

**Reproductive Hormonal
Issues:
Treating Mood Disorders
Associated with PMS and
Peri-menopause**

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Dr. Anna Cabeca

- Emory University trained, Board Certified Gynecologist and Obstetrician
- Board Certified in Anti-Aging & Regenerative Medicine
- Expert, Functional Medicine & Women's Health, Hormone therapy
- Lecturer, Consultant, and Trainer



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Objectives

- Identify important clues in the patient history and physical exam that identify mood disorders in PMS, postpartum, and the perimenopausal transition (PMT).
- Evaluate the role of diet, specific nutritional supplements, and hormonal and botanical therapies in improving mood disorders in women with PMS, premenstrual dysphoric disorder (PMDD), postpartum depression, and during the PMT.
- Promote hormonal balance through integrative medicine, detoxification, nutrition, alkalization, and digestive health.
- Empower our bodies, spirits, and minds to create balance and health.

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My Story - BEFORE

- 40 year old with 4 children
- Worked over 80 hrs/week
- Primary bread winner
- Losing hair
- 80 lbs overweight
- Menopausal and
- Depressed



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*The soul suffers when the body
is diseased or traumatized,
while the body suffers when the
soul is ailing - Aristotle*

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My Story - AFTER

- Hair grew back
- Lost over 80 lbs
- Fertile again... meet my miracle - Ava!
- Wake up excited each morning



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Head-to-Toe Approach

- Mind, Spirit, Energetics
- Environment
- Nutrition
- Digestion and Intestinal Health
- Detoxification
- Hormone Health and Balance
 - HPTAG Axis
 - Neuro-endocrine Health
- Structure and Function
 - Exercise & Mobility

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“75% of an individual’s health after age 40 is dependent upon what the person has done to his or her genes, not the genes themselves.”

25%

75%

Jeffrey S. Bland, Ph.D.
Genetic Nutritioneering,
1999, p. 65

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Linus Pauling’s Orthomolecular (right molecules) Medicine

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1. Everyone is different.
2. Each individual’s health benefits from having the right molecules in the right amounts.
3. *Before turning to medicines, we should attempt to adjust the normal body constituents to match the needs for optimal functioning.*

Individualized Care

- Physically
- Physiologically
- Biochemically
- Spiritually



Individualized evaluation
⇒⇒ Individualized treatment

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Inflammation & Hormone Imbalance

Precursor to disease states

- Diabetes mellitus
- Arthritis
- Alzheimer's disease, Cognitive decline
- Cardiovascular disease
- Stroke
- Cancer
- Endometriosis, Fibroids, Infertility
- PMS
- Depression
- Obesity

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Factors Creating Hormone Imbalance

- Stress
- Dietary Habits
- Certain nutrient deficiencies
- Dysbiosis
- Hormonal disruptors
- Toxins
- Other health problems such as adrenal, ↑ or ↓ BMI
- Natural aging
- Insomnia
- Genetics



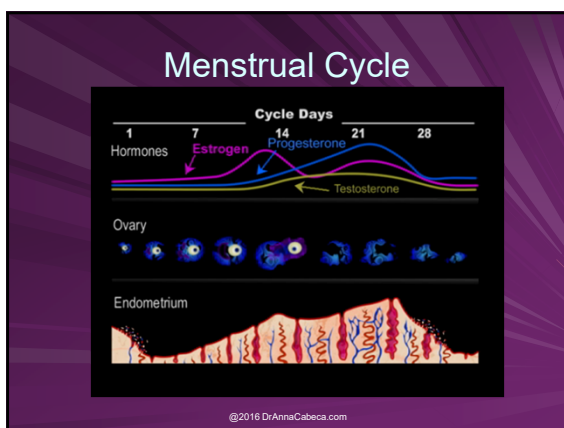
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Inflammation & Hormone Imbalance

- At time of menopause a woman's average life expectancy is 32.7 years
- 1:2 Osteoporotic Fracture
- 1:3 Coronary Heart Disease
- 1:5 Stroke or Alzheimer's
- 1:8 Breast Cancer

Kung HC, Hoyert DL, Xu J, Murphy SL. Deaths: final data for 2005. Natl Vital Stat Rep 2008;56:1-120

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Premenstrual Syndrome (PMS)

- **Definition of PMS:**
 - The cyclic appearance of one or more of a large constellation of symptoms (200)
 - Lifestyle or work is affected
 - Followed by a period of time entirely free of symptoms.
 - The most frequently encountered symptoms include the following: abdominal bloating, anxiety, breast tenderness, crying spells, depression, fatigue, irritability, thirst and appetite changes, and variable degrees of edema of the extremities
 - Occurring within the last 7 – 10 days of the cycle
 - Speroff L. Clinical Gynecologic Endocrinology and Infertility 7th ed 2005 pg 531-533.

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- According to the US Bureau of the Census, women aged 45-64 years, who are in their late and post reproductive years, constitute over 26% of the female population

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Zoe R. 36 y.o.

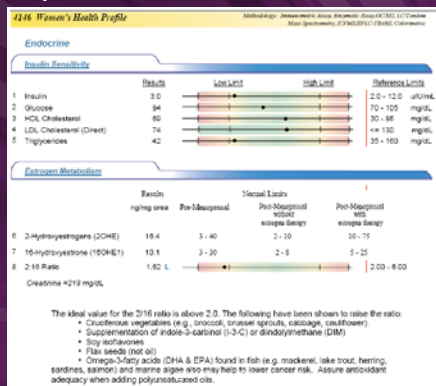
- Cc: PMS, moodiness, breast tenderness, having difficulty organizing tasks, memory loss, decreased libido
- PM/Shx: neg, G4P4004;
- WDWN, 5'11", 155 lbs., fcb b/l, areolar and vaginal mucosal palor

Hormone Test	Result	L	WR	H	Expected Range
Estriol	2.3	neg	X		(1) <30.0 females non-pregnant
Estradiol	45.0	neg	X		(1) 1-50.2 post; (2) 10-10.5 pre; (3) 1.5-10.5 supplementation; (4) <2.5 males
Progesterone	19.2		X		(1) 19-125 post; (2) 127-446 pre (r/tals); (3) 500-3000 supplementation; (4) <51 males
Ratio of Pg/E2	35.6	neg	X		(1) 200-600 females; (2) 200-300 males;
Testosterone	95.0	neg	X		(1) 30.1-142.5 males; (2) 6.0-49 females; (3) 30-60 therapy females; (4) 250-350 therapy males;
DHEA	7.3	neg	X		(1) 137-326 males; (2) 156-300 females
Cortisol Morning	0.8	neg	X		(1) 5.1-40.2
Cortisol Noon		neg	X		(1) 2.1-19.7
Cortisol Evening		neg	X		(1) 1.8-12.1
Cortisol Night		neg	X		(1) 0.9-9.2

*DHEA and Testosterone results are for investigational use only

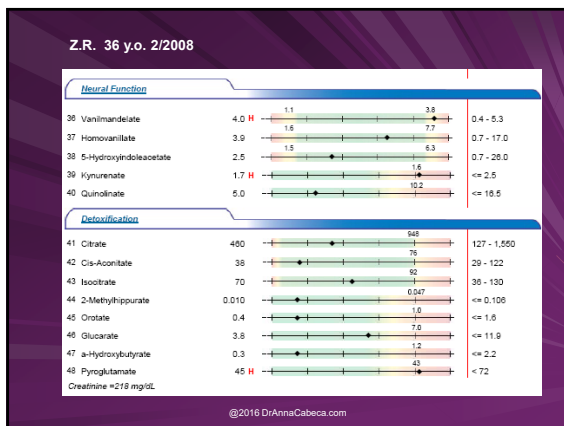
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Zoe R. 36 y.o



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Health and Nutrition





Zoe R.

- Therapeutic life style changes
- Dietary recommendations/detox program
- Progesterone cream 60 mg/ml ½ ml on cycle day 10 -28
- DHEA 15 mg/d
- Daily vitamin packs (multivitamin with minerals, MCHC calcium, Omega 3 360/240 mg EPA/DHA), Carnitine 500mg, Magnesium Glycinate, Zinc 50 mg, Glycine, NAC, Vitamin C 1000 mg, Vit E (mixed tocotrienols) 400IU, Iodide 25mg per day

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The Perimenopausal Transition (PMT)

- Average age of onset = 46 y
- Age of onset for 95% of women = 39 - 51 y
- Average duration = 5 y
- Duration for 95% of women = 2 – 8 y
- < 10% abruptly cease menses
- When FSH >20 IU/L, and LH >30 IU/L, pregnancy unlikely

■ Speroff L Clinical Gynecologic Endocrinology and Infertility 7th ed 2005

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Symptoms of Estrogen Dominance

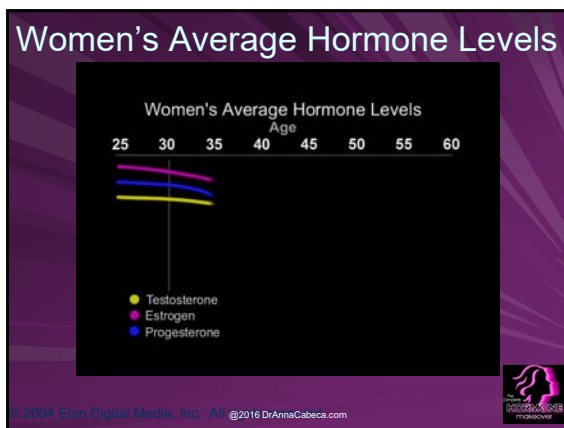
- Mood Swings
- Irritability
- Depression
- Irregular Periods
- Heavy Menstrual Flow
- Hot Flashes
- Vaginal Dryness
- Water Retention
- Weight Gain: Hips, Thighs and Abdomen
- Sleep Disturbance (Insomnia, less REM sleep)

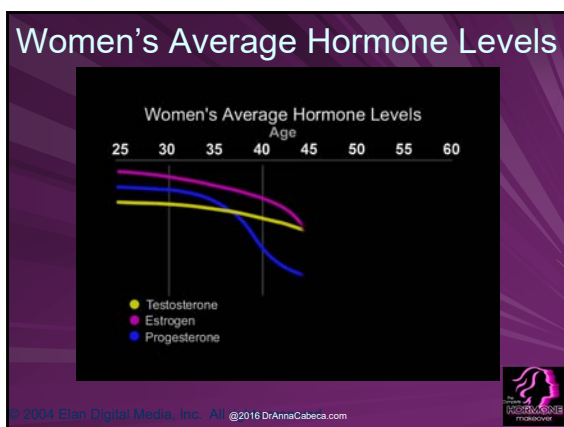
Prozac

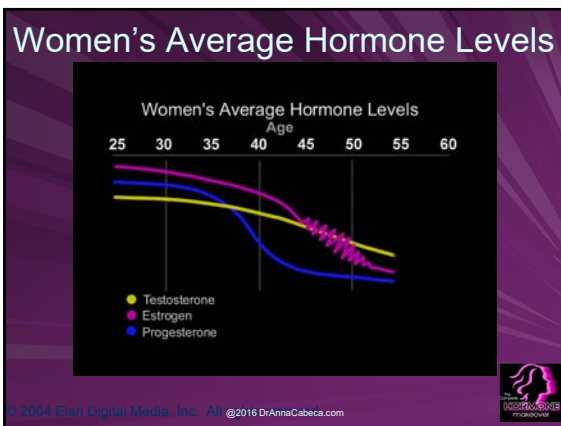
ACP's Hysterectomy

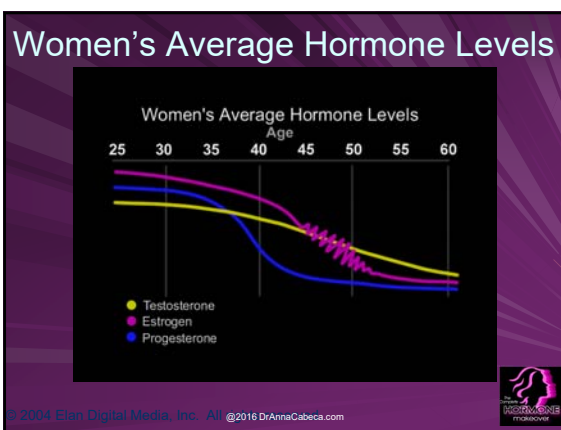
- Decreased Libido
- Headaches
- Fatigue
- Short-term Memory Loss
- Lack of Concentration
- Thinning of Scalp Hair
- Dry, Thin, Wrinkly Skin
- Increased Facial Hair
- Bone Mineral Loss (Osteoporosis) (Athletes Δ)
- Diffuse Aches and Pain

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Estrogens

- E2 receptors are present in the amygdala and hippocampus, which influence mood and behavior
 - Genazzani AR, Luchiesi A, Stomati M, et al. Effects of sex steroid hormones on the neuroendocrine system. *Eur J Contracept Reprod Health Care*. 997; 2: 63-69.
- ↑serotonergic receptors in the brain & ↑production of serotonin
 - Kugaya A, Epperson CN, Zoghbi S, et al. Increase in prefrontal cortex serotonin 2A receptors following estrogen treatment in postmenopausal women. *Am J Psychiatry*. 203;160:1522-1524.
- Modulates activity of the noradrenergic system and diminishes the number and sensitivity of dopamine receptors
 - Garlow S, et al. The neurochemistry of mood disorders: clinical studies. In: *Neurobiology of Mental Illness*, 1999.

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Progesterone

- calming, mood stabilizing effect
- modulates the brain's response to amino acid neurotransmitters that help regulate mood, sleep, cravings, etc.
- down-regulating the brain's GABA receptors. (Like Valium — except good for you!)

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Nutrient Deficiencies

Interfere with hormone actions

Nutrient	Hormone Action
■ Iodine	■ critical in thyroid, part of every hormone receptor
■ Zinc	■ E2, T, GH receptor
■ B6	■ fxns to clear E2 from receptor site, cofactor for NT
■ Calcium	■ Vit D
■ Magnesium	■ Nec. for phosphorylation of pyridoxine, EFAs, dopa
■ Methyl donors	■ (MSM, folic acid, DMG) needed for metabolism
■ Cobalt	■ E function
■ Chromium	■ ovarian P production
■ Boron	■ E and T

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Nutrient Deficiencies

Interfere with hormone actions

Drug	Nutrient Deficiency
Antibiotics: Penicillin, cephalosporins:	B Vitamins, Vitamin K
Tetracyclines:	Ca, Mg, Fe, B6, Zn
NSAIDs: Aspirin & Salicylates:	Folic acid Vit C, Ca, Folic acid, Fe, B5
Oral Contraceptives	Folic acid, B1, B2, B3, B6, B12, Vit C, Mg, Se, Zn

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Treatment Options

- Birth Control
 - Drospirinone (Yasmin/Yaz)
 - Nuvaring
 - Mirena IUD
- GnRH agonist (Lupron)
- Depo-Provera
- NSAIDs
- Spironolactone 100mg qd cd 15-28
- SSRIs
- Anxiolytics
- Endometrial Ablation
- BSO

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Treatment Options

- Cultural attitudes & personality
- Therapeutic Lifestyle Changes
 - Stress Management
 - Aerobic exercise
 - Dietary
- 25% of women low calcium
- 90% low folate, vit E
- 50% or more have deficiency in iron, manganese, and zinc
- 50% eat < 5 fruit & vegetables/day
- 33% meals eaten outside of home
 - a 66% increase over the last decade

-The American College of Obstetricians and Gynecologists. Practice Bulletin. Management of premenstrual syndrome. Clinical Management Guidelines No. 15. April 2000

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Treatment Options

- Dietary Recommendations
 - Fiber! (at least 25 g/day)
 - Flaxseed, fresh ground 1 – 2 tbsp daily
 - Avoid high fat diet but use good oils!
 - Choose Organic, free range
 - Limit Caffeine and alcohol
 - Limit refined carbohydrates

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Treatment Options

Supplements

- B6 (P5P) 50 - 100 mg/d
- Calcium 600 mg bid

■ Thys-Jacob S, Starkey P, Bernstein D, et al. Calcium carbonate and the premenstrual syndrome: Effects on premenstrual and menstrual symptoms. *Am J Obstet Gynecol*. 1998 ;179 :444 .

■ Wyatt KM, Dimmock PW, Jones PW, et al. Efficacy of vitamin B6 in the treatment of premenstrual syndrome: Systemic review. *Br Med J*. 1999; 318: 1375-1381.

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Treatment Options

Supplements cont'd:


- Omega's, Krill, GLA 2000 – 6000 mg/d
- Magnesium 200 – 400 mg/d (Magnesium Malate)
- Vitamin E (mixed tocotrienols) 400 IU/d
- Vitamin D, check level, optimal level between 50-70
- Zinc 25 – 30 mg/d
- Manganese 1.8 mg/d
- Chaste Berry (Vitex-agnus castus) 100mg
- Gingko 80 mg tid
- Licorice
- Potassium 400 – 600 mg/d (PMS H pts)

Dennehy CE. The use of herbs and dietary supplements in gynecology: an evidence-based review. *Journal of Midwifery & Women's Health*. 51(6):402-9, 2006 Nov-Dec.

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Treatment Options

- 5HTP 50 – 200 mg/d, L-tryptophan – PMS D
- Taurine – water balance - PMS H
- Phosphotidyl Serine 120 – 200 mg
- Phosphatidylcholine 200 mg
- Green Tea Extract 100 mg
- Calcium D Glucarate 300 mg
- Chaste Berry Extract 100mg
- Natural anti-inflammatory agents & anti-oxidants
 - DIM 200 mg
 - Turmeric 50 mg
 - Resveratrol 40 mg
 - Grape Seed Extract 25mg
- Detox – ph 1 & 2 support
- Get them to sleep!
 - Inositol 700 mg
 - Melatonin 1-20 mg



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MACA

■ Menopause. 2008 Nov-Dec;15(6):1157-62. ¹ Links

- Beneficial effects of *Lepidium meyenii* (Maca) on psychological symptoms and measures of sexual dysfunction in postmenopausal women are not related to estrogen or androgen content.
- Brooks NA, Wilcox G, Walker KZ, Ashton JF, Cox MB, Stojanovska L. School of Biomedical and Health Sciences, Victoria University, St. Albans, Victoria, Australia.
- OBJECTIVE: To examine the estrogenic and androgenic activity of *Lepidium meyenii* (Maca) and its effect on the hormonal profile and symptoms in postmenopausal women. DESIGN: Fourteen postmenopausal women completed a randomized, double-blind,

◆ **CONCLUSIONS: Preliminary findings show that *Lepidium meyenii* (Maca) (3.5 g/d) reduces psychological symptoms, including anxiety and depression, and lowers measures of sexual dysfunction in postmenopausal women independent of estrogenic and androgenic activity.**

Supplementing with a natural Maca extract (equivalent to 200 mg/mL Maca). CONCLUSIONS: Preliminary findings show that *Lepidium meyenii* (Maca) (3.5 g/d) reduces psychological symptoms, including anxiety and depression, and lowers measures of sexual dysfunction in postmenopausal women independent of estrogenic

3,3'-Diindolylmethane suppresses the inflammatory response to lipopolysaccharide in murine macrophages.

■ Cho HJ, Seon MR, Lee YM, Kim J, Kim JK, Kim SG, Park JH. Center for Efficacy Assessment and Development of Functional Foods and Drugs, Hallym University, Chuncheon 200-702, South Korea.

■ 3,3'-Diindolylmethane (DIM), a major acid-condensation product of indole-3-carbinol, has been shown to have multiple anticancer effects in experimental models. Because recurrent or chronic inflammation has been implicated in the development of a variety of human cancers, this study examined the antiinflammatory effects of DIM and the

DIM significantly decreased the release of nitric oxide (NO), prostaglandin (PG)E₂, tumor necrosis factor alpha, interleukin (IL)-6, and IL-1beta by RAW264.7 cells treated with LPS. DIM inhibited LPS-induced increases in protein levels of inducible NO synthase (iNOS), which were accompanied by decreased iNOS mRNA levels and transcriptional activity.

inflammatory responses.

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Treatment Options

■ **Hormonal balance (Bigger is not Better)**

- Address adrenaline, cortisol, insulin, thyroid
- Progesterone
 - 20 – 60 mg transdermal cream, qd – bid
 - cd 8 - 14 – menses
 - d 1-25
 - 50 – 400 mg oral compounded or micronized Progesterone
 - Progestin IUD insert (Mirena)
 - Vaginal suppository 20 – 50 mg
 - Injections

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Progesterone & Fertility

- Progesterone peak production at luteal phase: 25-30 mg/d
- Oral Micronized P form better absorbed
- Oral P rapidly metabolized - >90%
- IM – well absorbed
- Vaginal – no liver 1st pass effect, absorbed by lymphatics
 - 1st pass through the uterus
 - 50 mg/d for pregnancy support – 1st Δ

Practice Committee of the ASRM. Progesterone Supplementation during the luteal phase and in early pregnancy in the treatment of infertility: an educational bulletin. Fertil. Steril. 2008;89:789-792.

Effect of oral vs transdermal hormone therapy on lipid levels in postmenopausal women

	E	E+P	TD E	TD E+P
TC	↓	↓	↓	↓
LDL	↓	↓	↓	↓
HDL	↑	(↑)	↑	(↑)
TG	↑	(↑)	↓	↓

E + P, estrogen + progestin combination.
Parentheses indicate blunted effect relative to unopposed estrogen.
Adapted from Goddard IF. Fertil Steril. 2001;75:898-915. Shulman LP, Yankov V, Uhl K. Menopause. 2002;9:195-207.

Hormone therapy and venous thromboembolism among postmenopausal women: Impact of the route of estrogen administration and progestogens: the ESTHER study.

Canonica M, Oger E, Plu-Bureau G, Conard J, Meyer G, Levesque H, Trillot N, Barrellier MT, Wahl D, Emmerich J, Scarabin PY.
Circulation. 2007 Feb 20;115(7):840-5.

CONCLUSIONS: Oral but not transdermal estrogen is associated with an increased VTE risk. In addition, our data suggest that norepregnane derivatives may be thrombogenic, whereas micronized progesterone and pregnane derivatives appear safe with respect to thrombotic risk. If confirmed, these findings could benefit women in the management of their menopausal symptoms with respect to the VTE risk associated with oral estrogen and use of progestogens.

Inserm Unit 780,
94807 Villejuif Cedex, France.

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- (Canonico M 2007)
- Odds ratio for VTE for oral E = 4.2
- OR for VTE for transdermal E = 0.9
- OR for VTE for OMP = 0.7
- OR for VTE for synthetic progestin's = 3.9
- Oral but not Transdermal E assoc with incr risk of VTE.
- Synthetic progestin's may be thrombogenic, unlike OMP

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Programs

- www.Cabecahealth.com/feelfabulous
- www.WomensRestorativeHealth.com
- www.SexualCPR.com/helpdoctor
- www.MightyMaca.com
- Gims@Cabecahealth.com
- drcabeca@cabecahealth.com

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