogen is the increase seen in fatty acid esters which are key factors in the development of plaque and in preventing plaque deposition.**

  False, only oral E2 increases FAE.

- **One of the benefits of transdermal estrogen is a decrease in CRP levels.**

  False, however oral E2 did not raise CRP, only oral CEE does.

- **Researchers from the WHI recommend that ERT be prescribed for the shortest time possible and then stopped**

  True

This is because estrogen increases plaque formation over time and MI:

  False

- **…Colon CA**

  False

- **…Osteoporosis**

  False

- **…CVA**

  False

- **…Breast CA**

  False

- **…Death**

  False = makes no sense = MNS

Fe & Cu are free radicals

- **Copper is included in most vitamin and eye formulas to protect against AMD.**

  True, but it should not be = pro-oxidant.

- **NTX predicts future bone density.**

  True

- **NTX goals are < 38.**

  True

- **Estrogen metabolite goals are 2OH-estrone to be > 16αOH-estrone.**

  True, but who knows if that is of benefit.

Levels of 4OH-estrone might be more important then 16αOH-estrone.

True, but who knows. Who cares?

JNCI

- **A recent JNCI article demonstrated that the 2OH-E1/16αOH-E1 ratios were predictive of breast cancer risk.**

  False- showed no correlation

- **Oral testosterone (estratest) protects against CAD by lowering LDL and raising HDL.**

  False, does the opposite, but oral micronized testosterone is safe and ≠ harm of methyltestosterone.

- **Finasteride artificially lowers PSA by 50%.**

  True, so double the PSA to get the true PSA.

CRP is lowered by which of the following?

- Statins
- ASA
- CAL/MAG
- EFA
- Weight loss
- Testosterone
- Transdermal estrogen

Answer: All but estrogen

Which hormones are optimal at low levels and harmful at high levels?

- Cortisol
- Insulin
- Aldosterone

All, and each requires low levels for optimal health and high levels are harmful.

Doctor, Did You Test My Adrenals?

- If a patient requests testing for adrenal fatigue, what tests can be offered for diagnosing adrenal fatigue?

  Saliva cortisol

- As far as testing for cortisol, both saliva testing and serum levels are both equally accurate in diagnosing adrenal fatigue.

  False, as serum levels will show no fluctuation whereas saliva levels may show a diurnal flattening requiring treatment.

- What is the treatment for adrenal fatigue?

  Tx is adrenal support or cortisol in severe cases of fatigue/FMS.

Which of the following cause depression ?

- Provera
- Loss of progesterone post partum
- Low thyroid
- Finasteride

Answer: All and loss of all hormones can cause depression.

The Harm Of Estrogen In Men

- One legitimate use of anastrozole is in men with CAD.

  False, blocks estradiol that increases risk.

- Anastrozole lowers estrogen in men which in turn keeps SHBG low.

  False- SHBG is made in the liver and serum levels of estrogen do not affect SHBG levels. However giving oral estrogen to men will increase SHBG production as well as giving testosterone to ↓ VF and IR.

- Which in turn is beneficial in men.

  True as ↑ SHBG is good and desired for protection against CVD and CA and low levels are harmful.

What Day of the Cycle Is Best?

- In normally menstruating pre-menopausal women, when is the best day during the cycle to test for estradiol and progesterone?

  Test on day 35.

- The best day to test for progesterone level in a premenopausal woman treated daily for PMS?

  Test on day 34.

(If you have to think about this, then you need to go back and take Part I).

My Doctor Says…

- A patient's PMD is upset with the optimal levels of thyroid/testosterone on the patient's most recent blood test. The patient feels wonderful. Other than reducing the doses of hormones, what can be done to ease the concern of the PMD yet allow the patient to continue the same dose of HRT?

Retest but do not take the HRT on the day of or the day before the test. However that won't help you adjust any HRT.

DOCTOR I'M BLEEDING

- A 45 y/o premenopausal woman c/o prolonged periods and heavy bleeding. US shows no fibroids or polyps. ES is normal and EB is (-). Any endometrial pathology has therefore been excluded. Tx to diminish bleeding acutely?

1) BCP 2) Progesterone in high doses 3) Mirena IUD 4) Tranexamic acid (Lysteda) 5) Uterine (endometrial) ablation

All of the above can be used.

Antifibrinolytic agent = Lysteda

- Lysteda can be used if bleeding is due to fibroids?

  True-Yes it can be used for fibroids, polyps, and menorrhagia and metorrhagia, or any endometrial bleeding once a pathology (cancer) has been ruled out.

- Lysteda may be used in premenopausal women to decrease menstrual bleeding before endometrial ablation is attempted?

  True

- Lysteda may be also used in menopausal women with non-pathologic bleeding?

  True

- High dose progesterone should be tried first?

  True

LYSTEDA = TRANEXAMIC ACID

- This antifibrinolytic agent causes blood clots similar to oral estrogen?
- (Remember amino-caproic acid (Amicar) for prevention of re-bleed in SAH?)

False, as it prevents lysis of fibrin or clot breakdown as opposed to stimulating clots by increasing clotting factors.

No cases of DVT or thromboembolic events, in contrast to HRT, have been reported in the trials of Lysteda.

WEIGHT GAIN?

- ERT can increase leptin which increases appetite and weight gain?

False. ERT has not been shown to increase leptin or weight gain. Menopause transition does result in weight gain. Testosterone can ↑ wt. gain (muscle), and progestins ↑ IR and weight gain (fat).

- Weight gain can be due to increased appetite, decreased activity, progesterone, testosterone, fluid retention?

True

AMENORRHEA vs. ANOVULATION

- **Your 21 y/o daughter, track star, has no period for 2 years. No symptoms, HF, NS, or hormonal complaints. Recent OB/GYN tested DEXA and found T-score of -2.4. PMD gave her BCP to protect bones. She doesn't wish to take and refuses BCP. How would you treat your daughter? If it was you, how would you treat yourself?**

Anovulation=plenty of estrogen and testosterone produced but no progesterone = PCOS.

Amenorrhea= no estrogen, progesterone, or testosterone with low FSH/LH = hypothalamic failure.

P) Treat with all 3 hormones in low doses until weight increases or menstruation returns.

Testosterone

- Most common harmless side effect of testosterone that is commonly thought to be harmful by your peers?

  Erythrocytosis

- Most potential harmful side effect of testosterone that is most commonly overlooked or ignored?

  Transference to others

- Androgel, Testim, and Axiron have a BBW whereas compounded testosterone does not.

  True, but it should. Document on chart notes.

- Testosterone is Schedule III.

  True, it is controlled. HGH is not.

QUESTIONS: SECTION 2

- **Correct and appropriate treatment of PCOS can affect anovulation, infertility, hirsutism, CVD, endometrial cancer, breast cancer.**

True

- **The increase in aldosterone levels seen with PCOS can increase inflammation and plaque deposition, the treatment for which is spironolactone.**

True, to lower aldosterone levels

- **PCOS doesn't care if you are lean, medium weight, or over weight.**

  True
- **Lean women with PCOS may not be insulin resistant and will have normal insulin levels, yet will still respond to metformin therapy.**

  True
- **Over 40% of lean women with PCOS will have a fatty liver indicating some degree of insulin resistance.**

  True- The diagnosis is often missed if women are lean. I have been surprised and fooled so many times that I now routinely order FSH/LH ratios on any woman with any sort of complaints or symptoms, even psych symptoms.

- **The miscarriage rate for women with PCOS is 50% which can be lowered with thyroid, metformin, and progesterone.**

  True, however stop GLP-1 RA and DPP-4 I.

- **Metformin can lower the miscarriage rate to <10% if taken throughout pregnancy.**

  True

- **Progesterone lowers miscarriage rate and can be continued throughout pregnancy to increase smooth muscle relaxation.**

  True, but especially first trimester.

- **The minimal serum concentration of progesterone demonstrated in the literature to provide adequate endometrial protection is 5 ng/ml.**

  True- average is 10 ng/ml in most studies.

- **Studies demonstrate that MPA increases epithelial proliferation in breast tissue by 30% or greater.**

  True

- **All studies demonstrate decreased breast epithelial proliferation with progesterone administration.**

  True

- **Where would you like your levels to be?**

  10 ng/ml and not 2 ng/ml with TPC.

- **A woman who gains weight after starting HRT should be switched to a transdermal progesterone.**

False- fluid retention is treated with diuretic or switching to transdermal estrogen.

- **Oral progesterone lowers serum estradiol levels by 50% thereby necessitating an increased dose of estradiol to maintain adequate E2 levels.**

True - Oral progesterone can lower estradiol levels which is why we need to monitor levels to assure adequate replacement and protection. ∴ SL progesterone is preferred by providing better progesterone levels and better estradiol levels.

- **However MPA provides greater endometrial down regulation than progesterone.**

  False, it's no better but OB/GYN's think that it is a commonly switch from P4 to MPA.

- **Higher dose MPA reduces endometrial proliferation better than P4 due to its greater potency and effect on uterine tissue.**

False. MPA doesn't work any better than P4 and it is not tolerated in high doses that are usually required to treat endometrial proliferation.

- **80 y/o female with history of vaginal bleed and endometrial proliferation. The endometrial stripe measures 0.9cm; biopsy is negative. Can't stop estrogen due to vasomotor symptoms and osteoporosis. Did not tolerate Provera 5mg by PMD.**

Tx?

High dose progesterone at 200 mg TID resulted in serum levels of 95 ng/ml and a decrease in ES to 0.5 in one year.

- **52 y/o female c/o severe HF, FSH = 56, estradiol = 210.**

Tx?

Diagnosis is perimenopause with excess estrogen and lack of progesterone opposition. Even though HF and NS are present (due to loss of inhibin and not estrogen), prescribing estrogen makes symptoms worse as estradiol is already high. Tx with high dose progesterone @ 200 – 400 mg per day until the symptoms are no longer controlled by progesterone alone. Then start estrogen.

- **44 y/o female on BCP for PCOS, c/o PMS, fatigue, headaches, no libido.**
- **Total testosterone = 90 (high)**
  free testosterone = 0.2 (low)

Tx?

Symptoms are due to loss of free testosterone.

Treatment includes prescribing testosterone.

Take BCP continuously eliminates PMS.

Why is TT elevated and FT low?

Testosterone is ↑ due to adrenal hyperplasia from PCOS. Free testosterone is ↓ due to ↑ SHBG and suppression of ovarian function and production of testosterone.

- **A 72 y/o male who lives at Big Bear Lake at 7500 feet elevation desires HRT. However the H&H = 20.7/58**

Tx?

Once PV has been excluded by lab tests and (-) JAK-2 gene test, then testosterone is recommended. If another physician will be treating/monitoring, then recommend regular phlebotomy so that no one gets upset with the harmless erythrocytosis. Otherwise, erythrocytosis ≠ PCV and no treatment is necessary. High HgB is harmless in anyone that lives at altitude or has COPD.

- **72 y/o male, s/p brachytherapy for prostate CA, was cured with PSA < 1.0 for 5 years. Now PSA is 10 and climbing.**

- **Other than offering LHRH agonists, which other therapy would/should be offered.**

Treatment should be with high dose estrogen titrated upward monthly, with the eventual goal to a PSA < 1.

When should PSA/estradiol levels be retested?

Q 3 months.

- **53 y/o female on progesterone cream with constant vaginal bleed. Vaginal ultrasound- normal ES without polyp or fibroid. Progesterone salivary levels are 5 times normal, so PMD reduced dose of cream to 25 mg/day.**

Diagnosis? DUB

This is the problem with relying on salivary levels to guide therapy as levels will be high leading one to conclude that serum progesterone levels are too high. The opposite is true as the serum levels are too low and the dose of progesterone should changed and increased to provide levels of at least 10 ng/ml or more to control bleeding and endometrial proliferation and DUB.

Same Patient with PCa

- **Patient has a history of HTN, hyperlipidemia, and several heart attacks. You are concerned about prescribing oral estradiol as oral DES increases the risk of heart attacks. What to do?**

Tx?

Dose?

Patient has pre-existing CAD and potential plaque rupture from oral estrogen. Plaque rupture did occur with 5 mg DES but not with 1 mg DES or oral E2. Treatment could be with a transdermal patch if you are worried, starting at 0.1 mg patch and increased until PSA falls to less than 1. It takes 3 months for full effect to be seen. ∴ Adjust and test PSA with estradiol Q3M.

- **Which lab parameters are monitored?**

Monitor levels of testosterone, estradiol, & PSA.
Testosterone levels will fall to castrate levels, estradiol should elevate to >100 pg/ml, and PSA will continue to fall over 3 months and then level off.

- Rapid increase in estrogen can cause breast symptoms. To prevent this, doses should be increased slowly Q monthly.

True

- The goal of PSA should be to a level of < 1.0 and sometimes E2 levels need to be 300-500 pg/ml to achieve this.

True

- **A 65 y/o male is asymptomatic with CAD, on HRT. The Free T3 = 4.8 and the TSH = 8.9.**

Tx?

Patient needs more thyroid hormone to lower TSH to below 3.0. I would give 1 grain more of desiccated to maximize Free T3 that will lower VF and lipids and lower TSH too.

- **A 53 y/o female, newly menopausal feels good on HRT. Hx of PCOS, fatigue, no libido- all of which have improved on HRT. The PMD stops the testosterone claiming that it increases risk of CAD in women.**

Tx?

The physician is incorrect. Testosterone has been shown to be protective against CAD in women. It is the IR that is the culprit in causing the CAD and DM with PCOS, not the testosterone. If hirsutism develops, then treat with spironolactone and metformin.

When does PCOS end?

At death. Therefore may need to treat forever.

- **A healthy 65 y/o female on HRT for 15 years. Patient was told to stop HRT by her GYN who quotes from WHI that HRT causes strokes.**

Tx?

If patient is taking Prempro, then I agree patient should stop HRT. If patient is taking estradiol and progesterone, then the WHI recommendations do not apply and patient should continue her HRT to protect against strokes. Give patient the literature to support your position that E2/P4 ≠ CEE/MPA. We must be our patient's advocate, otherwise they will not know and their doctors certainly don't understand.

- **A 65 y/o healthy female on HRT for 15 years, has a small CVA. PMD tells patient to never take HRT again as that is what caused the stroke. However patient is miserable off HRT.**

Tx?

If patient is on Prempro, then stop (switch) that HRT. If patient is on BHRT, then she may continue as the RR for CAD and CVA is 0.6 as time progresses indicating that HRT was protective and did not cause the CVA. It is only during that first year of starting HRT that HRT poses a risk for plaque rupture. If patient has been on BHRT for 15 years, then the HRT is protective (and not harmful) and the CVA was not caused by the HRT, but rather by some other inflammatory agent. However Provera, long term, can continue to cause inflammation and negate any beneficial effect of estrogen. Stop CEE/MPA but not E2/P4.

- **There are multiple studies demonstrating that estriol is safe and beneficial.**

  False, it is safe but only benefits the skin.

- **There are two good studies demonstrating that estriol protects against breast cancer, as promoted by the compounding industry.**

  False. It is against the law to promote and advertise that which does not have FDA approval for that claim.

ED≠ED, Rather ED=IR

- **Estrogen dominance including the weight gain, fluid retention, fatigue, irritability resolves at menopause with loss of estrogen.**

  False, it only gets worse and is due to IR and not E2. In fact, blocking E2 makes IR worse!

- **Complete hysterectomy is the cure for estrogen dominance by getting rid of the estrogen that is causing all the symptoms.**

  False, all women gain weight after hysterectomy.

- **Estrogen dominance is actually Syndrome W which is due to IR and not ED.**

  True. Nowhere in any medical literature is the term estrogen dominance used!

Informed Refusal

- **Patients refusing treatment or stopping therapy should have an informed refusal documented informing them of the risks of not taking a therapy.**

True- as the risks of not taking hormones should be explained and documented.

Pseudo-period

- **A 53 y/o newly menopausal woman on HRT for 6 months, c/o severe bloating, cramps, dysphoria, feeling like she is going to have a period but can't. Going crazy and going to explode. Tx**?

Pseudo-period is treated with high dose progesterone as an IM shot of 100 mg progesterone in oil IM, or 6 progesterone tablets daily until better. Newly menopausal women will have 4 more periods until final cessation. Therefore many women will experience this. Tx is high dose P4.

- **Premarin & Provera combined have been implicated in provoking cancer, yet the literature demonstrates that the RR of statins, ETOH, and sedentary lifestyle are worse.**

  True

- **Statins ↑ breast CA risk.**

True

- **Estrogen ↓ breast CA risk.**

True

- **Should we raise or lower SHBG in women? How about in men? How?**

Raise in men, raise in women. Decrease the IR and VF by diet and hormones, and oral estrogen.

- **Just how bad is SHBG?**

SHBG is never bad, always good.

- **Testosterone administration lowers liver production of SHBG?**

False as the treatment eventually lowers visceral fat that then decreases IR that then raises SHBG.

- **High insulin levels lower SHBG?**

True as high insulin always lowers SHBG (blocks production in liver) and that is harmful for CA & CAD.

- **Does oral estradiol raise or lower body weight?**

Oral estradiol lowers visceral fat but may increase fluid retention, depends on genetics.

- **Does oral progesterone raise or lower body weight?**

Oral progesterone lowers fat slightly (progestins raise).

- **Does transdermal progesterone raise or lower body weight?**

Transdermal (SL or vaginal) raises weight slightly.

- **Oral progesterone when added to E2 lowers the serum level of E2 by 50%.**

True, ∴ increase dose of E2 and monitor it.

- **Researchers claim that elevated baseline levels of testosterone are associated with an increased risk of breast cancer and heart disease in women. Is there literature to support the opposite?**

Yes, testosterone administration is not harmful, only beneficial. Observation does not prove causation. Interventional RCT's prove benefit.

- **Hirsutism is a risk factor for CAD in women and the treatment is directed at the pancreas.**

True as hirsutism usually indicates IR and low SHBG, both of which increase risk of CVD.

Low serum androgen levels increase the risk of ICA atherosclerosis in women.

True, testosterone is protective and not harmful.

- **Statins are not beneficial for primary prevention of CAD in women. Neither is ASA.**

True, only estrogen is.

- **In men, estrogen is more protective than testosterone against development of CAD.**

True. Yes estrogen is protective in men and women. Block E2 in men causes increase in CAD.

This is the reason for maintaining low levels of estrogen in men.

False, makes no sense.

Pravastatin, lovastatin, simvastatin increase the risk of breast cancer greater than Prempro.

True, statins are oncogenic.

Norethsisterone (norethindrone) increases the relative risk of breast cancer even greater than Provera?

True, all progestins increase risk of breast CA.

CEE reduces risk of colon cancer by 37% whereas statins increase the risk of colon cancer by 46%.

True, hard to believe. Which one does everyone get?

- **A recent meta-analysis demonstrated a 33% increased risk of breast cancer with use of statins.**

True again.

- **In the frequently quoted article about breast CA from JAMA in 1968, the hormone estradiol prevented breast cancer just as well as the estriol and progestin groups.**

True, all did. Estriol is taken out of context.

- **In the WHI study ASA demonstrated no benefit in primary CAD protection.**

True

- **CEE & MPA increased risk of VTE (RR = 2.17) whereas there was no increased risk of VTE with esterified estrogen (RR = 0.78) or oral estradiol (RR= 0.8) in the WEST study.**

True and don't extrapolate CEE/MPA = E2/P4!

- **The risk of VTE with Tamoxifen or Evista is greater than CEE+ MPA.**

True

- **Tamoxifen, Evista, CEE + MPA all increase the risk of VTE whereas oral estradiol was demonstrated to lower the risk of VTE.**

True, but everyone thinks oral E2 increases DVT and that the world is flat.

- **In a recent meta-analysis, women younger than 60 who were randomized to receive HRT experienced an overall reduction in mortality compared to placebo.**

True and even with Prempro.

- **We reviewed which vaginal estrogens to use, which ones not to use, their mechanism of action, and % absorption. Which one increases serum levels of E2?**

Femring increases levels and requires opposition.

True

- **Optimal vitamin D levels are greater than 60 for optimal cancer and osteoporosis protection.**

True

- **Vagifem and estring require progesterone opposition.**

False

- **Low serum levels of estradiol in men are associated with an increased risk of prostate cancer.**

True

- **In men, the serum levels of estradiol are inversely related to the risk of prostate CA.**

True

- **The risk of prostate cancer was 30% lower for each doubling (increase) of the estradiol level.**

True

- **Low serum levels of estradiol in men are associated with an increase risk of CAD, CVA, dementia, osteoporotic fractures. Where would you like your levels to be?**

True and > 75 pg/ml or that of young men.

- **The current trend to keep estradiol levels low in men via use of aromatase inhibitors is not supported by any literature.**

True, there are no RCT's that show benefit to AI.

- **All literature supports low levels of estrogen in men are harmful.**

True

- **The current trend to keep estrogen levels low in men has demonstrated an increase risk of osteoporosis, insulin resistance, diabetes, heart disease and increased mortality.**

True

- **Long-term androgen deprivation therapy has consistently demonstrated increased mortality in comparison with placebo. This is primarily due to loss of estrogen's protective effects.**

True**.** Estrogen has the same beneficial effects in men as in women. E2 reverses harmful effects of LHRH agonists.

Progesterone

- **There have never been any negative medical studies published on micronized, natural progesterone.**

True, except for low levels providing no benefit.

- **SL or vaginal progesterone may increase weight gain in comparison to oral P4.**

True, it is slight and mechanism is unknown.

- **Oral P4 has been shown to inhibit the absorption of oral E2. However it does not increase weight gain.**

True as oral progesterone reduces intestinal absorption of estradiol but mechanism is unknown.

- **Transdermal estrogen therapy for treating prostate cancer is a better (potentially safer) therapy in older men than oral estrogen.**

True theoretically as high dose estrogen (DES) caused plaque rupture but not in any study of oral E2 or TE2.

- **Younger men with prostate cancer may benefit more from oral estrogen than transdermal.**

True. Transdermal E2 can prevent plaque rupture but has less effect on lipids. Oral may cause plaque rupture in older men (DES) but has a better effect on lipids than transdermal. Oral benefits and protects against CAD the best and for the same reasons as in women. Oral E2 reverses the adverse lipid effects of LHRH agonists the best. Therefore I prefer oral E2, and at high doses.

Understanding E2 & P4 Physiology

- **54 y/o on HRT complains of weight gain on oral E2 and SL P4. She claims that the estrogen is causing her to gain weight. Is she correct? Yes or No?**

No, not body fat. Yes, if fluid retention.

- **In every study to date oral E2 has not caused weight gain as it reduces visceral fat.**

True

- **The weight gain is more likely due to the SL P4.**

True, or perhaps fluid retention from E2. If patient gains weight, switch to oral progesterone, but make sure to raise and monitor estradiol level which can fall on oral progesterone. Low estradiol levels cause weight gain and increase VF; higher estradiol levels lower IR and VF but oral progesterone lowers estrogen. Therefore switch to oral progesterone and raise estradiol dose to compensate for poorer absorption of E2.

SHBG

- **Oral E2 raises TBG.**

True

- **Oral E2 raises CBG**.

True

- **Oral E2 raises SHBG.**

True

- **Doing this has never been shown to be harmful or detrimental to health or longevity.**

True-SHBG is good and not bad even though it binds testosterone and lowers free testosterone. Just simply Rx more testosterone.

Alzheimer's and Estrogen

- **The WHI observed a "105%" increase in AD?**

"True", but this was an incorrect statement as it was not Alzheimer's disease which was later corrected.

- **Even though the researchers reported an increase in AD, this was incorrect as it was actually vascular dementia and not AD.**

True

- **The actual % incidence of CAD, stroke, and vascular dementia was the same in the WHI.**

True, thereby proving that it is all the same vascular pathology related to plaque rupture by Prempro and not due to Alzheimer's disease.

QUESTIONS: SECTION 3

- **According to the literature, at what suppressed level does TSH cause osteoporosis?**

No level of TSH causes osteoporosis as it is not metabolically active. Only increased thyroid hormone levels metabolize bone. Just because TSH is suppressed does not mean hormone levels are increased. Therefore measure Free T4 and Free T3 to predict bone loss, not TSH.

- **Which medicine is indicated for a patient with hypothyroid symptoms and perfectly normal TSH levels?**

Thyroid hormone treats thyroid resistance. All hormones treat hormone resistance.

Sex hormones occur naturally in plants.

False. BHRT is derived from a cholesterol ring. Diosgenin (steroid ring) is extracted from a plant source and synthesized into BHRT.

- **Which two hormones have been recommended by medical studies to prevent migraine headaches?**

Melatonin and progesterone

- **Which medical journal recently published articles on the health benefits of DHEA in preventing Syndrome X and IR?**

JAMA

- **What is the best treatment to reverse hair loss in men?**

Avodart (dutasteride) which is a 5α-1 & 5α-2 inhibitor and hair is 5α-1.

- **What is the best treatment to reverse hair loss in women?**

Thyroid and spironolactone.

- **Which hormone might eliminate Raynaud's Syndrome?**

Thyroid

- **Patients taking HgH are prohibited from donating blood.**

True as the concern is about CJ disease.

Patients taking testosterone are prohibited from donating blood.

True, if the H & H is elevated, the BB thinks that the patient has PCV and they won't take blood from a patient that has any blood dyscrasia or pre-leukemic tendency.

- **Men that are taking finasteride are prohibited from donating blood.**

True

- **Perimenopausal women typically have elevated levels of estradiol due to increased ovarian activity due to elevated FSH.**

True

- **Progesterone is therefore the TOC for perimenopause symptoms as these women have elevated estrogen but loss of progesterone.**

True, and both progesterone and testosterone decrease HF and NS whereas using E2 here causes symptoms of ED.

- **As follicles age less inhibin is produced. Reduced inhibin results in increased FSH. Inhibin normally suppresses (inhibits) FSH and loss of inhibin no longer inhibits FSH thereby increasing FSH.**

True

- **Treatment for the above is therefore progesterone and not estrogen as estrogen is usually elevated early on by rising FSH levels to compensate for loss of inhibin.**

True

- **Inhibin is a sensitive marker of ovarian follicular function and elevated FSH is a sensitive marker of inhibin function.**

True

- **Inhibin regulates FSH the most; whereas estrogen does minimally. This is why prescribing estradiol does not lower FSH (BCP's do though) .**

True

- **If FSH >30 or LH >30 = infertile = no birth control needed.**

True

- **Anovulation = no ovulation or release of egg = no secretory (luteal) phase = no menstruation = no progesterone = no protection of breasts or uterus.**

True and common in perimenopause

- **No menstruation indicates a proliferative or hyperplastic endometrium = increased cancer risk.**

True

- **Loss of menstruation at any age does not usually require progesterone.**

False, as anovulation absolutely requires P4.

- **Natural HRT given continuously in high doses provides birth control.**

False-only potent synthetic BCP suppress FSH and ovulation, not BHRT.

- **Switch BCP to natural HRT when FSH >50. Wait 4 weeks off of BCP before measuring FSH.**

True

- **For adequate uterine down-regulation in treating endometrial proliferation, progesterone levels should be > 40 ng/ml to decrease ES.**

True, or 200 mg BID at the minimum.

- **Transdermal progesterone typically requires a TID to QID dosing in order to maintain adequate serum levels equivalent to SL or oral dosing.**

  (which can become a compliance issue)

True and levels > 10 ng/ml are necessary for secretory change.

- **Transdermal estrogen cream dose is usually the same as oral doses.**

False- as dose is usually double that of oral and taken BID (ie 3mg/gm at one gram BID).

- **Both the HERS study and the Pugent Sound Study showed that the longer the duration of Tx with HRT, the greater the risk & incidence of MI.**

False- as the RR decreases with time making HRT more protective as time goes on. Avoiding Provera (MPA) further reduces risk.

- **Thirty years of studies and data demonstrating estrogen's protective effect on CVD should be discarded based on the results of the WHI ?**

False!

- **The study in JAMA clearly demonstrated that CEE (conjugated equine estrogen) caused increased clotting whereas esterified estradiol did not.**

True (RR 1.6 vs 0.8)

- **CEE contains 10 or more estrogens not found in the human body that possess increased estrogenicity in comparison to estradiol.**

True

- **Other studies show no increased risk of DVT with oral estradiol.**

True, so why does everyone claim that oral estradiol causes thrombus. MNS. CEE ≠ E2.

True

- **Estrogen has been shown to be beneficial for <u>primary</u> protection of CHD.**

True

- **Estrogen has been shown to be beneficial for <u>secondary</u> protection of CHD.**

True – for estradiol, yes. For CEE, no.

- **In women over age 60 with pre-existing CAD, estrogen might exhibit a pro-coagulant effect (RR = 1.4) early on in the first year of treatment that is later offset by an anti-atherogenic effect (RR = 0.6) after year 5.**

True as in both HERS and WHI with CEE but not in E2 studies.

- **Progestins increase pro-coagulant effects in both arteries (MI) and veins (DVT).**

True- the only organ that MPA protects is the uterus. All other organs are harmed.

- **Progesterone increases coagulant effects.**

False- there is not one negative study on progesterone for DVT or otherwise (ESTHER).

- **In the EPAT trial estradiol decreased carotid artery intimal thickness = *secondary prevention.***

True = both secondary & primary prevention with E2.

- **Estrogen increases fibrinogen thereby increasing clotting.**

False- estrogen is the only thing that decreases fibrinogen.

- **The Nurses Health Study found a 50% reduction in CVD, CVA, and all cause mortality with HRT.**

True = longest and largest study to date.

- **Investigators from the HERS trial recommend that women continue ERT in light of the beneficial effects seen later in the study.**

False, even though the RR = 0.6 after 5 years.

- **Transdermal estrogen is safe in older women with potential CVD risk factors just starting to take estrogen.**

True-if comparing oral CEE but what study showed harm of oral E2?

- **Multiple studies demonstrate a weight gain of 10 lbs. in menopausal women taking hormones vs. women not taking hormones.**

False-as both gain weight and the women on HRT gain less weight than those not taking HRT.

Weight Gain

- The weight gain observed in the first month of HRT treatment is best treated with diet and exercise as it is due to fat gain.

False, as sudden weight gain in the first month is usually due to fluid retention easily treated with a diuretic.

- Testosterone is FDA approved only to treat symptoms of hypogonadism.

True, and it is not FDA approved to treat numbers.

- **Medical literature supports estradiol levels be at least 30 pg/ml for adequate cardiovascular protection and bone protection.**

False-needs to be 60 at the minimum; 80-100 is best.

- **Tx of endometrial hyperplasia is best accomplished by regular monthly bleeding by hormone cycling.**

False- as cycling or bleeding has nothing to do with it whereas constant opposition with progesterone does.

- ***Some women require up to 800 mg daily of progesterone to prevent and reverse endometrial hyperplasia.***

True, and it is not shedding of the lining but rather direct opposition that ↓ ES.

- **Estradiol increases the risk of breast cancer.**

False, not in any RCT.

- **Estriol protects against cancer.**

False, only confabulation.

- **Medroxyprogesterone increases the risk of all cancers.**

True, due to ↑ IR.

- **Transdermal estradiol provides better cancer protection than oral estrogen.**

False, oral ↓ IR better than transdermal. In European studies there was no difference.

- **Symptoms of estrogen excess – breast swelling, edema, irritability – with normal serum estrogen levels, are best treated by ↑ dose of medroxyprogesterone to balance the effect of estrogen.**

False-as MPA only makes symptoms worse (the 5 B's) by stimulating ER sites.

- **Standard doses of medroxyprogesterone usually provide better endometrial protection than micronized progesterone.**

False and women can't tolerate higher doses.

- ***If increasing the dose of progesterone doesn't shrink the ES, then one should switch to MPA and use higher doses to decrease endometrial proliferation.***

False, serum level is zero with MPA and prone to side effects.

- **Hot flashes not responding to oral estrogen (or for those not able to take estrogen) can be treated with:**
  - **Estrogen patch or transdermal cream**
  - **Testosterone**
  - **Progesterone**
  - **Effexor**
  - **Clonidine**
  - **Evista**

Answer: All except Evista

- **Which medicine is best at eliminating menstrual migraines:**
  - **Paxil**
  - **Vivelle patch**
  - **Provera injection**
  - **Progesterone**
  - **Sarafem**

Answer: Progesterone

–Estrogen dominance is well defined in the medical literature.

False- as no where is it defined nor treatment described. Symptoms are due to IR and not ED. Remove estrogen and ED gets worse.

- **Maintaining adequate serum levels of progesterone always guarantees adequate endometrial protection.**

False, progesterone resistance increases ES.

- **Maintaining adequate serum levels guarantees against symptoms.**

False, receptor site resistance increases symptoms and bleeding.

- **Estrogen decreases insulin sensitivity.**

False, oral ↓ VF which ↑ IS and more so than transdermal E2.

- **Which of the following have been shown to ⬇ LDL cholesterol and ⬆ HDL:**

HgH **Testosterone** **Estrogen**

Thyroid **DHEA** **MPA**

Answer: All except MPA as all can decrease VF.

Foam Cell Formation

- E2 decreases foam cell formation. P4 further decreases foam cell formation.

True, which is another reason for all women to take progesterone in addition to estrogen.

- **The hormone with the most potency to grow bone (not prevent loss of bone) is:**

  Estriol HgH Testosterone

  Progesterone DHEA

HGH improves bone growth the most (6-8%).

- **The 2nd most potent hormone to grow bone is?**

  Testosterone: testosterone stimulates osteoblasts and estrogen blocks osteoclasts.

- **The mechanism of bone growth from administering testosterone is via conversion to estradiol. Therefore the recommendation to block estrogen aromatization in men makes sense.**

False as it never makes sense to block estrogen in men.

- **Which of the following hormones do not increase T score on DEXA:**

  DHEA Progesterone Estradiol

  Estrone Estriol

  Estriol

- **Which of the following hormones prevent visceral fat gain at menopause:**

  Estrogen Testosterone DHEA

  Progesterone HgH

  All

- **Hormone administration can increase weight gain due to calorie content of each hormone.**

False

- **Which hormone increases VF, insulin or cortisol?**

Both, and all hormones ↓ VF.

- **Which of the following affect skin and prevent skin atrophy:**

HgH **Estrogen** **Testosterone**

Thyroid **Pregnenolone**

All but pregnenolone

- **Optimal levels of which hormones have been scientifically proven to ↑ energy and well-being in normal healthy adults:**

HgH **Pregnenolone** **Thyroid**

Testosterone **Progesterone**

All but pregnenolone

- **According to the JCEM, the best way to diagnose hypogonadism is by:**

a. symptoms **b. total testosterone level**

c. FSH **d. free testosterone**

Ans: symptoms (The PDR confirms this).

- **The most metabolic active hormone is:**

TSH T4 T3 HgH Testosterone

T3

- **The psychiatric literature recommends the addition of which hormone to augment the effects of antidepressants:**

estrogen progesterone HgH testosterone thyroid

Thyroid at 50 ug/day but all hormones have been demonstrated to improve depression.

- **The Rotterdam study showed that a deficiency of which hormone increases the risk of heart disease to that of tobacco use when levels are in lower 25% of normal:**

HgH estrogen DHEA
testosterone thyroid

Thyroid

- **Which hormone is used to treat cancer of the gland from where it is derived:**

HgH **DHEA** **Thyroid**
Progesterone **Pregnenolone**

Thyroid

- **In patients with severe fatigue, doses of thyroid should be titrated to a TSH of < 1.0 as that's where patients feel the best.**

True

- **HgH ↑ the risk of cancer.**
- *False*
- **IGF-1 ↑ the risk of cancer.**
- False
- **IGFPB-3 ↑ the risk of CA.**
- *False*
- **Testosterone ↑ the risk of CA.**
- *False*
- **DHEA ↑ the risk of cancer.**
- *False*
- **Medroxyprogesterone ↑ the risk of CA.**
- True
- ***Estrogen ↑ the risk of breast CA.***
- *False*

- **According to the medical literature, the addition of which hormone improves statin function by 25%:**

testosterone estrogen thyroid

progesterone HgH

Thyroid

- **Of the above hormones, which ones have literature support in lowering cholesterol?**

All lower cholesterol except progesterone which has no effect but also has no negative effect as does MPA.

- **Which of the following hormones has NOT been shown to decrease the risk of heart disease, CVA, Alzheimer's, osteoporosis, AMD, tooth loss, colon cancer, diabetes, muscle & strength loss, hyperlipidemia. This same hormone has never demonstrated any improvement in morbidity or mortality (as have all the other hormones), yet it is called the safe hormone:**

  Estradiol, estriol, testosterone, progesterone, HgH, DHEA, thyroid?

Estriol and it makes no sense to use it preferentially as so many are taught to do.

SECTION 4

Low testosterone has been associated with:

- **Obesity**
- **Depression**
- **CAD**
- **HTN**
- **Insulin resistance**
- **Low HDL and high LDL**
- **Prostate cancer**
- **All cancers**

Answer: All

- **55 y/o menopausal female on HRT for 1 year. C/O thinning hair since starting HRT. Has never felt better. Taking 2 grain thyroid BID. So what are the potential culprits in causing the hair loss?**
- **Menopause**
- **thyroid excess**
- **thyroid deficiency**
- **DHEA**
- **Testosterone**
- **telogen effluvium**

Answer: ALL

- **How does one diagnosis the cause of hair loss in women?**

Dermatologists typically don't know about hair loss as it relates to hormones. Therefore one should test routine labs, thyroid for both excess and deficiency, testosterone for excess.

- **Treatments?**

Treatment involves increasing or decreasing thyroid

Reduce testosterone (Rocky)

Spironolactone

Minoxidil

Telogen effluvium requires time and typical treatments = art of medicine.

- **Oral micronized testosterone absorbs well in capsule form.**

True, at 30 mg/day PO and 5 mg/day SL. PO lasts longer.

- **SL testosterone provides better levels than the cream.**

True and at a much lower dose but metabolizes rapidly thereby requiring frequent dosing.

- **Any male with a history of PE, VTE, or phlebitis is a contraindication for testosterone therapy.**

False (testosterone is not thrombogenic like oral estrogen) as per the literature. However be careful in congenital thrombophilias (Factor V Leiden) as per recent FDA BBW. If prior DVT, then don't use it to not upset PMD.

- **Testosterone causes erythrocytosis which increases blood viscosity thereby enhancing clotting risk.**

False, no increase in viscosity or thick blood.

- **Lowering DHT has been shown to decrease BPH.**

True (only in men with enlarged prostates, not with normal size prostates).

- **Lowering estrogen has been shown to lower BPH.**

False, and in studies giving estrogen to men, E2 decreased symptoms of BHP, mechanism unknown.

- **This is why all urologists use aromatase inhibitors to shrink prostates.**

False- There is no study to demonstrate that lowering estrogen is good; there is however data to support that lowering estrogen is harmful, the opposite of what the ROW believes.

55 y/o woman on natural HRT, had a recent DVT and PE. All her doctors told her to stop all HRT. Now she is miserable. Plan:

- **Give articles on transdermal vs oral estrogen and risk of clotting**

True

- **Patient argues back that doctors told her not to take estrogen as she would die.**

True

- **Support her doctors even though they do not understand.**

True

- **If she throws a clot again, everyone will blame you.**

True, 33% recurrence in non-provoked DVT.

- **Discuss risk vs. benefits.**

True

- **Just tell her to tough it out.**

True

- **Use vaginal estrogen which may absorb some and give some relief.**

True

- **Use SSRI's for HF.**

True

- **Progesterone and testosterone decrease HF and NS.**

True, if PMD allows them.

50 y/o female with CFS. Told by PMD to stop thyroid as it will kill her and give her osteoporosis.

Plan:

- **Explain to patient that you disagree, but we must do what her doctor says.**

True

- **Give her all the articles on thyroid not causing osteoporosis.**

True

- **Discuss risk vs. benefit**

True

- **Remember our first discussion on HRT and re-read booklet.**

True

- **If pt. continues to take thyroid, then stop thyroid before test for 3 days.**

True, but then you can't use this test to adjust thyroid.

45 y/o woman presents with stress, surgery, family death. C/O losing hair in clumps.

- **Dx is telogen effluvium = diffuse hair loss that is sudden.**

True

- **Treatment: Time and stress relief.**

True

- **Thyroid, SSRI, BCP in shampoo, minoxidil, topical E2 & P4 = art of medicine, plus reassurance.**

True

45 y/o male on HRT who C/O losing hair. Plan?

- **Switch testosterone to SQ or HCG.**

True

- **Minoxidil**

True

- **Propecia, Proscar, Avodart**

True

- **Eucapril (fluridil)**

True

- **Nizoral shampoo**

True

- **Climara and Femstat patches are changed once per week.**
- **True as they last 7 days.**

- **Vivelle-Dot is changed twice per week.**

True

- **Vivelle-Dot sticks better though.**

True

- **Women who do not tolerate the high release estrogen ring (Femring) will tolerate the slow release estrogen ring (Estring).**

True, Femring can be irritating due to potency but Estring is not.

- **55 y/o female in menopause cannot tolerate the progesterone in any form. Plan:**

Vaginal progesterone vs. norethindrone vs. MPA, vs. Mirena with yearly ultrasound of endometrium.

Try P4 suppository at 200mg PV BID and monitor levels = DOC.

- **The literature supports treating uterine cancer survivors with estrogen after being cancer free for:**

  A) 1 year B) 3 years C) 5 years

A) 1 year

- **The literature supports treating breast cancer survivors with estrogen who have been cancer free on tamoxifen for:**

  A) 1 year B) 3 years C) 5 years

C) 5 years

- **The literature used to recommend treating prostate cancer survivors after 5 years of being disease free.**

True

- **The literature now recommends treating hypogonadism in prostate cancer survivors as soon as the cancer is controlled with a PSA of less than 1.0 indicating a cure or remission.**

True

- **Newest, easiest, so far safest method of treating prostate cancer confined to within the capsule is:**

HIFU currently in phase 3 trials.

- Five years ago HIFU (high intensity focused ultrasound) was the best. Now laser ablation by MRI guidance is absolutely the best state of the art treatment vs. surgery or radiation.

55 y/o female with vaginal bleed for 3 months. Biopsy showed endometrial hyperplasia without atypia or metaplasia = benign. Tx is ?

Ans: Progesterone at higher dose (200mg BID) and titrate to effect (TID to QID) to decrease ES.

- **After 3 months the endometrial stripe went from 15mm to 16mm. Tx is ?**

Increase progesterone to 200mg TID. If ES increases, then increase to 200mg QID. Avoid TP4 cream = worthless to ↓ ES.

- **Patient should stop estrogen during this time?**

False as there is no need to. Just increase the P4 or you can stop estrogen if not too symptomatic off of E2.

- **Patient should cycle to shed the lining?**

False as sloughing the lining does nothing to the ES underneath the tissue that sheds.

- **According to the literature, transdermal (non-oral) estrogen has not had the problems with plaque rupture as does oral CEE (which is due to MMP).**

True

•However there is no evidence of plaque rupture in the WEST, EPAT, CORA, DANISH trials with oral E2 as there is with oral CEE.

True

•Oral CEE contains about 20% estradiol.

True, and 50% E1, equilin, and 10 more estrogens.

- **All estrogen is contraindicated if the PMD says so**

True, unless the patient changes PMD.

- **Why is it that many doctors that prescribe natural hormones are actually increasing the risk of CAD, CVA, fractures, and breast CA?**

This is due to the fact that the amount of hormone prescribed, or the blood levels of hormones attained, remain sub-therapeutic and too low to provide any protection. Most patients presenting to me for the first time while taking HRT prescribed by other BHRT physicians, will usually have baseline (zero) levels of hormones while on just creams or estriol. Inappropriately low concentrations of compounded hormones provide sub-therapeutic, non-efficacious levels of hormones that are not protective. Cheap compounded products provide poor levels. Premarin 0.625 has always produced therapeutic levels of estradiol! Use E2 to avoid DVT.

- **Adequate Vitamin D levels of 30 are said to be adequate.**

True, but barely adequate. Such low levels are not very therapeutic. Should be at least 60 as per most recent literature. Toxic levels are > 300.

- **Most women and men over 65 have baseline levels less than 25.**

True

- **The standard dose now recommended by IOM to maintain levels above 30 is 2,000 units daily.**

True, but that is not optimal.

- **The recommended dose of Vit D2 to raise levels into adequate and protective levels of at least 50 is 50,000 units of Vit D2 (ergocalciferol) Q week for 12 weeks.**

True, but D2 has to convert into D3 in the kidney. So just give D3, no reason to use D2.

- **Although different now than in the past, toxic levels of vitamin D3 are of concern when daily doses exceed 20,000 units daily.**

True

QUESTIONS: SECTION 5

- **Total testosterone is usually elevated in PCOS.**

False as it is usually the FT and not TT unless AH.

- **Free testosterone is usually elevated in PCOS.**

True, more so than TT due to low SHBG levels.

- **Normal testosterone levels are frequently found in PCOS but the sensitivity to free testosterone is increased which then causes the skin symptoms.**

True

PCOS Symptoms

- **The total testosterone can become elevated due to increased production of aldosterone which stimulates an increase LH production which stimulates the ovary to make more testosterone.**

True

- **Adrenal hyperplasia is common in PCOS and increases DHEA, testosterone and aldosterone.**

True

PCOS treatment

- **BCP decrease testosterone effects by what 2 mechanisms?**

A) Decreased production in the ovary. B) Increased production of SHBG to bind on to testosterone and decrease the free testosterone levels. Does not affect adrenal production though.

- **Transdermal patch or vaginal ring of BC also decreases symptoms of excess testosterone.**
- True, but not as well as oral BC that ↑ SHBG.

•Testosterone in high doses that produce high, supraphysiologic levels can have an adverse effect on lipids.

True

• The PDR now lists blood clots as a possible complication of testosterone therapy.

True, although it is not reported in any RCT, only an observational study that retrospectively “looked” for harm.

•Progesterone can increase inflammatory cytokines.

True, but only in men which is why it is contraindicated in men. This can lead to an increase in CAD and prostate cancer.

- **What is the first test (tricky) to do in a man with a newly elevated PSA that costs $4 to perform.**

Therapeutic trial with Bactrim to Tx prostatitis.

- **There are over a dozen RCT's that show adding T3 to T4 has no benefit.**

True, and all used low dose T3 which is not potent enough to have any benefit.

- **Which of the following drugs that are not used for CVD can increase CO and ejection fraction: HGH, T3, testosterone.**

Ans: All increase cardiac output. Too bad the cardio world is oblivious to them.

- **Propecia, Proscar, Avodart are banned in the Olympics.**

True

- **5-alpha reductase inhibitors raise testosterone levels and are therefore banned.**

True

- **Aromatase inhibitors are banned in the Olympics.**

True

- **Aromatase inhibitors raise testosterone levels.**

True

- **Heavy dysfunctional uterine bleeding causing acute anemia can be immediately controlled by IV Premarin &/O Tranexamic acid (Lysteda).**

True

- **Postmenopausal vaginal bleeding with intercourse is treated how?**

Estrogen stops dysfunction uterine bleed, or Ovral BID. Topical vaginal estrogen treats atrophic vaginitis, and increasing progesterone prevents uterine bleeding.

ALL WOMEN ARE LIKE SNOWFLAKES

A woman's idiosyncratic response to hormones are due to a multitude of reasons which include:

- **Different absorption of hormones.**
- **Different serum levels.**
- **Different metabolism.**
- **Increase or decrease in sensitivity of receptor sites.**
- **Different production of metabolites**
- **Poor compliance**

True

- **It has been reported that over 90% of women on HRT will experience breakthrough bleeding.**

True (educate!)

- **Most cases of persistent breakthrough bleeding can be remedied by increasing progesterone dose, assuming vaginal US is normal.**

True (educate!)

- **Sometimes excess estrogen levels cause this as in perimenopause.**

True, and treat with mo' progesterone.

Patients not on HRT

- 50 y/o with DM, high lipids, HTN.
  - Oral or transdermal estrogen?
- - Oral
- 55 y/o with above.
  Oral or transdermal estrogen?
- - Oral
- 60 y/o with above.
  Oral or transdermal?
- - Oral
- 70 y/o with above
  Oral or transdermal?

Oral E2 but not Premarin

If afraid, use transdermal but no study demonstrated oral E2 was thrombotic, only CEE.

- **55 y/o on HRT X 5 years with the above illnesses, just had an MI?**

MI is only seen during the first year of HRT and the RR at 5 years is 0.6, therefore HRT did not cause the MI.

- **70 y/o perfectly healthy without any risk factors at all. Wants to start HRT. Oral or transdermal?**

Oral

- **70 y/o perfectly healthy without any risk factors except HTN. Oral or transdermal?**

Transdermal if Hx +DVT, otherwise oral if healthy.

HF WITH NS

Which is better to control early menopausal symptoms:

- **Oral**
- **Cream**
- **Patch**

Patch due to steady state, 24 hour levels or oral BID.

- **Which is best to use in general, an estrogen patch or a cream?**

Patch due to better compliance and better maintenance of levels, but allergy to patch is common and sometimes poor absorbtion.

- **Which is best to use in general, a cream or oral estrogen?**

Oral due to better compliance and cardiovascular benefits, but only oral E2.

- **If the patient is compliant, transdermal estrogen cream once daily is just as beneficial as oral estrogen and provides the same levels?**

False, as transdermal usually requires BID dose (which = less compliance). Use cream if oral contraindicated and allergic to patch.

A 70 y/o woman on oral estrogen for 20 years develops CVA. So now what?

1) **Patients will still have CVD in spite of HRT. HRT did not cause this stroke as RR <.6 after 5 years.**
2) **WHI and HERS trials both demonstrated less risk on HRT than off HRT after first year and thereafter.**
3) **There was increased harm only during the first year, and only protection after that (RR was less that 0.6 thereafter) meaning that patients will still derive some protective benefits from HRT.**
4) **However peers will not understand this, therefore estrogen should be stopped if PMD demands.**
5) **Otherwise continue the same oral (E2) regimen.**

- **Stopping would further increase growth of plaque, not stop it.**
- **However, oral estrogen may be thrombotic (only in the first year) in presence of heavy plaque even though studies show continued secondary protection against further plaque development with E2. (EPAT)**
- **Stop estrogen if peer pressure dictates it - you can't argue.**
- **Explain to family the risk vs. benefit.**
- **For me or mine, I would continue oral as the plaque rupture was due to other inflammatory process, not E2.**

PERIMENOPAUSE

- **Is defined as signs and symptoms of excess and deficiency of hormones that can fluctuate from day to day.**

True

- **This erratic ovarian function can last for 5 years with irregular bleeding and spotting and signs of estrogen excess.**

True

- **Any symptom is considered normal.**

True

Peer Recommendations

- **ACOG & NAMS recommend menopausal HRT be given at the lowest dose for the shortest period of time and then stopped.**

True, but I agree if HRT is CEE/MPA.

- **The end-point being studied in the ELITE study is IMT reversal.**

True, and only with E2 at 2 mg PO and P4 at 200 mg PO.

Men and Estrogen

- **Testosterone administration always raises estrogen levels in men.**

True (Always)

- **Therefore, testosterone administration in men also raises SHBG levels.**

True: SHBG is a protein produced in the liver that increases when insulin decreases. Since T lowers insulin, it will eventually raise SHBG but not by raising estrogen.

A 70 y/o man with CVD is treated with Casodex and Lupron for prostate CA. Recent bone scan demonstrates significant osteoporosis.

- **What therapy is best for osteoporosis?**

Estrogen, not biphosphonate.

- **Which type of this therapy is best?**

Transdermal as oral may increase thrombosis as did DES in older men with CAD if high dose oral E2 is used. Otherwise oral OK.

- **Which therapy will further decrease growth of prostate cancer?**

Estrogen decreases PSA and cancer growth.

- **Which therapy is best for HF?**

Transdermal estrogen patch for 24 hour relief.

- **Some studies demonstrate that transdermal E2 has no effect on lipids and lipoproteins which had no effect on plaque reversal.**

True

- **Oral E2 raises SHBG, fatty acid esters, HDL, and apo-lipoprotein A as well as lowers LDL, apo-lipoprotein B, and fibrinogen, all of which are much more affected by oral than transdermal E2.**

True

- **Testosterone lowers triglyceride levels in women on oral estrogen.**

True

- **IR can lead to dyslipidemia causing CVD. Hypertriglyceridemia is the most predictive of CVD best treated with what drug.**

Niacin (nicotinic acid), then any hormone that ↓ VF.

- **Which illness predisposes women to hirsutism.**

IR and DM

- The best treatment to prevent the hirsutism is:

Metformin and HRT to lower IR, which is the cause.

- **A study showed that mice given both estrogen and testosterone caused prostate cancer to rapidly grow thereby suggesting that estrogen causes prostate cancer to grow.**

True

- **Estrogen has been an excellent therapy to treat prostate cancer for over 50 years.**

True

- **Testosterone has been shown to be harmful to women as demonstrated by its detrimental effects in PCOS patients in causing increase in DM and CAD.**

False, testosterone is an innocent bystander.

- **It is the excess testosterone that results in these problems.**

False, it is the IR that causes the problem, not the testosterone. Remove the testosterone and the IR still persists with all the pathology.

- **Injectable testosterone in low doses has been shown to benefit some women.**

True

- **This is probably due to receptor site down regulation which requires more stimulation.**

True, but God only knows.

- **High dose transdermal T may accomplish the same if there are no side effects.**

True

- **55 y/o woman now in menopause. She c/o severe HF, NS, mood swings, miserable. Desires HRT but oral not controlling HF. Both parents with severe CAD and she wants to protect herself. Tx?**

Estradiol patch is best to control HF symptoms due to 24 hour effect, not oral.

- **After 1 year all symptoms have resolved. Now what?**

Yes change after one year to oral, perhaps BID to control symptoms, and better protect against CAD with oral as opposed to transdermal.

Alzheimer's and Estrogen

- **The WHI observed a "105%" increase in AD**.

True as that is what the authors claimed but that was incorrect and false also. The study incorrectly claimed an increase in AD whereas it truly was not AD but rather vascular dementia that occurred at the same incidence as did CAD and CVA.

- **For women starting HRT at menopause, there was an 83% reduction in AD risk.**

True as per the Cache County Study. E2 can protect against AD and VD.

Gambrel and NAMS 2012

- **“The lowest effective dose for the shortest period of time” is invalid according to Gambrel as the benefits of long term ERT far exceed any risks.**

True

- **The data from all studies do not support strict limitations on duration of ERT.**
- True, as recent recommendations from NAMS support the safety for ERT but not for HRT.
- **However HRT can be problematic.**

True if Prempro.

- **However HRT with progesterone eliminates that concern.**

True, absolutely.

Switch or Stop Estrogen

- **A 65 y/o woman on oral HRT for 15 years since menopause suffers an MI. Knowing the RR of oral estrogen, this MI was probably caused by the estrogen and the patient should be switched to transdermal E2.**

Very False as the harm with administration oral estrogen occurs within the very first year only. Every year subsequent to the first year has demonstrated a RR < 0.6 which indicates that estrogen is protective and not causative in an MI. Stopping the estrogen at this point would further increase risk by reducing further protection and cause increase in plaque growth.

- **The patient should be taken off of E2 and P4.**

False as there is no risk of continuing the HRT as E2 and P4.

- **The patient should be taken off of Prempro.**

True, absolutely as MPA can continue to negate the positive benefits of estrogen and cause plaque to rupture in arteries and veins.

Understanding Risk of Clots

- **The RR of oral HRT causing MI during the first year of administration was RR = 1.6.**

True

- **The RR at 5 years was 0.6.**

True

- **The RR for DVT's is identical to that of CVD in that there is a higher risk during the first year, and then it is lower each subsequent year thereafter.**

True, however all of the above is true for Prempro but not for estradiol with progesterone. No study showed increase in MI during the first year with E2 or DVT.

- **QUESTIONS: SECTION 6**

- **Pregnancy rates in PCOS patients increase when Femara is used to decrease excess estrogen.**

True, and the goal is to decrease excess free estrogen that is seen in PCOS due to low SHBG.

- **The MCC of hirsutism in postmenopausal women on HRT is the same as that in pre-menopausal women.**

True (PCOS = insulin resistance that only gets worse with time).

- **Both metformin and Actos should be continued throughout pregnancy in patients with PCOS.**

False (Metformin is OK, Actos is a teratogen and should not be used any more. Use Januvia or GLP-1 agonists but not in pregnancy).

- **PCOS patients with irregular periods, or in non-PCOS patients without periods, require no treatment if entirely asymptomatic.**

False as they need progesterone to decrease the risk of cancer.

- **Amenorrhea requires BCP or estrogen due to no production of estrogen, as well as progesterone opposition.**

True

- **Anovulation requires progesterone to oppose estrogen.**

True. You must differentiate between the two as both produce no periods but the treatment for each is entirely different as one needs estrogen replacement (amenorrhea) and one produces plenty of estrogen (anovulation).

- **A 52 y/o newly menopausal woman took BCP for the last 20 years without problems. Now she has HTN, DM, and smokes, and Syndrome X. Due to the WHI results, this patient should only take transdermal estrogen and never oral estradiol.**

False (She is within the 10 year window and needs the oral estrogen for maximum protection against plaque development as she is at tremendous risk for MI and less risk for DVT).

- **A 65 y/o woman with CAD on Premarin for 15 years just stopped HRT 2 years ago after MI. She wants to restart HRT. Do you start oral or transdermal ERT?**
- Continue the oral estrogen but switch to E2 and add P4. The medical literature actually demonstrates that maintenance on oral estrogen after an MI results in less morbidity & mortality long term than stopping estrogen. However you will be hung by your peers for starting estrogen, so make sure it is OK with other doctors first.

- **Transdermal estrogen causes less breast CA than oral estrogen.**

False, studies show the risks are equal and both < 1.0.

- **In early menopause, hot flashes have nothing to do with estradiol levels.**

True as HF are due to loss of inhibin initially and then later on the HF are due to loss of estrogen.

- **HRT is only as effective as long as the patient takes it.**

True

- **Creams tend to have poor compliance.**

True

- **Estrogen patches have better compliance.**

True, but are irritating.

- **Transdermal cream is beneficial for vaginal atrophy but compliance is poor.**

True, so use either PO or SL for improved compliance.

- **Norethindrone (NETA)(Aygestin) is a synthetic progestin that enhances the anti-artherosclerotic effects of estrogen as opposed to MPA.**

True

- **Oral estrogen increases CRP, triglycerides, protein S, apo-e, all of which may increase inflammation and cause arterial and venous clotting.**

True, however CEE much more likely to induce these changes than E2.

- **Perimenopause = high estrogen and low progesterone = no man's land.**

True

- **Uncontrolled symptoms of perimenopause can be treated with BCP taken daily without cycling.**

True

- **An alternative to BCP would be daily high dose progesterone.**

True

- **Which hormone is entirely absent in menopause?**

Progesterone

- **Saliva levels are accurate in diagnosing a deficiency.**

True

- **Saliva levels are accurate in monitoring transdermal therapy.**

False, as transdermal progesterone is impossible to monitor due to incredibly high levels in saliva and low levels in serum. No study shows correlation for treatment levels with transdermal HRT.

- **MCC of women stopping HRT is vaginal bleed.**

True

- **The second MCC of stopping HRT is fear of breast CA.**

True

- **The third MCC of stopping HRT is that women don’t think that they need it anymore due to WHI trial.**

True, therefore educate

Benign, recurrent vaginal bleed is best managed &/O prevented by progesterone administration BID to TID.

True, and the DUB is due to decreased progesterone sensitivity or resistance.

Transdermal progesterone is best to achieve high levels (trick question).

True, (SL is also transdermal (transmucosal) and is the best. However the transdermal creams are poorly absorbed and provide very low serum levels making the transdermal creams the worst).

- **Postmenopausal HRT decreases production of testosterone.**

False, oral E2 increases binding.

- **Postmenopausal HRT decreases bioavailability of testosterone, thyroid, cortisol.**

True, but only with oral estrogen.

- **Transdermal estrogen can decrease libido.**

False, as TE has no effect on any protein produced in the liver from first pass effect.

ARMOUR vs CYTOMEL

- **A patient switches from 25ug of cytomel to 2 grains of Armour. She states that feels worse because she went from 25ug of T3 to only 18ug that is in 2 grains of Armour. Is she correct?**

True but False. Correct in calculation, but not in bioavailability. 25ug of T3=1 grain of Armour as far as bioactivity is concerned. Therefore 2 grains of Armour is bio-equivalent to 50ug of T3. She was only getting 25 ug of T3, so she is getting a better dose equivalent than what she was taking prior.

- **The starting dose of metformin ER is 500mg BID with meals.**

True, then titrate upwards slowly.

- **Very young women with PCOS may not tolerate metformin.**

True, so stay low on dose to increase tolerability.

- **Treat these woman with BCP, diet, exercise.**

True

- **What other hormone makes them feel and function better and increases metabolism?**

Thyroid

- **Lean women may not show much IR but they still respond to metformin.**

True

- **Newly menopausal women that develop breast pain on HRT are best treated how?**

Stop estrogen until symptoms resolve which are due to fluid retention. Then take QOD for 1 month to adapt to dose. Then increase back to 1 capsule per day as tolerated. This applies only if patient is to stay on oral estrogen. Slowly titrating up on the estrogen works the best.

Start diuretic immediately to diurese the fluid retention.

Switch to transdermal estrogen (that causes less swelling and lowers estriol) if oral is still not tolerated.

Measure serum levels of estradiol to assure level of estradiol is not too high.

- **The best tolerated treatment for reducing symptoms in adolescent women with PCOS is:**
  - **Metformin XR**
  - **Actos**
  - **BCP**
  - **Spironolactone**

  Answer: BCP

- **Best BCP is?**

Yas or Yasmin are least androgenic but not well tolerated; law suits.

- **Natural HRT made by compounding pharmacies is FDA approved.**

False

- **Natural HRT is subject to the same regulations as FDA approved drugs in that pharmacists must dispense the same warning for the natural hormones as with the synthetics.**

False, there are no BBW.

- **The two natural hormones that are important in treating PCOS that the medical literature never mentions are:**

Thyroid (to improve metabolism), progesterone (to protect breasts and uterus).

- **A 50 y/o women with a HX of PCOS, and now in menopause, should not be treated with testosterone.**

False, but she may be very sensitive to testosterone.

- **Same patient refuses testosterone or spironolactone. Measurement of what 2 hormones might change her mind?**

One can measure testosterone (which will be low and needed) and aldosterone (which increases HTN, CAD, inflammation, and should be lowered with spironolactone). Remember breast CA protection in women with PCOS!

- **Which estrogen would you use?**

You should use oral estrogen to increase SHBG and decrease sensitivity of testosterone and CVD protection for which she is at risk.

- **Transdermal estrogen can be safer than oral estrogen but oral estrogen can be more protective that transdermal.**

True

- **The risks of oral estrogen are very small in comparison to the tremendous benefit.**

True with less heart disease that kills 90% of women.

- **Women with PCOS or IR have less conversion to T3 due to decrease in 5'deiodinase enzyme.**

True which is why all IR patients need optimization of T3.

- **T3 administration augments the effects of antidepressants.**

True, 25 to 50 ug/day in addition to optimizing with desiccated thyroid.

- **T3 administration suppresses T4 production.**

True, therefore don't just give pure T3.

- **T4 primarily crosses the BBB whereas T3 does not.**

True

- **The brain has plenty of 5'deiodinase enzyme whereas the body does not.**

True, and that's why we use both T4 and T3.

PCOS

- **The miscarriage rate in patients with PCOS is 50%.**

True

- **Metformin, when taken throughout pregnancy, lowers the miscarriage rate from 50% to 10%.**

True, and it also prevents gestational diabetes.

- Thyroid and progesterone round out the optimization for prevention of miscarriage.

True

- **A 40 y/o patient with PCOS presents without symptoms of acne or hirsutism. Patient does have insulin resistance and Syndrome X and HTN that are all controlled on meds. Does she need spironolactone?**

Yes, as spironolactone decreases aldosterone. Aldosterone increases inflammation, HTN, and CAD and therefore should be lowered with spironolactone in spite of no signs or skin symptoms of excess testosterone.

DOCTOR, I'M BLEEDING

- **53 y/o doctor c/o bleeding whenever she takes HRT. Progesterone increase did not help and level still 11, estradiol level of 70. Ultrasound shows ES of 4mm and 2cm fibroid. Now what?**

Change progesterone to RDT 200mg SL in AM and PO capsule @ HS.

Dose @ QID to attain levels of > 40 to attain maximum down regulation.

Assure estradiol is not > 80.

If still bleeding, then the cause is fibroid; needs embolization or tranexamic acid (Lysteda).

ORAL ESTROGEN

- **Many studies failed to demonstrate much cardiovascular benefit with transdermal estrogen.**

True

- **Most studies demonstrated CVD protection with oral estrogen.**

True, CORA, EPAT, WEST, DANISH, ELITE.

- **This was felt to be due to the strong, beneficial effect on serum lipids, lipoproteins, SHBG, and estradiol fatty acid esters.**
- True

QUESTIONS: SECTION 7

- **High estrogen level is the most common cause of hypogonadism symptoms in older men.**

False, just the opposite. Blocking E2 ↑ symptoms.

- **Men on testosterone that have polycythemia and get sent to get phlebotomized usually cannot donate blood and have to pay for phlebotomy.**

True, and this is because 1) PCV is a blood dyscrasia or blood cancer and 2) men on finasteride cannot donate blood.

- **Testosterone can assist in Tx of ED by applying it to the penis.**
- True-*apply to frenulum or foreskin.*

- **The best way to achieve consistent daily blood levels using injectable testosterone and avoid the ups and downs of IM testosterone is to administer testosterone by daily SQ route.**

True – give 0.15 ml SQ daily.

- **Fluridil (Eucapril) is a better topical solution than minoxidil for hair loss.**

True, available on internet and in phase 3 trials.

- **Cortisol dosing at 10 mg BID usually causes adrenal suppression and should be monitored using ACTH test.**

False, not suppressive at 20 mg/day. For flat diurnal curves give just AM dose of 10 mg.

- **Epidemiologic suggests that the ratio of 2-OH-E1/16-αOH-E1 predict cancer although the 4-OH pathway is probably more cancer causing.**

True, however no outcome studies have demonstrated this, it's only theoretical and conjectural and observational by looking at urine levels.

- **The most recent study from the NEJM 2013 demonstrated that aromatase inhibitors used in men on testosterone cause:**

A) Decrease in libido

B) Decrease in sexual performance

C) Increase in visceral fat

D) Increase in subQ fat

E) Adverse change in lipids

Answer: All

- **Natural thyroid is best administered as a BID dose for fatigue.**

True-as the half-life of T3 is 8 hours, so treat fatigue and weight issues with BID dose.

- **It is safe for women to not have periods by taking BCP continuously instead of cycling.**

True, which has been the Tx for PMS & perimenopause.

- **It is safe for women with PCOS to not have periods either.**

False (Increased breast CA and endometrial CA)

Anovulation → no release of egg → no corpus luteum → no progesterone → estrogen stimulation without opposition → ↑ risk of uterine and breast CA.

OK not to have periods but must treat with progesterone (and enough of it!)

- **Recent medical studies have demonstrated a benefit in having postmenopausal women cycle their hormones thereby causing monthly menstruation similar to BCP.**

False

- **Cycling further reduces risk of endometrial cancer.**

False**:** The protection is from direct effect on the tissue and not from cycling. Cycling actually = ¼ less protection than continuous.

True

- **The medical literature has never demonstrated any harm in erythrocytosis after 50 years of study.**

True, no arterial or venous thrombosis. However recent PDR warnings state otherwise for thrombophilias by only one individual. Multiple RCT's and meta-analysis show no increase risk.

- **Injectable testosterone reduces the incidence of erythrocytosis.**

False, increases it more than any other treatment, so use it subq.

- **All testosterone preparations (except HCG and clomiphene) can adversely affect fertility.**

True, and don't forget to advise the patient of this. Document loss of fertility, loss of testicle size, irreversible loss of testicular function, and increase risk of DVT and CAD (but only based on recent flawed studies).

- **In men, what level of estradiol requires Tx with an aromatase inhibitor?**

No level needs treatment-what does the literature suggest? The only Tx should be for symptomatic breast tenderness (not gynecomastia) and only for short term 1-2 months.

- **What dose of anastrozole is adequate for Tx of breast tenderness (mastalgia)?**

Dose of Arimidex is 0.5 mg @ 2 X per week X 2 months and stop. Remember nocebo phenomenom vs. NEJM RCT.

- **A free PSA of < 10% is indicative of what % risk of CA ?**

Ans: *50%*

- **The best test to localize a prostate cancer before biopsy is:**

MRI-S

- **Which RCT recently demonstrated that estrogen caused cancer?**

No RCT has demonstrated that estrogen causes cancer.

- **Which RCT recently demonstrated that estrogen/progestin caused cancer?**

WHI: There were many successful suits (3,000) against Wyeth (CEE/MPA) but no suits ever against estrogen (CEE) alone.

What are the differences between MP vs. MPA

PROGESTERONE

- **Down-regulates breast tissue**
- **Decreases breast density**
- **↑ HDL**
- **↓ LDL**
- **↑ Mood**
- **↓ Foam cell formation**
- **Diuretic**
- **Hormone of pregnancy**

Everything progesterone does is beneficial.

MPA

- **Up-regulates breast tissue**
- **Increases breast density**
- **↓ HDL**
- **↑ LDL**
- **↓ Mood**
- **↑ Foam cell formation**
- **Teratogen**
- **↑ Edema**
- **↑ DVT**

Except for protecting the uterus, everything that MPA does is harmful.

- **Normal levels of hormones always imply normal physiologic effects.**

False: Hormone-protein binding, receptor site sensitivity, loss of signal transduction are all responsible for clinical and symptomatic response.

- **The association of HDL with cardiovascular disease was consistent regardless of cholesterol total or LDL level.**

True

- **For every 1% increase in HDL, there was a 3% reduction in death or MI, a therapeutic benefit that eclipses the benefit associated with LDL reduction.**

True

- ***Am J Cardiol 2000:868;19-22***

- **Most cardiologists are aware of this which is why they so routinely recommend hormones, niacin, low carb diets.**

False (cardiologists are unaware),

- **ASA eliminates niacin flush.**

True

- **5 yrs of statin Tx ↓ MI recurrence in 100 of 1,000 with previous MI; in 900 of 1,000 patients it does not.**

True, buy you have to treat everyone.

- **In the vast majority of studies, angioplasty reduces MI and saves lives.**

False

- **Medicare reimburses for a screening DEXA in men.**

False (must have Dx first)

- **If the level of estrogen is measured during a hot flash, the level is typically low as it is the lack of estrogen that causes the hot flashes and temperature dysregulation.**

False as high estrogen compensates for loss of inhibin.

- **Administration of growth hormone increases cancer risk due to increased levels of IGF-1 which is mitogenic.**

False, as IGFBP-3 goes up simultaneously also which is apoptotic and opposes any effect of mitosis from IGF-1.

IGFPB-3 increases simultaneously which protects against cancer.

- **Progesterone increases endothelial dysfunction in women.**

False, as it lowers it whereas MPA ↑ it)

- ***Progesterone induces endothelial dysfunction in men.***

True, so then why do some doctors give progesterone to men?

- **44 y/o female, s/p complete hysterectomy, developed blood clot post surgery. Now on Premarin and wants refills?**

P) work up for clotting disorder or refer to hematologist. Use transdermal estrogen only even though thrombophilia w/u is negative. Again there is a 33 % chance of recurrent DVT that is non-provoked and w/u for thrombophilia was (-). PMD's will resist any oral estrogen so it is safe to go with any trandermal E2 and hopefully they will understand this aspect of HRT, so show them ESTHER trial from part II.

- **52 y/o female c/o severe night sweats while on oral estrogen. Tx?**

P) ↑ estrogen to 2, 3, 4 caps QHS; then switch to patch if not successful in reducing NS as the patch decreases catecholestrogens that oral estrogen increases and can make HF worse.

- **52 y/o female with persistant subtherapeutic levels of estradiol on oral biest. Not absorbing yam based E2. Tx is:**

To treat oral estrogen failure, use patch, cream, pellet, or simply switch to soy based estradiol. There are now problems with commercial products that are generic.

- **T3 (triiodothyronine) reduces cardiac output.**

False, ↑ CO.

- **T3 reduces systemic vascular resistance.**

True and ↑ CO too, thereby unloading the heart.

- **The impact of thyroid hormone on lipid levels is primarily mediated through T4 bound thyroid protein binding.**

False, as T3 MRNA binding effects change and not T4.

- **Normalizing TSH levels, but not T3 levels, always leads to improvement in T4. The body self regulates the amount of T4 to T3 conversion based on health and metabolism needs. If the body doesn't need it, then the body produces less T3. (As so stated in the bible of endocrinology).**

True according to AACE. However this is definitely not what we see clinically nor in the literature. It's someone's opinion but not helpful clinically.

- **The conversion of T4 to T3 is via the 5'deiodonase enzyme that is most commonly found in the liver and kidney.**

True

- **According to Ann Intern Med (132:780,2000) statins are cost effective for secondary prevention of CAD but not for primary prevention.**

True

- **Niacin lowers fibrinogen, lipoprotein A, apo-liproprotein B.**

True

- **Niacin raises HDL, apo-lipoprotein A.**

True

- **Niacin in the form of niacinamide is the most efficacious form of niacin due to the non-flush characteristics.**

False

- **Decreasing visceral fat raises HDL levels.**

True

- **Estrogen, testosterone, DHEA, thyroid, and growth hormone reduce visceral fat.**

True

- **High carbohydrate diet lowers HDL.**

True

- **Progestins nullify estrogen's beneficial effects on visceral fat.**

True

- **Progesterone increases pro-coagulant effects.**

False**, has no adverse effects on clotting as does MPA.**

- **Elevated fibrinogen increases clotting which is a contraindication to testosterone use.**

False (E & T lower fibrinogen)

- **60 y/o men typically have more estrogen than 60 y/o women.**

True

- **Estrogen has been shown to cause prostate cancer in men.**

False as studies fail to show that elevated baseline levels, raising levels via aromatization, or by administration of E2 cause cancer. Only the reverse is true.

- **Erythrocytosis involves ↑RBC, ↑WBC, ↑ platelets, splenomegaly, MDS.**

False, that's for PCV.

- **A 65 y/o male developed thrombosis post hip surgery. This patient should not receive testosterone.**

False, although the PDR lists DVT as a precaution. Test for thrombophilia and if (-) then treat.

- **After 3 months on HRT, 60 y/o female loses hair 3 months after CABG. TX?**

Observation as telogen effluvium resolves with time. However one may add minoxidil, nizoral, Eucapril.

- **55 y/o female with vaginal bleeding on HRT. TX?**

1. **Double progesterone, stop estrogen.**
2. **Vaginal ultrasound.**
3. **Biopsy if stripe is greater than 6mm.**
4. **Progesterone 100 mg/ml in oil – 1 ml IM**

For the vaginal bleeding, all listed are appropriate for vaginal bleeding.

- **Biest causes breast pain & swelling = fluid retention. TX?**

  a. test estradiol level

  b. eliminate estriol – causes edema

  c. switch to transdermal

  d. diuretics

  e. adequate progesterone

All assist in treating breast pain.

- **Overall, which estrogen is preferable for most women – oral or transdermal?**

For compliance and CV protection, it is oral.

- **A 53 y/o woman with elevated triglycerides of 1000 and HDL of 30 should not take oral estrogen.**

(tricky question)

False, as oral will provide better protection against plaque development.

- **A 63 y/o women with elevated triglycerides and low HDL should not take oral estrogen if starting for the first time.**

True if for Premarin. However E2 reverses plaque.

- **A 63 y/o women with ↑ triglycerides and low HDL has been on oral estrogen for years. Should she continue oral or switch to transdermal?**

She should continue oral as it is more protective against development of fibrous cap and necrotic core. Especially with her risk factors.

- **A 65 y/o female with HTN, DM, +FH, PPP and wants to start estrogen for the first time. Is oral OK?**

No, oral is not OK if CEE. E2 has less estrogenicity than CEE and so far is safe in oral E2 studies.

- **65 y/o female with HTN, but Hx DM, ↑ cholesterol, wants to start estrogen for the first time. Is oral OK?**

No, CEE would be contraindicated (use transermal to prevent thrombus rupture or low dose oral E2).

- **65 y/o female above, was on estrogen but stopped one year ago after the scare. Was on for 15 years. Is oral OK?**

Yes oral is OK to continue as a patient on estrogen for 15 years should be protected against any development of a fibrous cap and necrotic core that could rupture (RR=0.6 at 5 years = protective and is within 10 year window.

- **Older women tend to be more compliant with transdermal than with oral estrogen.**

False

- **There was a relative risk (RR) of 2.5 in the HERS study for women to develop CVD within the first year of HRT.**

True

- **All of these women had HTN.**

True, so don't give older women beyond 10 year window oral CEE, only transdermal E2 or oral E2.

- **After the first year, the RR was less than 0.6 for CAD which meant that there was protection against CAD the longer the estrogen was continued.**

True

- **The experts therefore recommend terminating estrogen as soon as possible or after symptoms resolve.**

True: but why stop if the risk is < 1.0 (decreases to 0.6) as time progresses for BC risks and DVT.

- **The cardiovascular risks and CVD risks and outcomes for HRT were similar for the HERS Trial and the WHI Trial.**

True

- **53 y/o woman on HRT recently perimenopausal, c/o feeling like she's going to have a severe period… Going to explode! TX?**

  A. stop HRT and bleed

  B. progesterone in oil 100 mg/ml 1 ml IM

  C. Six SL progesterone daily until better.

  – Stop HRT and give IM progesterone is best, or SL if IM not an option.

- **35 y/o women +BRCA gene, s/p hysterectomy, oophorectomy, mastectomy.**

1) Which hormones should she get?

All hormones are indicated as there is no risk of causing cancer as the organs have been removed and studies show no harm.

2) She complains of vaginal dryness:

Femring or Estring or Vagifem?

Femring, Estring, Vagifem are all OK, with Vagifem least irritating but all are expensive.

- **55 y/o female s/p mastectomy one year ago for CA, off HRT, c/o severe vaginal dryness.**

  P) Femring or Estring ?

  Estriol Vag Cream?

  Estradiol Vag Cream?

  Vagifem ?

Estring, estriol cream, and vagifem are indicated and will not raise estradiol levels. Femring contraindicated due to systemic absorption. Estradiol cream may be contraindicated if it raises systemic estradiol, so don't use high dose= < 1mg/gm.

- **40 y/o female on BCP, c/o ↓ libido.**

  TX?

Testosterone & stop BCP to avoid SHBG binding by BCP.

- **Above female, c/o vaginal dryness.**

  TX?

Estring, Vagifem, creams, and testosterone will help vaginal dryness.

- **55 y/o female feels out of balance – on HRT, levels are good, but depressed, manic. TX?**

SSRI vs. Valproic acid, lamictal, etc.

- **63 y/o male DDS with osteoporosis seen on wrist x-ray for wrist fx.**

  test: DEXA, parathyroid level, DHEA, Testosterone, Alk Phos, Vit D, NTX, thyroid, calcium, IGF-1.

Test all to work up osteoporosis

- **The predominant premenopausal hormone is estradiol. The literature demonstrates postmenopausal estradiol levels should be maintained at levels of: 20, 40, 60, 100, 120?**

>60 pg/ml at the minimum.

- **Long term elevation of FSH is due to loss of inhibin.**

True

- **This is why treatment with estrogen can be monitored by measuring FSH.**

False, as FSH levels still remain elevated on E2 except for pellet therapy.

- **Cardiovascular disease can be reduced by 50% by all of the following except:**
  - **Life-long ERT**
  - **Testosterone**
  - **Exercise**
  - **Life style change**
  - **Estrogen for <5 years**

  estrogen for < 5 yrs, so then why do the experts say to stop?

  The average daily premenopausal level of estradiol is:

  10, 30, 60, 80, 100, 120?

  Average daily level is 100 with midcycle levels of > 400 pg/ml.

- **Estrogen enhances bone mineral density by inhibition of osteoclasts.**

True

- **Estrogen enhances bone mineral density by stimulation of new bone formation by osteoblasts.**

True

- **Estrogen enhances bone mineral density by renal activation of Vit D.**

True

- **Estrogen enhances bone mineral density by enhanced intestinal absorption of calcium.**

True

- **Estrogen slows the progression of Alzheimer's Disease.**

True but use transdermal only in older women with severe active disease to prevent vascular dementia.

- **The average risk of breast cancer is:**

1 in 20 1 in 15 1 in 10 1 In 8 1 in 5

Ans: 1 in 8

- **All of the following are advantages of transdermal estrogen patch:**
  - **Steady state serum levels**
  - **True**
  - **Minimal risk of thrombosis**
  - **True**
  - **Lack of first pass**
  - **True**
  - **Equivalent effect on lipids & CVD**
  - **False**
  - **Once weekly application**
  - **True**

- **48 y/o female with no menses in 6 months, no symptoms, no HF, no night sweats.**
  - **What tests?**
  - FSH & HRT levels
  - **What tx?**
  - Tx with progesterone
  - **Dx?**
  - Dx is anovulatory cycle

- **40 y/o female, no menses in 8 months, feels OK.**
  - **Test? FSH & LH to R/O PCOS**
  - Yes, test FSH/ LH and hormone levels**.**

  FSH-5, LH-15 Dx?
  - **Any risks?**
  - Dx is anovulation with the risk of CA uterus & breast secondary to PCOS.

  Tx?
  - Tx is daily progesterone, thyroid, metformin.

- **55 y/o female with vaginal bleeding on & off x 3 months. Changing around HRT has no effect. Most important Dx to rule out?**

Endometrial CA by ultrasound and biopsy**.**

- **Tx?**

High dose progesterone as most women can't tolerate high dose MPA.

- **Always document that HRT was discussed in detail, risks & benefits.**
- **Document that pt chooses to initiate and continue HRT.**
- **Recommend annual tests by PMD.**

- **A 65 y/o female on PremPro for 15 years, hx HTN, tobacco use, hyperlipidemia. Presents as new pt.**

- **Which estrogen – oral or transdermal-even though she has been on estrogen consistently for 15 years?**

Oral as less than 10 year window and RR = 0.6. The estrogen has protected her from plaque build-up.

- **PEPI Trial proved progesterone protected against endometrial hyperplasia equally as well as MPA.**

True

- **PEPI Trial: Premarin & Provera had worse cardiovascular outcomes than Premarin and progesterone.**

True

- **Estrogen plus progestin negates estrogen's lipid lowering properties.**

True

- **Testosterone serum levels are at highest in AM or PM?**

AM

- **Therefore we should always measure baseline testosterone levels in the AM or PM?**

Test in the PM if you want to document low testosterone levels or in the AM if wanting to document higher levels which may not qualify patient based on AACE quidelines.

- **Chronic narcotic use causes hypogonadism by:**

  a. inhibition of testosterone production in the testis.

  b. increases prolactin.

  c. inhibits gonadotropin-releasing hormone.

Answer: C

- **The metabolic syndrome, or Syndrome X, consists of:**

  a. low HDL

  b. ↑ triglycerides

  c. abdominal obesity

  d. HTN

  e. insulin resistance

Answer: All = Syndrome W or Syndrome X that worsen at menopause. It is not estrogen dominance.

CASE STUDIES: SECTION 8

- To understand the appropriate use of oral vs. transdermal estrogen.
- To review various scenarios that might change the HRT prescription.
- To review different types of progesterone & estrogen & testosterone.
- To understand men and HRT.
- How to hit a curve ball.

49 Y/O female with normal heavy periods becoming heavier. She complains of severe HF and NS. (Hint-severe NS).

Treatment: oral or transdermal estrogen?

Treatment: oral or transdermal progesterone (remember that there are two types of transdermal progesterone)?

Same 49 y/o female with normal periods whose NS are not controlled with 100mg PO P4 at HS.

- At what day of the cycle do you measure E2 levels to determine if estrogen is needed for control of NS?
- At what day of the cycle do you measure E2 levels in a 30 y/o that c/o NS in order to know if she needs estrogen?
- How about a 19 y/o?

- Under what circumstances would a 19 y/o female need/require estrogen?
- What lab tests would you order and what levels would you expect to see.

- Hypothetically, what treatment option could you offer/tell a young female patient that would provide natural BC assuming that the patient refused to take any medicine, drug, or surgery for BC. (Hint: What could you do to mess up her periods and cycles)?

- 53 Y/O with recent complete hysterectomy, requests HRT for HF & NS. Hx of DM, smoker. Treatment should involve which type of estrogen? Which type of progesterone?

- 53 Y/O female in menopause, LMP 9 months ago, c/o HF & NS. Hx of BCP for 20 years but now refuses. Family history of breast cancer. Treatment?

- 53 Y/O woman in menopause, s/p bilateral mastectomy 6 years prior for breast cancer, took Tamoxifen for 5 years, and now is a BC survivor. Patient still has ovaries. Recent + BRCA-1 gene. Treatment for menopause?

- **55 Y/O woman in menopause, c/o severe HF & NS. Hx complete hysterectomy at age 32. History of HTN and ↑ cholesterol. Her PMD took her off your HRT advising her that it will increase risk of heart attacks and strokes.**

Plan and explanation?

55 Y/O woman in menopause for 23 years

- **Same patient but she doesn't look healthy, BMI > 40?, takes diabetes medicine.**

Plan?

- **Contraindications to oral E2?**
- **Why does everyone fear oral E2?**
- **What RCT proved that E2 was harmful?**

- 62 Y/O woman requests HRT for HF & NS. Never has taken HRT before. Hx only + for family history of CAD. After treatment with HRT she develops severe acne and hirsutism. She reports the same symptoms when younger. Treatment and diagnosis?

- **82 Y/O healthy woman wants HRT as recommended by her 60 y/o sons and daughters on HRT. Her PMD and you are hesitant to prescribe HRT.**

What are you afraid of?

- **61 Y/O woman wants HRT to feel better, falling apart. C/O severe fatigue, overweight, never exercised. History of elevated cholesterol treated with statin for 10 years. PMD refused to give estrogen because she weighs 200 pounds and makes enough estrogen on her own. Treatment?**

- **65 Y/O woman on Prempro for 12 years and wants off. History of DM, elevated cholesterol, HTN.**

Treatment? (Remember the RR of HERS and WHI results after 5 years of HRT).

- **Same patient, complete hysterectomy at age 40. Stopped Premarin 15 years ago and wants to restart HRT. Treatment?**

- **59 Y/O woman desires HRT. Menopause at age 53. History of syndrome X on metformin.**

Treatment?

- **What about SHBG in this patient?**
- **What about the best CV protection?**
- **What about her BMI of 35?**
- **What is going to kill her, CAD or DVT?**

- **53 Y/O woman desires HRT to feel better and decrease HF. Healthy and active except smokes. History of DVT at age 50 that was unprovoked.**

Treatment?

- **68 Y/O male on Casodex and Lupron. Feels like crap, healthy and active, ran daily and played tennis but not now. Feels terrible. C/O HF, NS, and depression.**

Treatment?

- **68 Y/O male on Casodex and Lupron, s/p proton gun and brachytherapy. Now feels like crap. Feels fatigued but otherwise has been healthy and active. No other meds. PSA recently was 5.1.**

Treatment?

- **60 Y/O male s/p radiation and brachytherapy. The original PSA of 0.1 has now increased to a PSA of 4.1. Hx of CAD. Urologists want to put him on LHRH agonists.**

Treatment?

When To Change From Oral To Transdermal?

- Oral estrogen (CEE) has been shown in some studies to increase the risk of a thrombus (MI & CVA) in older women. At what age should a menopausal woman be switched over from oral to transdermal estrogen to avoid the complications of long term oral estrogen?
- What if she has an MI?
- What if she has a DVT?

Oral to Transdermal?

- Never if after the first year of Tx. Unless…
- Only if patient has developed a DVT.
- Immediately if you realize there is a risk, like diagnosis of thrombophilia.
- The RR of CVD decreases after the first year on CEE/MPA, therefore not need to stop HRT but need to change to E2/P4.

When To Switch?

- A 65 y/o female with HTN and hyperlipidemia desires HRT after reading books and listening to Oprah. Since she is beyond the safe 10 year window and has several risk factors, so you Rx a transdermal estrogen to avoid causing a thrombus. At what point (how many years) is it safe and recommended to switch to oral estrogen?
- The question is: Why did you Rx TE2 in the first place?

Transdermal To Oral E2?

- 65 y/o menopausal woman on transdermal E2 patch for 15 years presents for HRT replacement. Wants off patches and creams to switch to orals. Hx of HTN, DM, and hyperlipidemia.
- Treatment?
- Safety concerns?

Heart Disease ≠ Heart Disease

- Estrogen both causes heart disease and protects against heart disease. Explain.
- The main culprit that causes the thrombotic type of CVD is MMP?
- If MMP could be eliminated, what harm would oral estrogen still have?

What Is The Harm Of Transdermal E2?

- Side effects if too much.
- The only harm is not enough!
- What study proved harm of transdermal E2?

The 5 B's of Menopause

- 52 y/o woman desires HRT. Hx of irregular heavy menstrual bleeding but now has no period in 2 years. She complains of NS. FSH is 5 and estradiol is 20. Tx?

Prior patient is now 53 and experiencing severe HF and NS

- Patient starts estrogen and develops severe bleeding for one month straight. Tx?
- What test is most important to run?
- ES measures 1.3cm. Tx?
- Hormone tests & adjustments?

Endometrial biopsy is negative for CA

- Treatment?
- Patient c/o persistent menopausal symptoms which necessitates increasing estrogen to control her symptoms. Repeat US in 3 months indicates increased ES to 1.5 cm.

Treatment?

- Patient read where HRT is harmful if it goes through the liver and she wants all HRT changed to transdermal creams.

What is the harm of doing this?

Age and BHRT?

- 75 y/o woman with severe incontinence requests HRT.
- Type of progesterone to use?
- Type of testosterone to use?
- Type of estrogen to use vaginally?

Treatment for Syndrome X?

- 57 y/o female with Syndrome X on no meds presents requesting HRT. Presently takes HRT cream: transdermal testosterone, progesterone, estrogen. She c/o severe acne and hirsutism on testosterone in spite of normal levels. Other than spironolactone, what should be done with all 3 of her other hormones and why?
- Could this have been predicted?
- What should she have been treated with and when, or was wrong with her current regimen?

What Is The Importance of SHBG?

- The above patient was diagnosed with PCOS 15 years before menopause. What treatment could be used to raise SHBG?
- Is SHBG associated with longevity?
- Is SHBG beneficial in women?
- In men?

Safe vs. Best E2

- Is transdermal estrogen appropriate for a woman starting menopause who has Syndrome X and a BMI < 30?
- What about a 65 y/o woman with Syndrome X who has never been on HRT?
- What does Syndrome X do to E2 levels and inflammatory cytokines, cancer risks?
- How do you fix that?

What about men?

- 58 y/o male with Syndrome X is treated with testosterone. Total testosterone is 1800 but the free testosterone is 75ug/ml (Quest normal 50-210).
- Should the testosterone Rx be lowered?
- Raised?
- Treatment for Syndrome X?

- Is SHBG good in this situation?
- Should SHBG be lowered or raised?
- What would cause an increase in SHBG?

- 63 y/o female with partial hysterectomy at age 40. Took Premarin for 6 years and stopped 7 years ago. No HTN, DM, ↑ lipids. BMI = 40.
- Treat with oral or transdermal for maximal cardiovascular protection?
- Treat with oral or transdermal for maximal DVT safety. (Remember RR = same for both).
- So is the risk of DVT greater now than 5 years ago?

- 63 y/o female experienced menopause at age 50. Hx of DM, HTN, hyperlipidemia that are well controlled on meds. Started BHRT at menopause and continues through today which included Triest (2, .25, .25), progesterone & testosterone creams.
- Now wants to start BHRT with you. Treatment?

- 54 y/o female on BHRT with creams and wants to continue them. Read they are the best. Hx. HTN, DM, + family Hx.
- Best treatment?
- If creams are used, what dose of each?

- 53 y/o female still menstruates, only on oral progesterone for severe PMS. She develops a DVT and PE. Her PMD tells her to stop the hormones as it caused the PE.
- Treatment?
- Switch to transdermal progesterone?
- What one study showed an increased risk of DVT with oral progesterone?
- What is the RR of recurrence? Spell?

Prior patient still menstruates normally at age 54

- Progesterone QD is no longer helping control symptoms. Tx?
- FSH level tested during hot flashes is 45 and estradiol level is 250. Tx?

Prior patient stops menstruating and c/o severe symptoms of menopause.

- PMD states that she can never take estrogen. Plan and explanation?
- What is in Part II that the PMD needs to read and understand?

Prior patient's husband develops a DVT while on testosterone. His PMD states that he must stop testosterone and never take it again as it caused the blood clot because his blood is too thick.

Tx?

NEJM?

65 Y/O healthy male with prostate cancer with extension outside the capsule, S/P proton gun radiation. PSA is now 10 and climbing in spite of LHRH agonists.

- Tumor is no longer androgen sensitive.

Treatment?

- Another patient with the same problem except for a history of DVT secondary to Factor V Leiden?

Treatment?

70 Y/O male with metastatic prostate cancer, PSA of 150. Hx of DM, HTN, hyperlipidemia which are all controlled. Recently placed on chemo which is his only hope according to heme-onc. Protocol involves addition of prednisone mandating addition of Lantus insulin to other DM meds to control BS of 400. Both doctors continue LHRH agonists.

- Treatment?
- Should LHRH agonists be continued?

DIAGNOSIS & TREATMENT of PROSTATE CANCER

- 65 Y/O male with PSA of 8.4 and Free PSA of 9%. Diagnostic tests?
- First try Bactrim and repeat PSA. If elevated, then work up with:
- MRI with Tesla 3.
- Biopsy under MRI guidance.
- Laser ablation under MRI guidance.
- Avoids usual side effects and complications of conventional therapy but expensive.

65 y/o male is diagnosed with prostate CA by MRI scan.

- Patient wants to know if he should stop the testosterone?
- Patient has other doctors?
- Patient states you are his only doctor?
- What would you do if it was you?

65 Y/O MALE WITH PSA OF 6.5. TRUS BIOPSY (-). PMD REFUSES TESTOSTERONE?

- What test will alleviate fear of possible prostate CA?
- What is the risk that patient still has CA?
- If patient/insurance refuse this test, is testosterone still indicated in light of still having possible prostate cancer?
- What is the risk of causing further CA progression with testosterone Rx?

54 Y/O female who is intolerant to PO or SL progesterone. Treatment?

- Incidence of intolerance to P4?
- Options include vaginal P4, transdermal cream QID, Mirena IUD, a progestin.
- Advise of increased risk of CA of uterus and breast if progesterone is not taken.

54 Y/O female c/o weight gain on HRT program oral E2 and SL P4

- If swelling, edema, sudden weight gain in one month time frame, then Tx is?
- What should be done with oral E2?
- What should be done with SL P4?
- What effect will oral P4 have on estradiol levels?
- What should be done with testosterone dose?

64 y/o female on your HRT program for 13 years suffers an MI.

- What do you do with her HRT program?
- What does the literature say about continuing HRT after an MI?
- What if her PMD insists that she stops HRT?

At what point can hormones be resumed, based on literature from Part II, after diagnosis of CA?

- Breast CA?
- Uterine CA?
- Ovarian CA?
- Prostate CA?

Progesterone and Breast CA?

- 42 y/o female with breast CA is receptor site (+) for both estrogen and progesterone. S/P mastectomy; no chemo or radiation. She continues to menstruate normally. Only medication is Tamoxifen for estrogen (+) receptor tumor. If she is (+) for progesterone receptor also, and is menstruating normally, then what progesterone blocker should be used to prevent stimulation of (+) progesterone receptor on tumor?

65 y/o woman with diabetes and HTN has an MI.

A) While on PremPro. What to do?

B) While on oral BHRT. What to do? (Think timing and RR).

C) Develops DVT while on oral HRT. What to do?

D) Develops DVT while on transdermal HRT. What to do?

ESTROGEN AND THE TREATMENT OF PROSTATE CANCER

65 y/o male with prostate cancer treated with Proton Gun 10 years ago. PSA has remained 0.1 for 10 years and now has been increasing to 4.2. A urologist started patient on Casodex and Lupron which caused severe rash and side effects and was stopped. The patient presents requesting alternative therapy. Additional Hx of CAD, HTN, DM.

Estrogen in Men

- Oral DES at a 5mg dose has been shown to be harmful to men in that it increases the risk of heart disease. T or F

- Oral DES at a 1mg dose demonstrated the same harm. T or F

- Oral estradiol has been shown to be harmful to men also. T or F

Oral vs. Transdermal E2?

- The WHI demonstrated an increase in MI with the use of oral estrogen in women over 60 years of age with risk factors for CAD.
- Studies demonstrate the same effect in men that were prescribed oral high dose DES.
- Studies also demonstrate a significant increase in morbidity and mortality from CAD and CVA in men treated with LHRH agonists.
- Knowing this…

Estrogen in Men: EBM?

- Transdermal estradiol has been shown to be not only safe in men but also protects against heart disease. T or F
- Estrogen has long been a standard therapy for treating prostate cancer in men. T or F
- The higher the serum estradiol level in men, the greater the risk of prostate cancer. T or F

Evidenced Based Medicine

- Since the medical literature demonstrates protection against cardiovascular disease, bone loss, diabetes, prostate cancer, Alzheimer's disease, and dementia with estrogen administration in men, it makes perfect sense to routinely lower estrogen levels in men with aromatase inhibitors. T or F
- There is EBM showing that lowering E2 levels in men is beneficial. T or F
- Understanding the above, it also makes sense to raise progesterone levels in men based on EBM. T or F