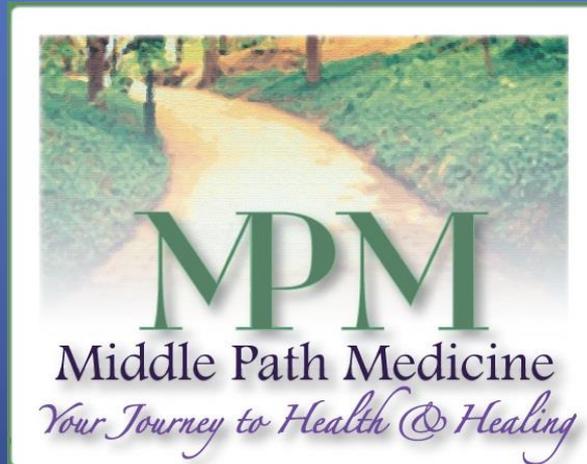


# The Symphony of Hormones

Gary E. Foresman, MD

August 2011



# TRANSCEND

Ray Kurzweil, Terry Grossman MD (2009)

**T**alk with your doctor

**R**elaxation

**A**ssessment

**N**utrition

**S**upplements

**C**alorie Reduction

**E**xercise

**N**ew Technologies

**D**etoxification

# Talk With Your Doctor

- No lecture or presentation is meant to replace the honest and thorough communication between you and your personal physician.
- Your doctor's knowledge of you as the person who has the signs or symptoms or disease allows them to treat you as the individual who has the disease (or dis-ease) not treat the disease where you happen to be the victim.
- Definition: "Authority" - One who has a particular interest in a subject and lives at least one hundred miles away!
- Your best reference for authoritative Integrative Medicine information: [www.middlepathmedicine.com](http://www.middlepathmedicine.com).

# Relaxation: Stress Management

- As a physician, meditation practitioner for 25 years and meditation instructor for 16 years I am in a unique place to emphasize a meditation practice as the single most important thing we can do individually or collectively as a species.
- For our *Stress Management Series* please go to:[www.middlepathmedicine.com/ArticlesandPublications/ArticlesP-T/Stress\\_Management\\_Series.pdf](http://www.middlepathmedicine.com/ArticlesandPublications/ArticlesP-T/Stress_Management_Series.pdf).
- The necessity of the Middle Path: being and doing, feminine and masculine, saving and spending...

# Assessment

- The most important things in life are those things we can not measure, but measure *everything* that you can, when the knowledge of that data can refine your approach to your health, your happiness.
- Male Hormonal Panel: Testosterone, Free Test, DHT, Estradiol, prolactin, others
- Female Hormonal Panel: Estradiol, estrone, estriol, progesterone, testosterone, free test, prolactin, others
- Adrenal: minimum of AM Cortisol with DHEA-S, consider diurnal variation with salivary samples through the day
- Thyroid: TSH, free T4, free T3, reverse T3, and appropriate thyroid antibodies as indicated
- Growth Hormone: IGF-1 and IGFBP-3

# Nutrition

- Please review my “orienting generalizations” found in the Foundations of Health ([http://www.middlepathmedicine.com/ArticlesandPublications/ArticlesF-J/Foundations\\_of\\_Health.pdf](http://www.middlepathmedicine.com/ArticlesandPublications/ArticlesF-J/Foundations_of_Health.pdf))
- Of course, **TRANSCEND** chapter 11, p207-312.
- Most Americans spend too much time on education about nutrition and too little on practicing self-awareness and eating awareness. You are your own personal authority on how to eat for you. Don't acquiesce your personal authority on what to eat to someone else. (Don't ask someone else what to eat...past a few orienting generalizations!)
- If you experience digestive difficulties review our version of the 4R Program (PowerPoint presentation on our website)

# Supplements

- Lifestyle starts with the Foundations of Health and then we build a supplement routine around our Multivitamin, Fish Oils (EPA/DHA) and Vitamin D3 as discussed in our Basic Nutritional Protocol (BNP)  
([http://www.middlepathmedicine.com/ArticlesandPublications/ArticlesA-E/Basic\\_Nutritional\\_Protocol.pdf](http://www.middlepathmedicine.com/ArticlesandPublications/ArticlesA-E/Basic_Nutritional_Protocol.pdf) )
- The antioxidant cocktail adds to this for those under significant physical or psychological stress (also found in BNP)
- Allow your Integrative Medicine Practitioner to review every supplement you take as the quality of every supplement can vary so significantly and your goals for your routine can easily change from month to month. 95% of my most educated and well-intended patients, if not directly guided by me, chose supplements with devastatingly negative consequences on their physiology. Unless you treat hundreds of patients every month with a variety of health conditions, you can NOT do this on your own!

# Calorie Reduction

- The most proven strategy for detoxification, regeneration and life extension. Heck, it even saves money!
- Developing a comfort with hunger and satiety can be very liberating.
- If weight loss is also a goal, I recommend our recent Weight Loss PowerPoint Presentation on our website.

# Exercise

- There are three levels of fitness and I recommend a minimum of seven hours per week on developing these specific lines of development.
- **Stretching Fitness:** Whether yoga, or good old American stretching our physical flexibility mirrors our mental flexibility. Our direct body awareness holds so many keys to our long-term health, not just in the prevention of injury. (10-15 minutes per day)
- **Aerobic Fitness:** The best form of exercise: the one you will do! Whether hiking, kayaking, or biking, or a gym membership, commit and be consistent. (20-30 minutes per day, if less time, then increase the intensity!)
- **Resistance Fitness:** Whether yard work or more commonly today, some weight training, there is almost no way to maintain lean body mass without some form of resistance training. (20-30 minutes per day)

# New Technologies

- This is where Kurzweil and Grossman excel and provide a fascinating view of the not so distant future.
- You must learn about genomics and how to “play the hand you have been dealt”. I am beginning with [www.23andme.com](http://www.23andme.com) and will also pursue the other genetic result companies as I am able.
- Stay on the “cutting edge” of research with the daily newsletter from [www.kurzweilai.net](http://www.kurzweilai.net)
- “Chance favors the prepared mind.” -Louis Pasteur

# Detoxification

- There are as many ways to detox as there are cultures, and I am a strong believer in doing something to enhance our bodies natural detoxification abilities on a routine basis.
- FIR (Far Infrared ) Sauna dramatically enhances detoxification through the skin.
- The UltraClear Renew/ Advaclear program through Metagenics stands above many others for enhanced liver and colon cleansing
- Intravenous Nutritional Support with glutathione and nutritional support drips like the Modified Meyers' Cocktail can significantly ease the “pain” of detoxing.
- The HEEL Detox system remains one of my favorite balanced detox supports as it enhances the lymphatic, renal and hepatic pathways.

# Far Infrared Sauna

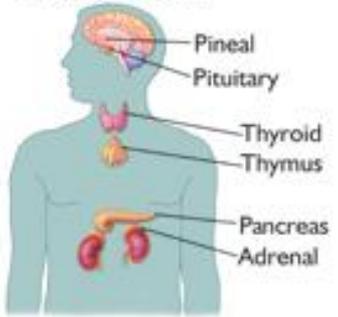
- Enhances cellular repair
- Increase toxic content of sweat from 5% to 15%
- Increased blood flow throughout
- Use when patient can not exercise
  - FM
  - RA
  - CFS

# The Symphony of Hormones

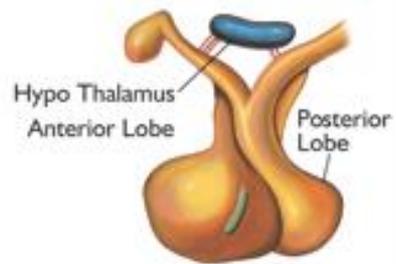
- Credits go to so many for the creation of this PP presentation.
- Miranda Foresman for her editorial expertise.
- The entire team At the Fellowship for Anti-Aging, Regenerative, and Functional Medicine.
- Specific authors whose slides have been adapted for this presentation include James Wilson ND,DC, PhD (Adrenal Fatigue), Sangeeta Pati MD (Andropause), Eldred Taylor MD (Menopause) and Pamela W Smith MD, MPH (Thyroid)
- The grand squad at Middle Path Medicine

# HUMAN ENDOCRINE GLANDS

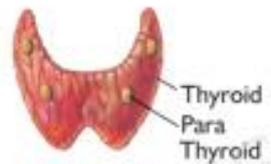
## Glands In Situ



## Pituitary



## Thyroid



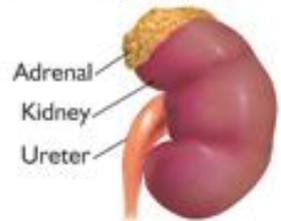
## Thymus



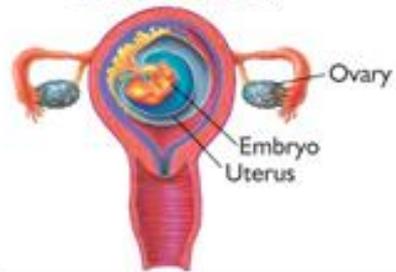
## Pancreas



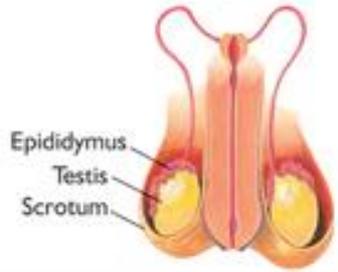
## Adrenal



## Ovary ( Female )



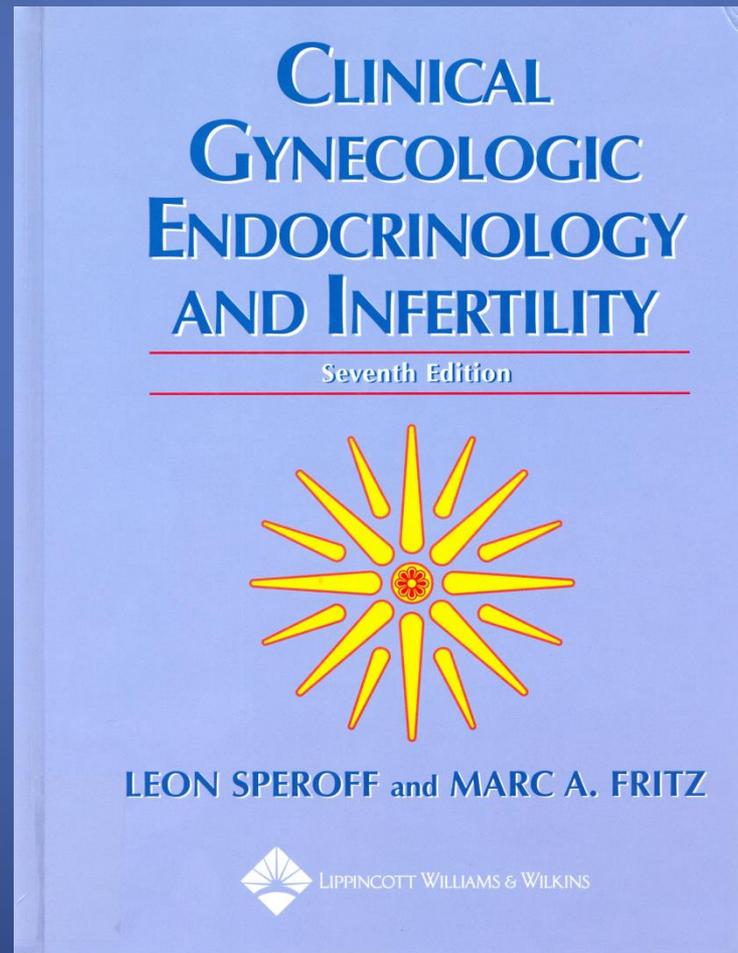
## Testis ( Male )



# Menopause

Myths & Misconceptions

# Hormone Replacement Therapy By The Book: What Does Speroff Tell Us About Bio-Identical Hormone Replacement?



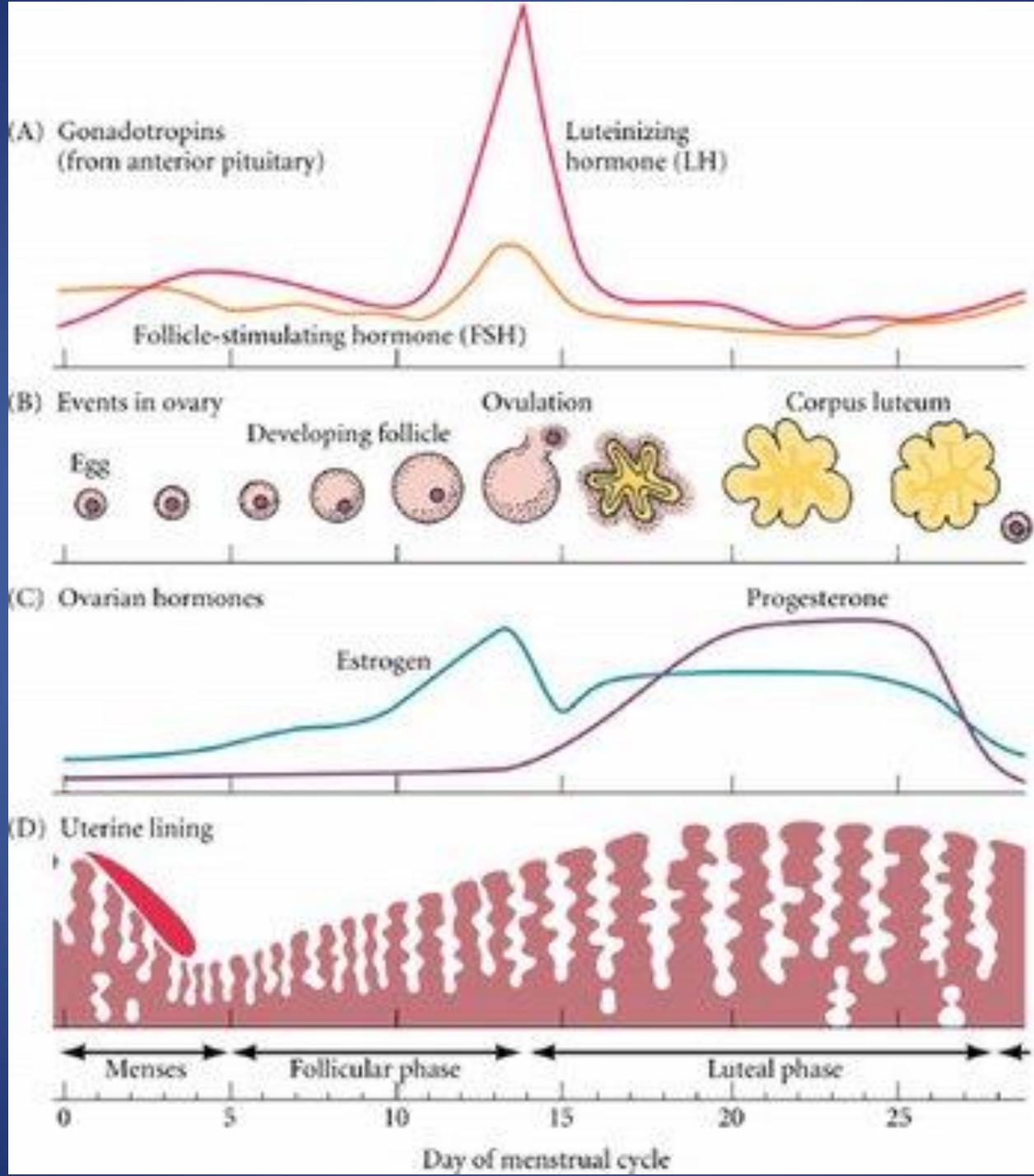
"I tell clinicians that until we have definitive randomized trial data—which we may never have—whatever the patient wants to do is the correct decision. It takes about 10 minutes talking to a patient to know what she wants. However, it's important to point out to her that in case series involving over a thousand patients, whether your tumor

**'I tell clinicians that until we have definitive randomized trial data—which we may never have—whatever the patient wants to do is the correct decision.'**

receptor was positive or negative, it didn't make any difference."

Out of the controversy over the link between hormone therapy and coronary heart disease (CHD) there has emerged a theme, or hypothesis, that it

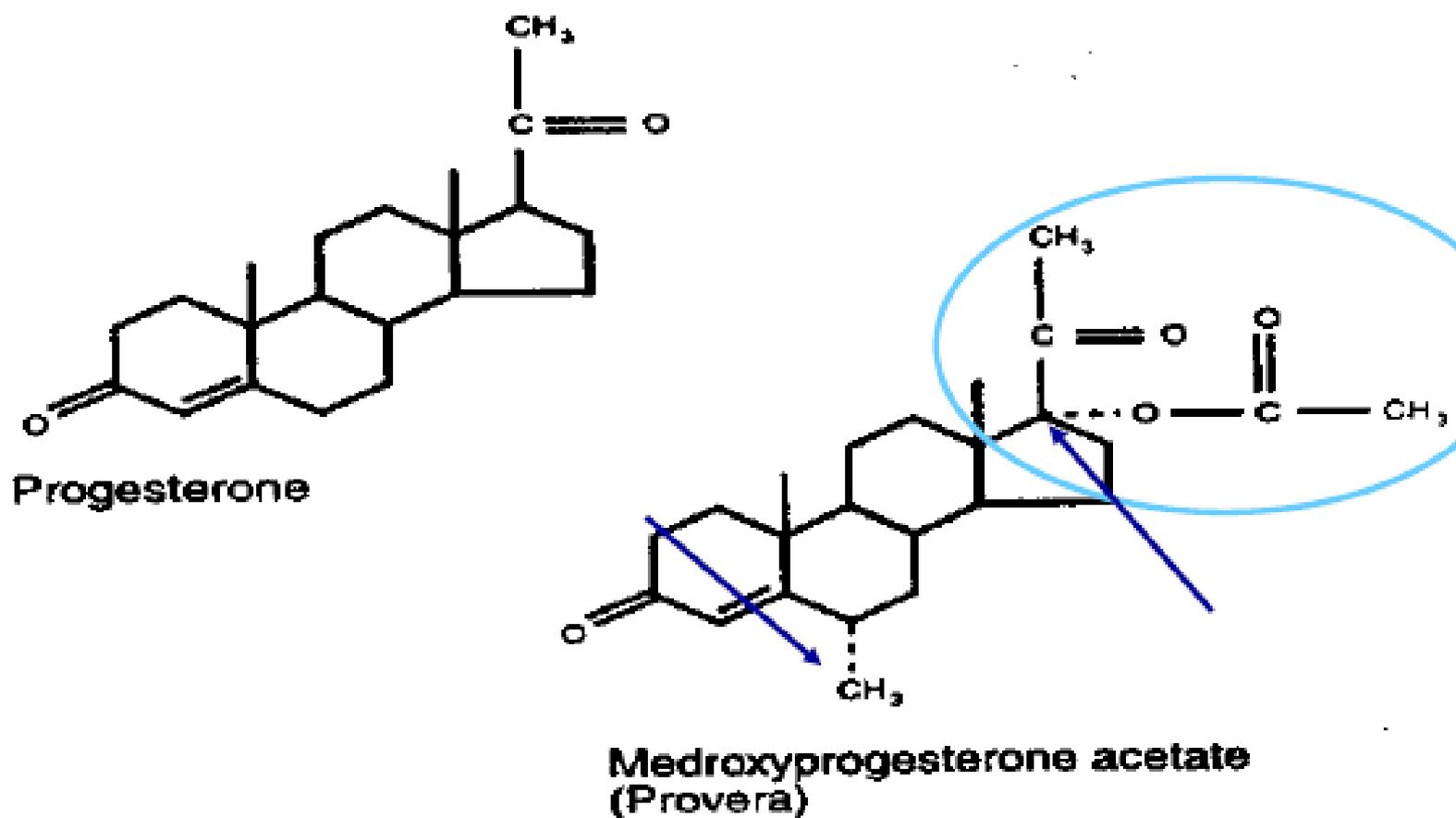
takes healthy cardiovascular endothelium to have a maximal beneficial response to estrogen exposure, continued Dr. Speroff.



# What is a hormone

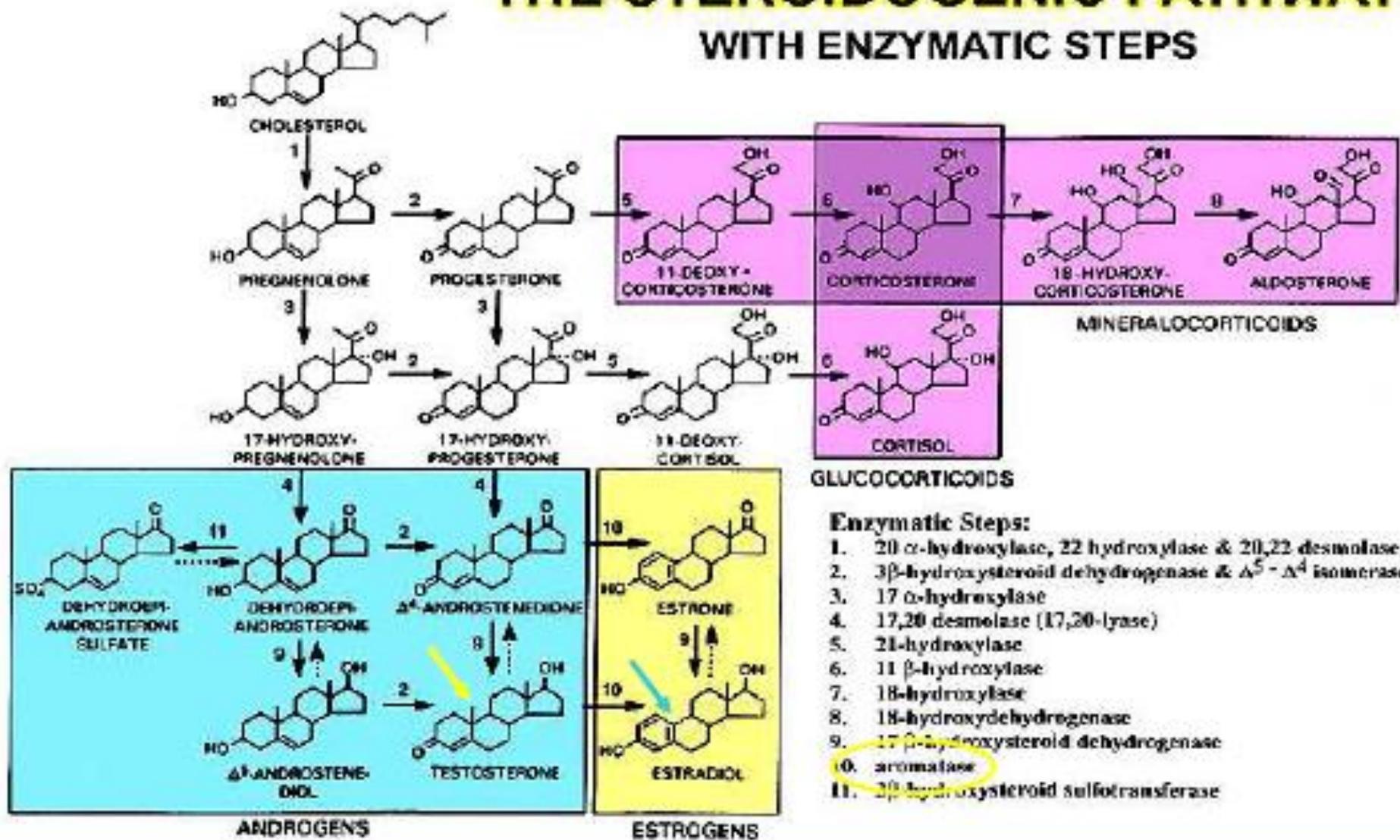
- A hormone is a substance that is produced in a special tissue where it is released into the bloodstream and travels to distant responsive cells in which the hormone exerts its characteristic effect.

Speroff L, Glass R, Kase N. *Clinical Gynecologic Endocrinology and Infertility*. 7<sup>th</sup> Edition, Lippincott Williams and Wilkins, Baltimore, MD, 2005, Pg. 25



**Figure 1.**—Differences in the chemical structures of natural progesterone and synthetic progestogens.

# THE STEROIDOGENIC PATHWAY WITH ENZYMATIC STEPS



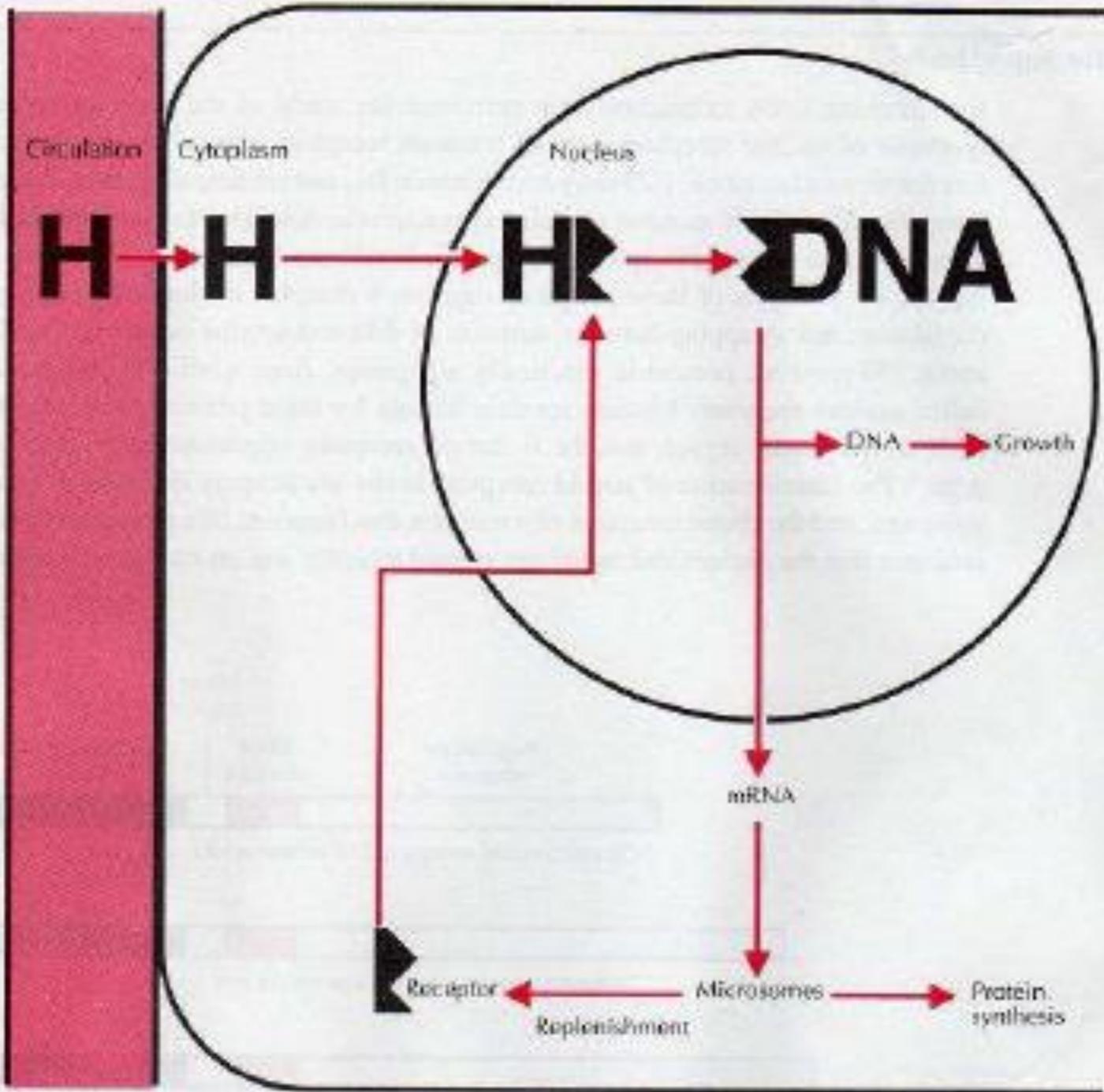
# Bound Vs. Free

	<b>Free (Unbound)</b>	<b>Albumin-Bound</b>	<b>SHBG-Bound</b>
<b>Estrogen</b>	1%	30%	69%
<b>Testosterone</b>	1%	30%	69%
<b>DHA</b>	4%	88%	8%
<b>Androstenedione</b>	7%	85%	8%
<b>Dihydrotestosterone</b>	1%	71%	28%

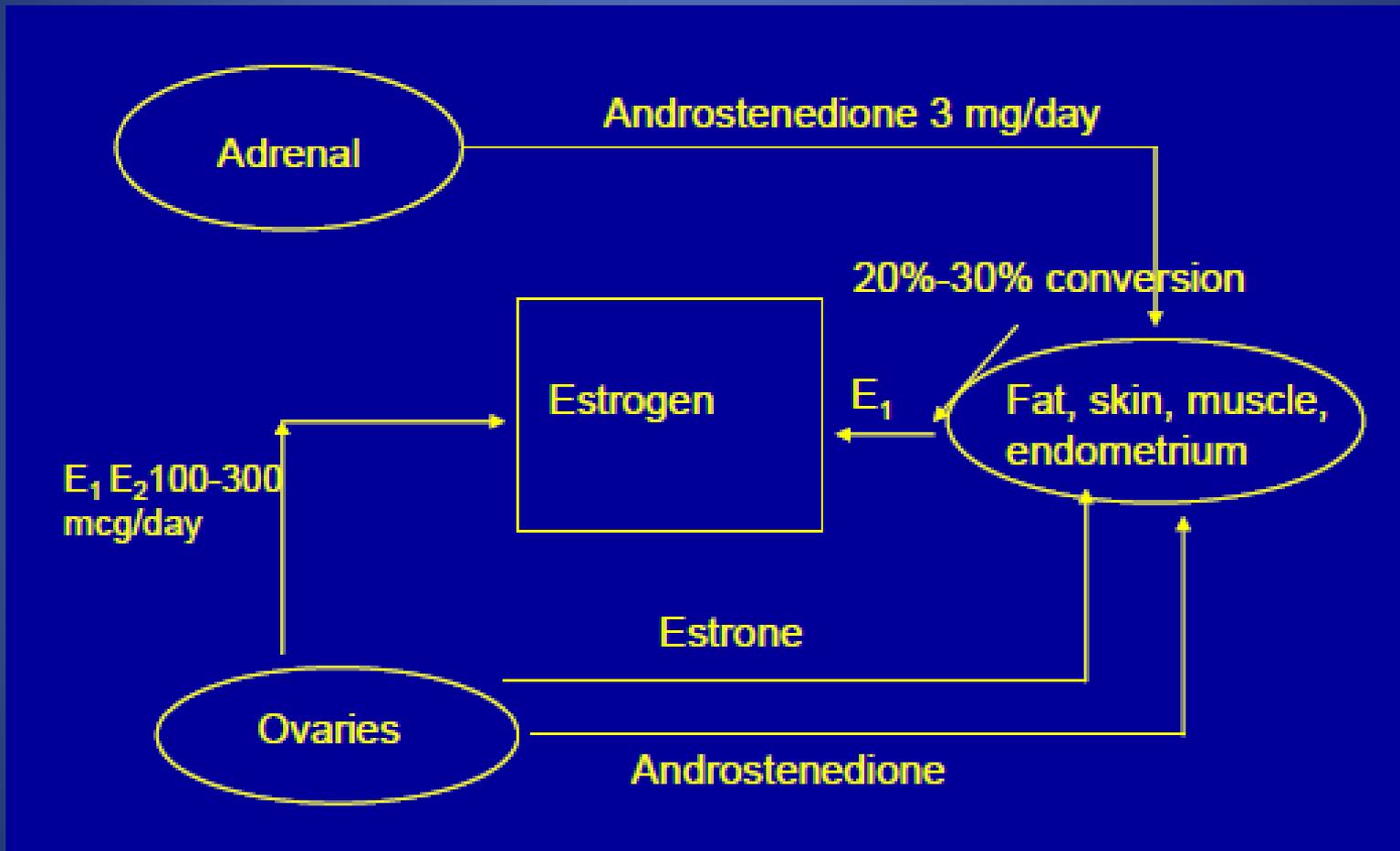
From Mendel<sup>9</sup>

- Steroid hormones cross the cell membrane by simple diffusion.
- The concentration of FREE hormone in the bloodstream seems to be an influential determinant of cellular function.
- Biologic activity is maintained only while the nuclear site is occupied with the hormone-receptor complex.

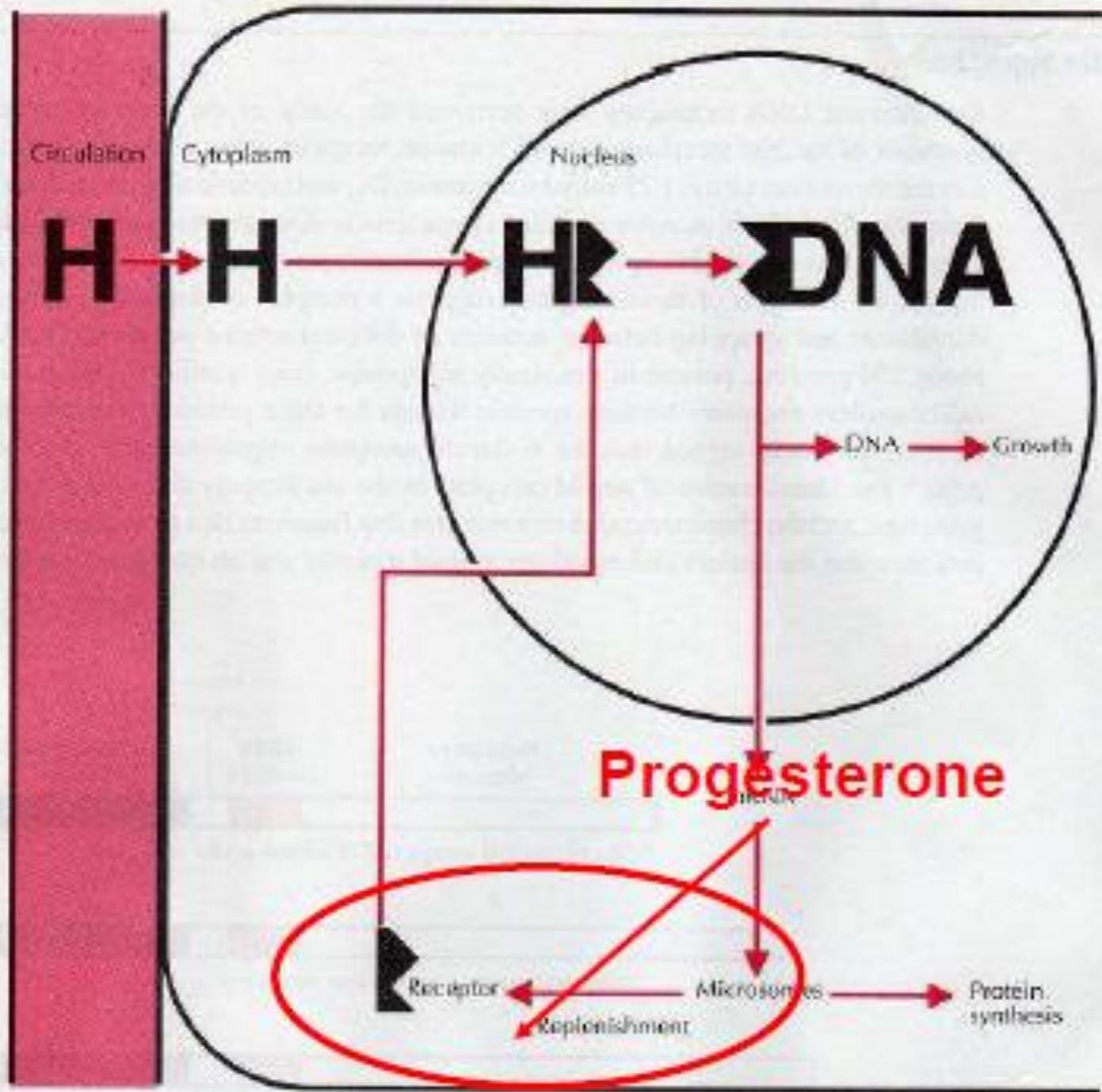
Speroff L, Glass R, Kase N. *Clinical Gynecologic Endocrinology and Infertility*. 7<sup>th</sup> Edition, Lippincott Williams and Wilkins, Baltimore, MD, 2005, Pg. 46



Because androstenedione is secreted in milligram amounts, even a small percent conversion to estrogen results in a significant contribution to estrogens



- DURATION of exposure to a hormone is *more important* than the DOSE.
- Estrogen increases target tissue responsiveness to itself and to progestins and androgens by increasing the concentration of its own receptor and that of the intracellular progestin and androgen receptors.  
(Replenishment). Progesterone blocks replenishment.

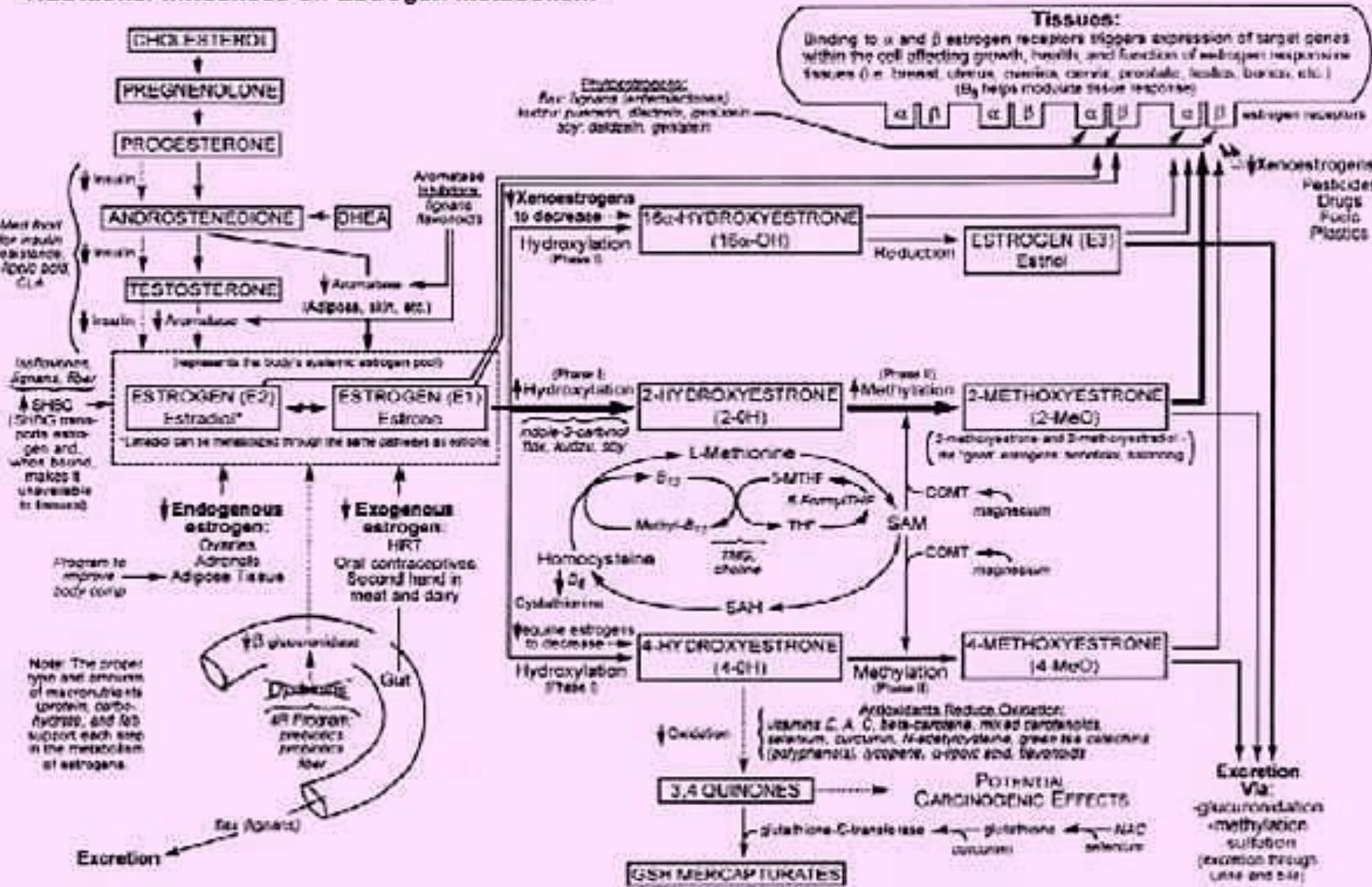


# Duration of Exposure

- Estriol has only 20%-30% affinity for the estrogen receptor compared with estradiol; therefore, it is rapidly cleared from a cell.
- But if the effective concentration is kept equivalent to that of estradiol, it can produce a similar biological effect.

Figure 1.

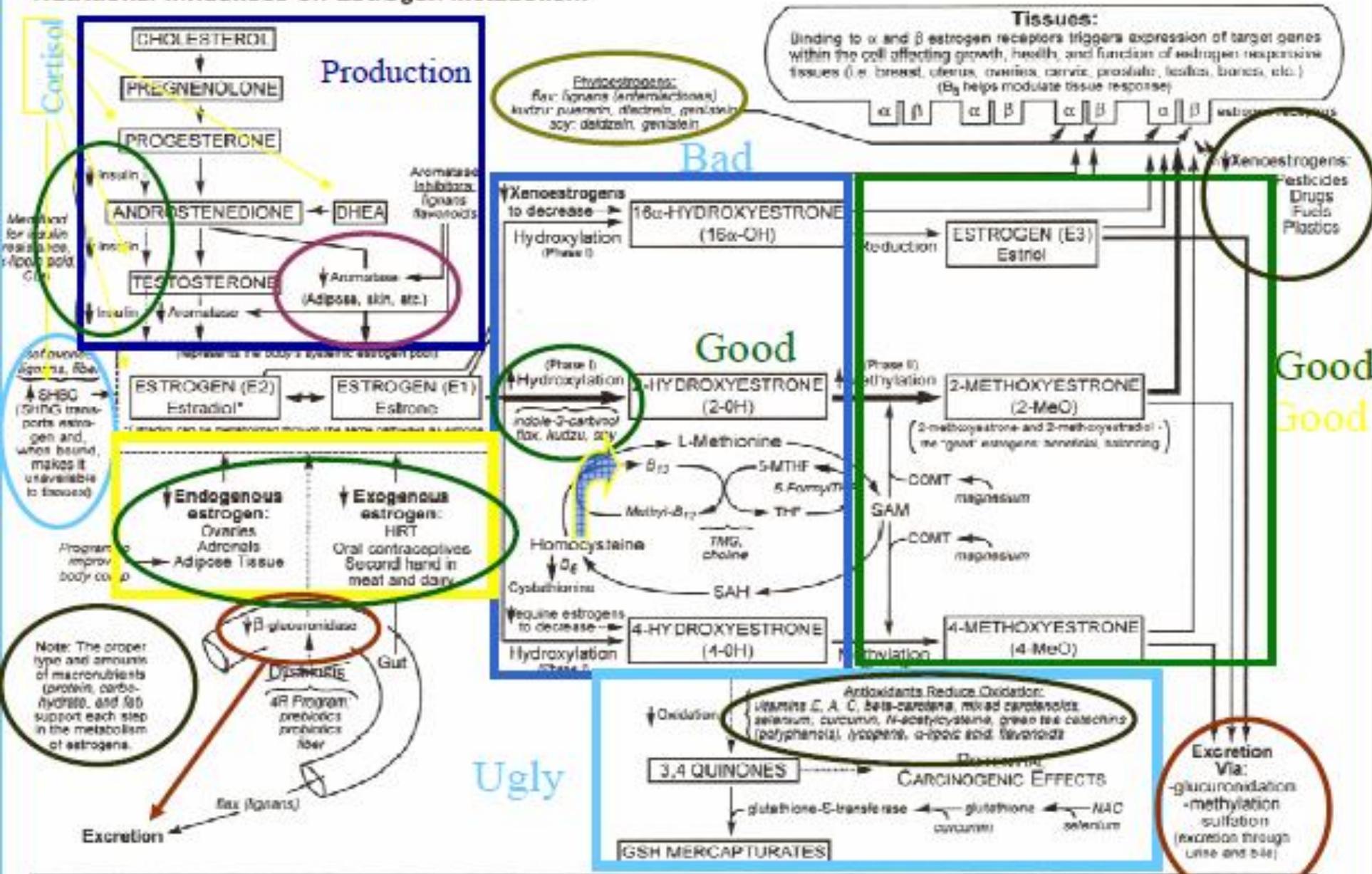
# Nutritional Influences on Estrogen Metabolism



Acronym Key: CLA: conjugated linoleic acid, COMT: catechol-O-methyltransferase, DHEA: dehydroepiandrosterone, S-Fornyl/THF: S-formyltetrahydrofolate, HRT: hormone replacement therapy, S-MTHF: S-methyltetrahydrofolate, NAC: N-acetylcysteine, SAM: S-adenosylmethionine, SAH: S-adenosylhomocysteine, SHBG: sex hormone binding globulin, THF: tetrahydrofolate, TMO: trimethylglycine, GSH: glutathione

Figure 1.

# Nutritional Influences on Estrogen Metabolism



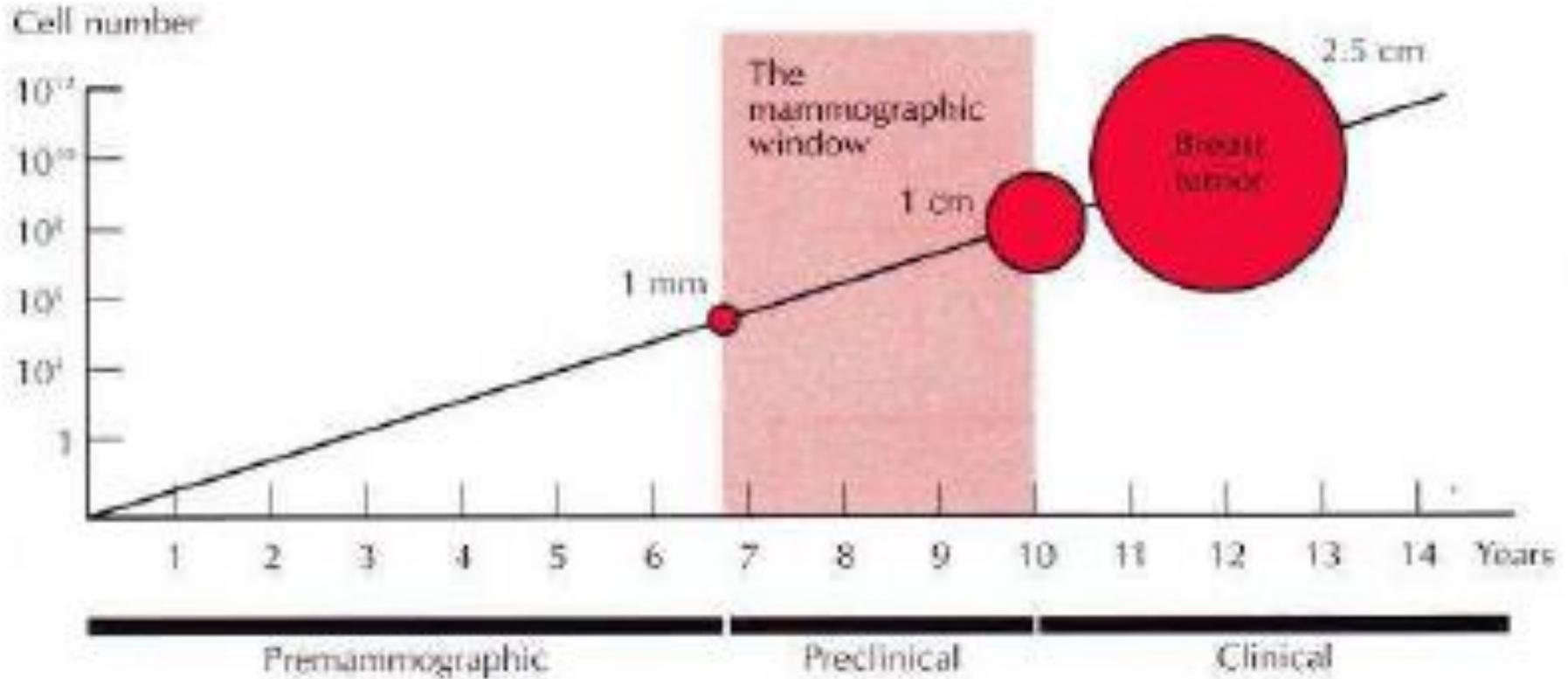
# Gynecology Made Simple

## Key Question:

*How Old Are You?*

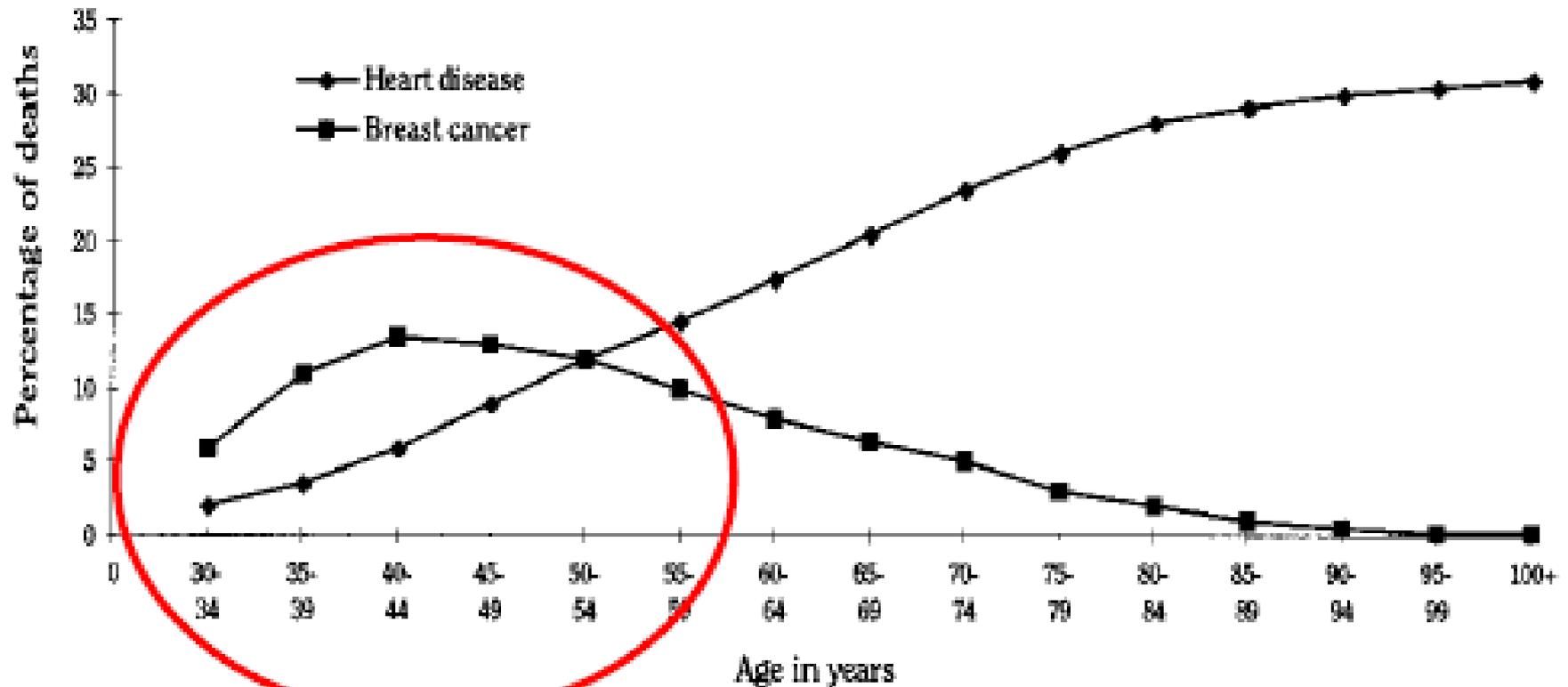
- < 45.....Birth Control Pills
- > 45.....Hormone Replacement
- < or > 45 Antidepressant
- No response to therapy.....Surgery

# Breast Cancer Detection



Speroff L, Glass R, Kase N. *Clinical Gynecologic Endocrinology and Infertility*. 7th Edition, Lippincott Williams and Wilkins, Baltimore, MD, 2005, Pg. 610

## Deaths from Heart Disease or Breast Cancer in Women in the U.S.



Breast cancer deaths peak between ages 40 and 50. The average age at menopause in the United States is 51, after which deaths due to coronary artery disease rise.

Source: National Center for Health Statistics: *Vital Statistics of the United States*. Vol. 11, Mortality, part B. OHHS Public Health Service Pub. No. (PHS) 90-1102, Washington, DC, US Government Printing Office, 1990.

# ACOG NEWS RELEASE



For Release: October 31, 2005  
Contact: ACOG Office of Communications  
(202) 484-3321  
[communications@acog.org](mailto:communications@acog.org)

## **No Scientific Evidence Supporting Effectiveness or Safety of Compounded Bioidentical Hormone Therapy**

**Washington, DC** – There is no scientific evidence to support claims of increased efficacy or safety for individualized estrogen or progesterone regimens prepared by compounding pharmacies, according to a new Committee Opinion released today by The American College of Obstetricians and Gynecologists (ACOG). Furthermore, hormone therapy does not belong to a class of drugs with an indication for individualized dosing. ACOG's opinion also points out that salivary hormone level testing used by proponents to "tailor" this therapy isn't meaningful because salivary hormone levels vary within each woman depending on her diet, the time of day, the specific hormone being tested, and other variables.

Compounded "bioidentical hormones" are plant-derived hormones that are prepared, mixed, assembled, packaged, and labeled as a drug by a pharmacist. These preparations can be custom made for patients according to a physician's specifications. "Bioidentical hormones" refer to hormones that are biochemically similar or identical to those produced by the ovaries or body.

According to ACOG, most compounded products, including bioidentical hormones, have not undergone rigorous clinical testing for either safety or efficacy. Also, there are concerns regarding

# Standard of Care is Determined By:

- Media
- Insurance reimbursement
- Drug patent
- Number of studies
- Number of drug representative visits
- CME sponsorship

# Good is the ENEMY of Great

John Collins author of  
Good to Great

“The Reason we Don’t have  
*Great*  
doctors is because we have  
*Good*  
Doctors.”

# Thinking for a Change

By John Maxwell

“The difficulty lies not so much in developing new ideas as in escaping the old ones.”

“Until we can get used to living with something that is not comfortable we cannot get any BETTER”

**“Even when we know the changes are going to be better for us and our Patients, we don’t make them because we feel uncomfortable or awkward.”**

**“*COURAGE:*  
The Power To Let  
Go of the Familiar.”**

**-John C. Maxwell**

# Menopause Summary

- Menopause is not a disease, but a time of transition and adaptation. The acute symptoms (hot flashes, night sweats, vaginal atrophy) give way to the chronic menopausal symptoms of accelerated aging.
- Start with the **TRANSCEND** approach if you are having a difficult menopause at any age.
- For mild to moderate discomfort start with herbal adaptogens such as Source Naturals' Hot Flash, Vitanica's Phase II, or MPM's RR-MSR.
- Especially if therapy is initiated before the age of 60, and carefully guided by your physician, true bioidentical hormone therapy with topical Bi-Est (80% E<sub>3</sub>/20% E<sub>2</sub>), topical or oral progesterone, and often topical testosterone can not only be symptom-relieving but essential to a healthy aging - well program.

# Thyroid

A Total Assessment

# Lab Studies to Evaluate Thyroid Function

- TSH
- Free T4
- Free T3
- Reverse T3
- Thyroid antibodies
  - Antithyroglobulin antibody
  - Antimicrosomal antibody
  - Antithyroperoxidase (anti-TPO) antibody

# Thyroid Hormone

- T4 – What is secreted from the thyroid, the storage form of thyroid with a long half -life, “ money in the bank”
- T3 – The bioactive form, “cash in the wallet”
- T2 - increases the metabolic rate of our muscles and fat tissue
- T1

# Signs and Symptoms of Low Thyroid Production

- Depression
- Weight gain
- Constipation
- Headaches/migraine headaches
- Brittle, ridged, striated, thickened nails
- Rough, dry skin
- Menstrual irregularities
- Fluid retention

# Signs and Symptoms of Low Thyroid Production

- Poor circulation
- Elbow keratosis
- Slow speech
- Nails that are easily broken
- Anxiety/panic attacks
- Decreased memory
- Inability to concentrate
- Muscle and joint pain

# Signs and Symptoms of Low Thyroid Production

- Reduced heart rate
- Slow movements
- Morning stiffness
- Puffy face
- Swollen eyelids
- Decreased sexual interest
- Cold intolerance
- Cold hands and feet

# Signs and Symptoms of Low Thyroid Production

- Swollen legs, feet, hands, abdomen
- Insomnia
- Fatigue
- Low body temperature
- Hoarse, husky voice
- Low blood pressure
- Muscle weakness
- Agitation/irritability

# Signs and Symptoms of Low Thyroid Production

- Sparse, coarse, dry hair
- Dull facial expression
- Yellowish discoloration of the skin
  - Inability to convert beta carotene into vitamin A
- Muscle cramps
- Drooping eyelids
- Carpel tunnel syndrome
- Sleep apnea

# Signs and Symptoms of Low Thyroid Production

- Endometriosis
- Hypercholesterolemia
- Infertility
- PMS
- Hyperinsulinemia
- Fibrocystic breast disease
- Nutritional imbalances
- Paresthesias
- Myxedema

# Signs and Symptoms of Low Thyroid Production

- Down turned mouth
- Acne
- Allergies
- Painful menstrual cycles
- Tendency to develop allergies
- Loss of the later 1/3 of the eyebrows
  - “Queen Anne’s sign” or “sign of Hertoghe”
- “Fat pads” above the clavicles

# Signs and Symptoms of Low Thyroid Production

- Hair loss in the front and back of head
- Loss of hair in varying amounts from legs, axilla, and arms
- Poor night vision
- Loss of eyelashes, or eyelashes that are not as thick
- Blepharospasm is more common
- Ear canal that is dry, scaly, and may itch
- Excess formation of cerumen in the ear canal

# Signs and Symptoms of Low Thyroid Production

- Iron deficiency anemia
- B12 deficiency
- Tinnitus
- Delayed DTR
- Low amplitude theta and delta waves on EEG
- Bipolar disorders
- Schizoid or affective psychoses

# Signs and Symptoms of Low Thyroid Production

- Dizziness/vertigo
- CHF
- CAD/MI
- Decreased CO
- Arrhythmias
- Increased risk of developing asthma
- Hypertension

# Signs and Symptoms of Low Thyroid Production

- Mild elevation of liver enzymes
- Gallstones
- Bladder and kidney infections
- Eating disorders
- Increased appetite
- Deposition of mucin in connective tissues
- Muscular pain

# Signs and Symptoms of Low Thyroid Production

- Arthralgias/joint stiffness
- Menorrhagia
- Recurrent miscarriage
- Nocturia
- Easy bruising
- Erectile dysfunction
- Hypoglycemia

# Signs and Symptoms of Low Thyroid Production

- Osteoporosis
  - Bone structure can become abnormally thickened and then weakened
  - Remodeling to stronger and thinner bones occurs with thyroid replacement
  - Takes 6-12 months for remodeling to occur

# Does Suppressing The TSH Cause Bone Loss?

- NO!
  - Wenzel, K., “Bone minerals and levoythyroxine,” *Lancet* 1992; 340:435-36
  - Franklin, J., et al., “Long term thyroxine treatment and bone mineral density,” *Lancet* 1992; 340:9-13.
  - Muller, C., et al., “Possible limited bone loss with suppressive thyroxine therapy is unlikely to have clinical relevance,” *Thyroid* 1995; 5(2):81-7.
  - Baldini, M., et al., “Treatment of benign nodular goiter with mildly suppressive doses of L-thyroxine: effects bone mineral density and on nodule size,” *Jour Int Med* 2002; 251(5):407-14.

# Factors That Cause Decreased Production of T4:

- Deficiency of zinc, copper, vitamins A, B2, B3, B6, C

# Conversion of T4 to T3

Requires 5' deiodinase production. There are three types of deiodinases.

- Type 1
  - Located in the thyroid liver and kidney
  - Plays an important role in the production of T3
- Type II
  - Found in the pituitary, hypothalamus, and brown fat
  - Converts T4 to T3
- Type III
  - Catalyzes deiodination of the inner ring of T4 and T3 which inactivates the hormone

# Elements That Affect 5'deiodinase Production

- Selenium deficiency
- Stress
- Cadmium, mercury, or lead toxicity
- Starvation
- Inadequate protein intake
- High carbohydrate diet
- Elevated cortisol

# Elements That Affect 5' deiodinase Production

- Chronic illness
- Decreased kidney or liver function
- Inflammation
  - Jakobs, T., et al., “Proinflammatory cytokines inhibit the expression and function of human type I 5' deiodinase in HepG2 hepatocarcinoma cells,” *Eur Jour Endo* 2002; 146(4):559-66.

# References

- Nishiyama, S. et al., “Zinc supplementation alters thyroid hormone metabolism in disabled patients with zinc deficiency,” *Jour Amer Coll Nutr* 1994; 13:62-7.
- Meinhold, H., et al., “Effects of selenium and iodine deficiency on iodothyronine deiodinases in brain, thyroid and peripheral tissue,” *JAMA* 1992; 19:8-12.
- Berry, M., et al., “The role of selenium in thyroid hormone action,” *Endocrine Rev* 1992; 13:207-20.
- Kohrle, J., “The deiodinase family, selenoenzymes regulating thyroid hormone availability and action,” *Cell Mol Life Sci* 2000; 57:1853-63.

# Other Factors That Cause an Inability to Convert T4 to T3

- Nutrient deficiencies
  - Iodine
  - Iron
  - Selenium
  - Zinc
  - Vitamins A, B2, B6, B12

# Factors Associated with Low T3 or Increased Reverse T3

- Increased E, NE
- Free radicals
- Aging
- Fasting
- Stress
- Prolonged illness
- Diabetes
- Toxic metal exposure
- Elevated levels of IL-6, TNF-alpha, IFN-2

# Treatment

- Detoxification
- Medication
- Nutrition
- Is soy intake a problem?

# Detoxification

- After detoxification, some patients no longer need treatment for hypothyroidism. All of these toxins affect thyroid function.
- PCBs
- Dioxins
- DDT
- HCB (hexachlorobenzene)
- Phthalates
- Heavy metals – lead, arsenic, mercury

# Treatment

- T4 has little physiological activity
- T4 must be converted to T3 to be utilized by the cells – conversion takes place in the liver and kidneys
- T3 is five times stronger than T4
- T4 has never been proven to be effective for treating the symptoms of hypothyroidism in any long-term study.

# Treatment

- Intracellular thyroid hormone receptors have a high affinity for T3.
- 90% of the thyroid hormone molecules that bind with the receptors are T3 and 10% are T4.
- If a patient is not able to metabolize thyroid (convert T4 to T3, then T3 to T2, and T2 to T1) then they will not be as healthy.
  - Kelly, G., “Peripheral metabolism of thyroid hormones: A review,” *Alt Med Rev* 2000; 5(4):306-33.
- Desiccated thyroid solves this problem

# Important to Replace Both T4 and T3

- T4 alone
- T3 alone
- Desiccated thyroid (both T3 and T4)
- Compounded thyroid replacement (both T3 and T4)

# Functions of T3

- Has direct effects on the mitochondria
  - Wrutniak-Cabello, C., et al., “Thyroid hormone action in mitochondria,” *Jour Mol Endocrin* 2001; 26:67-77.
- Has direct effects on the heart
  - Klein, I., et al., “Thyroid hormone and the cardiovascular system,” *NEJM* 2002; 344:501-09.

# T4 (Levothyroxine Sodium)

- Synthroid
- Levothyroid
- Levoxyl
- Eltroxin
  - All are immediate release
  - May contain lactose which can interfere with thyroid absorption. Absorption can vary from 48-80%.

# T3 (Liothyronine Sodium)

- Cytomel
- Triostat (injection)
- Liothyronine sodium (generic)
- All are immediate release

# Desiccated Thyroid Hormone

- Nature-Throid (T4 4.2 to T3 1)
- Armour (porcine) (ratio: T4 4 to T3 1)
- Thyroid USP (ratio: T4 4.2 to T3 1)
  - May contain lactose, sucrose, dextrose or starch – more than 99% of the contents are not thyroid hormone
- Liotrix (ratio: T4 4 to T3 1)
- Thyrolar (ratio: T4 4 to T3 1)
- Euthroid (ratio: T4 4 to T3 1)

# T4 vs. T3 + T4

- Lab results were not better but patients felt better when both T3 and T4 were replaced.
  - Escobar-Morreale, H., et al., “Thyroid hormone replacement therapy in primary hypothyroidism: a randomized trial comparing L-thyroxine plus liothyronine with L-thyroxine alone,” *Ann Int Med* 2005; 142(6):412-24.

# Optimal Thyroid Replacement

- TSH
  - 0.3-5.5 (N)
  - want below 2.0 (optimal)
- FT3
  - 2.3-4.3 (N)
  - 3.5-4.3 (optimal)
- rT3
  - 90-350 pg/ml (N)
  - 50-150 (optimal)

# What To Do If rT3 is Elevated

- Excess rT3 (stored thyroid hormone) will further inhibit conversion from T4 to T3.
- FT3 and rT3 occupy the same receptor sites. However, T3 will activate the receptor, rT3 will not. If rT3 is high the patient will have symptoms of hypothyroidism, even if labs are normal.
- Since rT3 is derived from T4 then lower the T4 dose or take the patient off of T4.
- Give T3. T3 will lower the TSH and subsequent production of T4 by the thyroid gland and inappropriate conversion to rT3.

# Other Genetic Thyroid Problems

- About 100 different mutations have been found in one of the primary genes for thyroid receptors. Receptors that are not functioning optimally may prevent a sufficient supply of hormones that are in the blood from reaching the mitochondria and the nucleus of the cell.
  - Brucker-Davis, F., et al., “Genetic and clinical features of 42 kindreds with resistance to thyroid hormone, The National Institutes of Health prospective survey,” *Ann of Int Med* 1995; 123(8):572-83.

# Thyroid and CRP

- Elevated CRP levels are associated with hypothyroidism.
  - Christ-Crain, M., et al., “Elevated c-reactive protein and homocystiene values: cardiovascular risk factors in hypothyroidism? A cross-sectional and double-blind, placebo-controlled trial,” *Atherosclerosis* 2003; 166(2)379-86.

# Increased Homocysteine and Hypothyroidism

- Homocysteine levels are commonly elevated in hypothyroid patients. Mean level of this study was a homocysteine level of 16.3.
  - Nedrebo, B., et al., “Plasma total homocysteine levels in hyperthyroid and hypothyroid patients,” *Metabolism* 1998; 47(1):89-93.

# Thyroid Function and Cardiac Death

- Low T3 is a strong predictor of death in cardiac patients.
  - Iervasi, G., et al., “Low T3 syndrome, a strong prognostic predictor of death in patients with heart disease,” *Circulation* 2003; 107:708.

## **rT3 and CV Disease**

- Elevated rT3 strongest predictor of mortality in first year post acute MI.
  - Friberg, L., et al., “Association between increased levels of reverse triiodothyronine and mortality after acute myocardial infarction,” *Amer Jour Med* 2001; 111(9):699-703.

# Thyroid Hormone Summary

- Every one who has a low body temperature does not necessarily have hypothyroidism.
- Even with a comprehensive panel (including TSH,  $fT_3$ ,  $fT_4$ , and reverse  $T_3$ ) your doctor can't tell for certain whether your overall thyroid metabolism is optimal without discussing your symptoms.
- We can measure the "keys" (hormones) to the doors (receptors), but there is no certain way to assess how well the hormone-receptor complex is activating its specific effects.
- If your doctor refuses to measure anything other than a  $T_4$  and TSH, you need a new doctor. Endocrinologists are the last MDs to discuss this with, as they have been the most resistant to even try to understand this material.
- Max Planck - **A new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die, and a new generation grows up that is familiar with it.**

# Adrenal Fatigue

Adrenal Fatigue: The 21st  
Century Stress Syndrome  
*Anti-Aging & Functional Medicine  
Fellowship*

James L. Wilson, DC, ND, Ph.D.

September 10, 2009

San Jose, CA

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Adrenal Fatigue is one of the most pervasive, yet under-diagnosed health conditions affecting people today.

- The decrease in optimal adrenal function has become a common occurrence in modern society with far reaching implications for most organs and systems.
- It includes all ages, occupations, races, social and economic groups.
- In older persons, it contributes to the combined processes of aging.

Adrenal Fatigue occurs both as a distinct clinical disorder and as a contributing factor to many chronic illnesses.

- However, in a typical clinical practice, the concept of low adrenal function is usually limited to the more or less classic Addison's disease with all the subtle increments between normal and Addison's being ignored.
- Doctors see Adrenal Fatigue sufferers in their offices every day.

Yet Adrenal Fatigue is seldom detected by most practicing health care professionals.

- It is not looked for.
- It is not properly diagnosed when the signs & symptoms are present.
- It is seldom properly treated even if recognized.
- Their patients are left to wander from doctor to doctor in search of help that often never comes.

# Difficulties in Determining Subtle or Sub-clinical Endocrine Problems

1. Difficulties in relying primarily on endocrine lab test interpretations
2. The classic signs & symptoms are not the common ones.
3. Symptoms usually precede signs, which usually precede syndromes; but diagnosis is usually from syndromes.

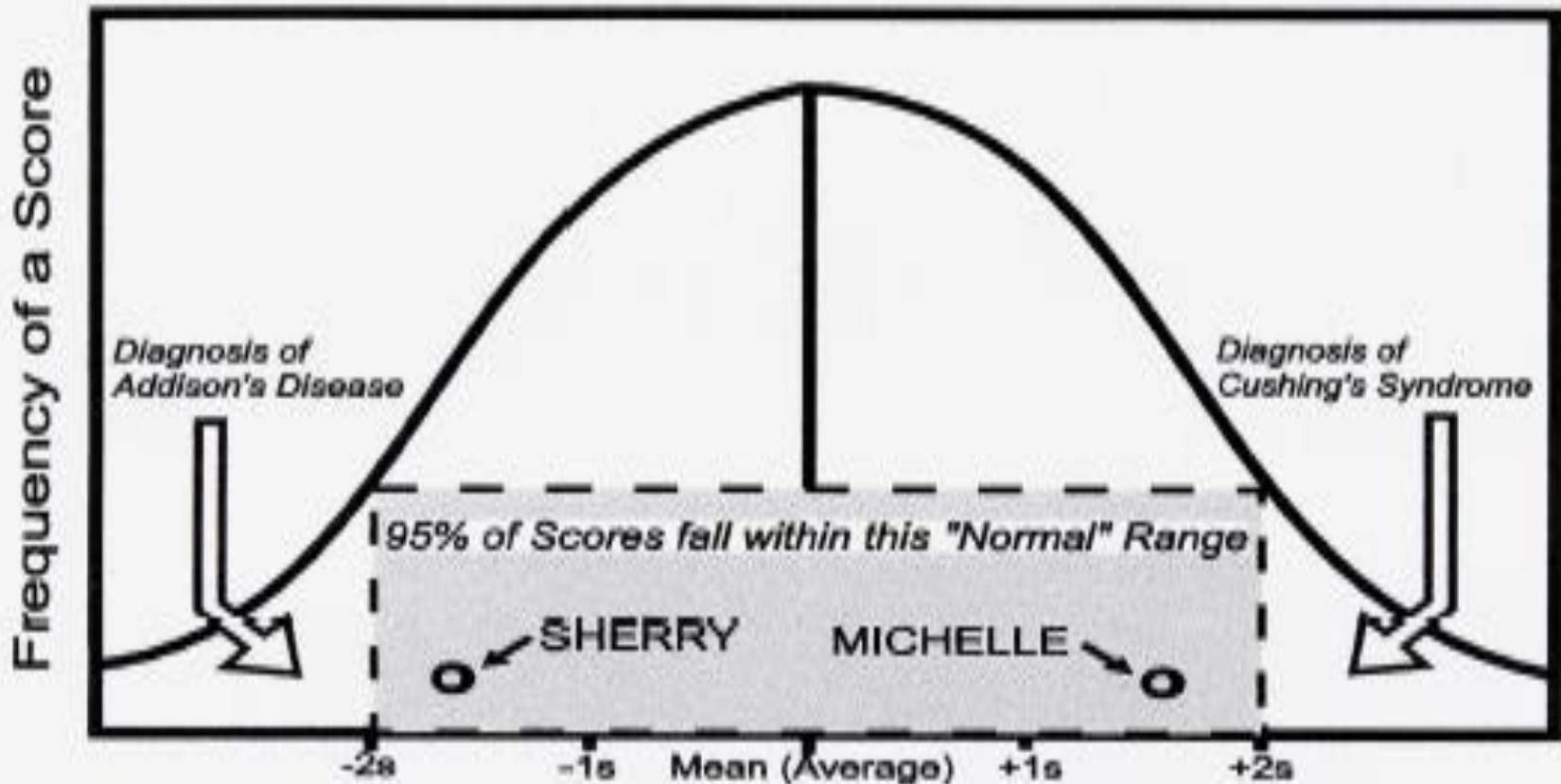
# Difficulties in relying primarily on endocrine lab test interpretations

- Tests are defined according to statistical norms instead of physiologically optimal norms, leading to a deceptively broad laboratory range of “normal” functioning
- No reference ranges for optimal functioning or allowance for biochemical individuality

# Difficulties in relying primarily on endocrine lab test interpretations

- Hormone receptor sensitivity usually not measurable
- Blood concentrations of some hormones change so subtly that the changes cannot be detected by standard lab tests
- Diurnal or cyclic hormonal variations typically not provided as part of standard reference ranges

## Variation in "Normal" Values between Individuals



*Both test results shown would be considered to have Normal Cortisol Values*

# *What are the Adrenal Glands?*

- The adrenal glands are two small glands that sit over the kidneys.
- They secrete over 50 hormones such as:
  - epinephrine (adrenaline)
  - Cortisol
  - Progesterone
  - dehydroepiandrosterone (DHEA & DHEAs)
  - Estrogen
  - Testosterone

# The Adrenal Glands

## In Females:

- The only appreciable source of DHEAS and testosterone in females.
- After menopause, are the major sources of estrogen and progesterone.

## In Males:

- Are the only source of DHEAS, estrogen and progesterone in males.
- After andropause, are the major sources of testosterone.

# *The Adrenal Glands Are Necessary for Life*

- Energy Production – controls carbohydrate, protein and fat conversion to blood glucose
- Fluid and electrolyte balance in cells, interstitial fluid and blood stream
- Fat Storage
- Sex hormone production - especially after menopause

# Optimal Adrenal Health is One of the Major Keys to the Enjoyment of Life.

- We can't live without the adrenals.
- We can't live very well when the adrenals are depleted.

# Adrenal Fatigue Is Adrenal Depletion

- If the adrenals are totally depleted, it is called Addison's disease and can be a medical emergency, that can even result in death.
- However, most people who have depleted adrenal glands are not medical emergencies, but drag themselves through life not knowing what is wrong with them.
- These people are suffering from Adrenal Fatigue.

# Definition of Adrenal Fatigue

- The sub-optimal functioning of the adrenal glands:
  - At rest
  - Under stress
  - In response to constant, intermittent or sporadic demands

- 1898 - Adrenal Fatigue was first described by Emile Sargent in France as a sequela to severe influenza.
  - (Sargent, Emile. *Estudies cliniques sur l'insuffisance surrenale*. A Maloine et fils. 1920 Second Edition. Paris: p423.)
- During the 1930s Adrenal Fatigue was recognized and successfully treated by tens of thousands of physicians.
  - (Harrower'39)

- The adrenal glands are the glands of stress, but are the first glands to fail under stressful conditions. (Selye)

## Stresses are Additive and Cumulative:

- The more stressors,
- The greater the intensity of each stress,
- And the longer they last,
- The higher the cumulative stress load.

“In the beginning, disease is difficult to recognize but easy to cure. In the end, disease is easy to recognize, but difficult to cure.”

(Mesmer - 1777)

# Onset of Adrenal Fatigue

- After a long period of stress or one severe stressful event (mental stress, trauma, burns, toxemia, auto accident, etc.)
- After someone has driven themselves to exhaustion
- Overwork with little play or relaxation for extended periods
- After extended or severe respiratory infections - flu, bronchitis, pneumonia, tuberculosis

# Onset of Adrenal Fatigue

- History of a “nervous break-down”
- Previous heavy or binge drinking or drug intake
- Intense participation in competitive sports
- After \_\_\_\_\_, I was never the same.

# Human Stress Adaptation Model Varies From Selye's G.A.S. Animal Model

“The phenomenon of hypocortisolism has received growing attention in the field of stress research, in as much as it challenges, or virtually reverses, prevailing concepts on the neuroendocrinology of stress.”

# Human Stress Adaptation Model Varies From Selye's G.A.S. Animal Model In That:

- A person may remain in the resistance or mild exhaustion phase for months or years
- There are variable patterns of collapse & recovery
- The person usually remains somewhat functional
- Adrenal Fatigue is frequently related to other clinical conditions
- Recovery is possible

# Blood Tests Indicating Adrenal Fatigue

- Plasma Free Cortisol - Reference ranges
  - 8:00 AM 2-25 mg/dl (optimal 15-22)
  - 4:00 PM 3-16 mg/dl (optimal 10-14)
    - > 4 years of age= same ref. range as adult
  - Typical lab reference ranges are excessively broad and therefore, do not detect most cases.
  - Suspect low adrenal function if symptoms are present and results are lower than optimal levels.

# Salivary Adrenal Function Test:

## The Preferred Test for Adrenal Fatigue

- Use 1 day collection (4 vials) as baseline.
- Have patient record S&S, date and time of sample on separate sheet.
- If possible, take blood sugar at same time as cortisol level.
- Test other steroid hormones.

# Salivary Adrenal Function Test:

Adrenal Cortex – salivary adrenal hormone test

- Salivary cortisol (4 times daily)
- DHEAS
- Progesterone
- Estrogens
- Testosterone

# Adrenal Fatigue: Lifestyle Changes

- Laughter - very important\*
- Lie down during work breaks
  - Brief (15-30 minute rest) at 10:00 AM &
  - Brief (15-30 minute rest) between 3-5:00 PM
- Regular relaxation\*

# Adrenal Fatigue: Lifestyle Changes

- Breathing exercises
- Daily break for enjoyment\*
- Regular meals - chewing food well\*
- Exercise - avoid highly competitive events
- Early to bed 9-9:30 PM
- Sleep in until (9AM) whenever possible

\*= Parasympathetic enhancers (remember the adrenals have no parasympathetic nerve control)

# Nutritional Support for the Adrenals

- Diet
  - Combine unrefined carbohydrates (whole grains) with good quality protein and oils (nuts and seeds) at most meals
  - Use cold pressed oils - olive, walnut, filbert, flax
  - Eat by 10:00 AM and again before noon
  - Eat regular meals
  - Avoid junk food
  - Especially avoid hydrogenated fats and caffeine

# Nutritional Support for the Adrenals

- Phenylalanine (DLPA) 1,500-2,250 mg/ day
- Vitamin C 2-4 gm/ day
  - with bioflavonoids in a 2:1 ratio of ascorbic acid to bioflavonoids
  - sustained release
  - pH balanced
  - contains mineral for metabolizing Vit. C in adrenals
- Pantothenic acid 1,000-1,500 mg/ day

# Nutritional Support for the Adrenals

- Vitamin E with mixed tocopherols 800 IU
- B-complex high in niacin(25+ mg) and niacinamide (125 mg)
- B6 (pyridoxine) 250 mg/day with pyridoxal 5' phosphate (10 mg). B6 is both a fatty acid metabolizer and a cofactor for several adrenal hormone enzymes
- Biotin (1000 mcg)

# Nutritional Support for the Adrenals

- Calcium(malate, citrate, glycinate) 800 mg
- Magnesium (malate, citrate, glycinate) 400 mg
- Organic trace minerals - calming effect – see note below
- Electrolyte replacement fluids high in sodium and chloride - if hyperirritability or other side effects develop upon their administration, adrenal failure may be suspected.

# Glandular Extracts

- The Key to Recovery
- Multi-glandular extracts designed for adrenals
- The best ones contain adrenal, hypothalamus, pituitary, thyroid, and gonadal tissue.

# Herbal Remedies

- Licorice, a specific for hypoadrenia, do not exceed  $\frac{1}{4}$  lb per day to avoid increase in BP (contraindicated in cases of hypertension)
- Ashwagandha
- Maca
- Siberian Ginseng
- Korean Ginseng (for men)

The above multi-glandulars, nutrients and herbals are now available in precisely balanced formulas to save you time, effort and money.

## Steroid (Adrenal & Gonadal) Therapy

- Hormones should never be given without continual monitoring including baseline levels before therapy is begun.

# Adrenal Hormones

## DHEA

- Male dosage 25-200 mgs/day divided into 2-4 doses
- Female dosage 5-25 mgs/day divided into 2 doses
- Signs of excess DHEA supplementation:
  - Females - acne & facial hair usually the first signs of excess. Weight gain.
  - Males - increased aggressiveness, hostility, mood swings, irritability.

# DHEAS

## GENERAL COMMENTS

- Cortisone (cortisol) treatment may decrease DHEAS levels. (Neilson, et al '94)
- Hyposecretion of DHEAS was more pronounced in the obese.
- “Sympathetic hyperactivity may be a common denominator for low levels of DHEAS in inflammatory and noninflammatory diseases.”
  - (Kizildere, S et al '03)

# Adrenal Hormone Precursors

- Pregnenolone
  - 10 - 50 mg bid male & female (or 150 mg micronized, time released/day)
  - Signs of excess - acne & facial hair usually first signs of excess
- Progesterone transdermal (female) –  $\frac{1}{4}$  to  $\frac{1}{2}$  tsp (5-50 mg) twice per day

# Adrenal Comments:

- Adrenal Fatigue takes time to heal
  - Mild – 6 to 9 months with treatment
  - Moderate – 12 to 18 months
  - Severe – 12 to 24+ months
- Suspect Adrenal Fatigue whenever morning fatigue is present.

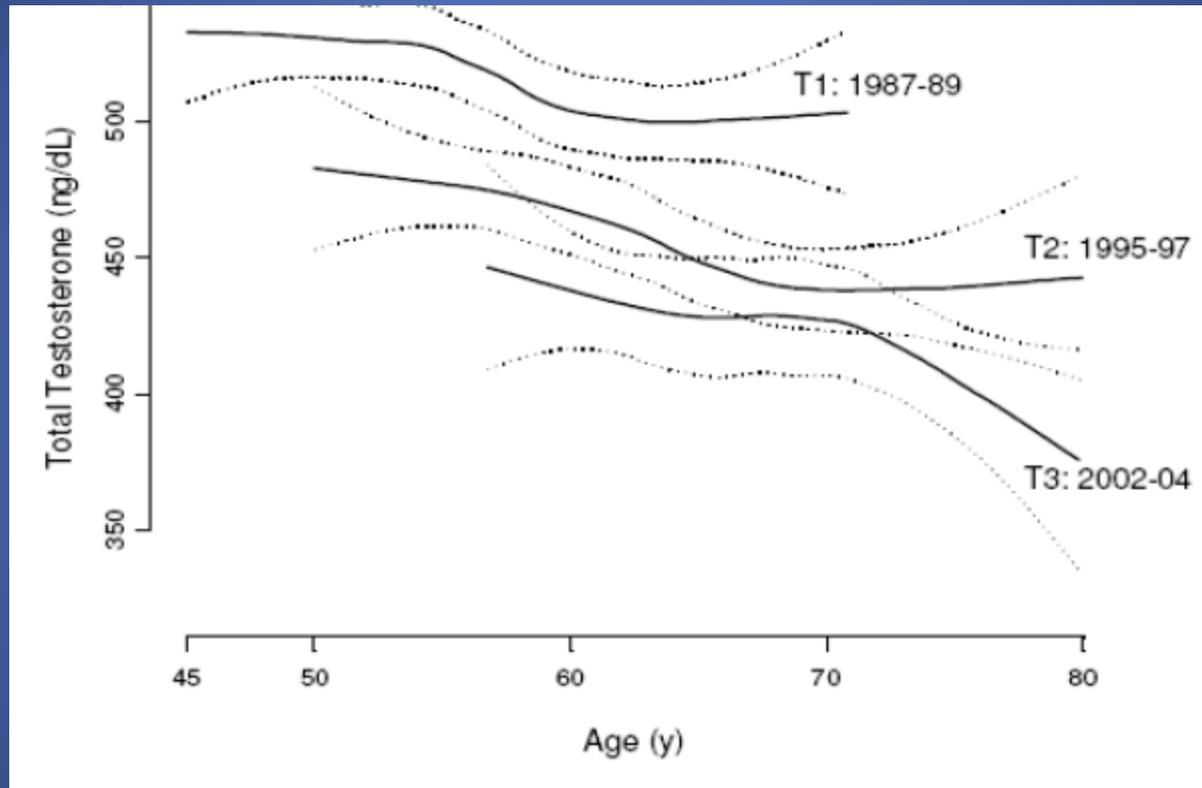
# Testosterone

Andropause: The Male  
Menopause

# Testosterone Levels Decline From 30's

- Testosterone decline occurs in men from late 30's onwards:
  - decline of total testosterone is slow and gradual as are appearance of symptoms.
  - Decline of bioavailable T is profound with decline of approx. 50% by age 50 because SHBG goes up.

# Testosterone levels have declined ~15% from 1987 to 2004



Travison TG et al. *A population-level decline in serum testosterone levels in American men.* J Clin Endocrinol Metab. 2006 Oct 24

# Testosterone

## Major Symptoms of Deficiency

- Decreased sex drive and sexual function
- Poor cognition, memory
- Fatigue
- Pain in joints and muscles
- Loss of muscle/ fat gain
- Loss of bone
- Loss of confidence
- Depression/ anxiety in men

# Testosterone Deficiency: Major Associated Diseases

- Bone loss, osteoporosis
- Weight gain
- Sarcopenia, increased fat
- Arthritis
- Poor cognition, brain fog, Dementia, AD
- High cholesterol
- Diabetes
- Heart attacks and stroke

Stress associated pituitary suppression is the major cause of low levels in young men, therefore reduction of stress and pituitary stimulation are to be considered in younger men (<45 years old)

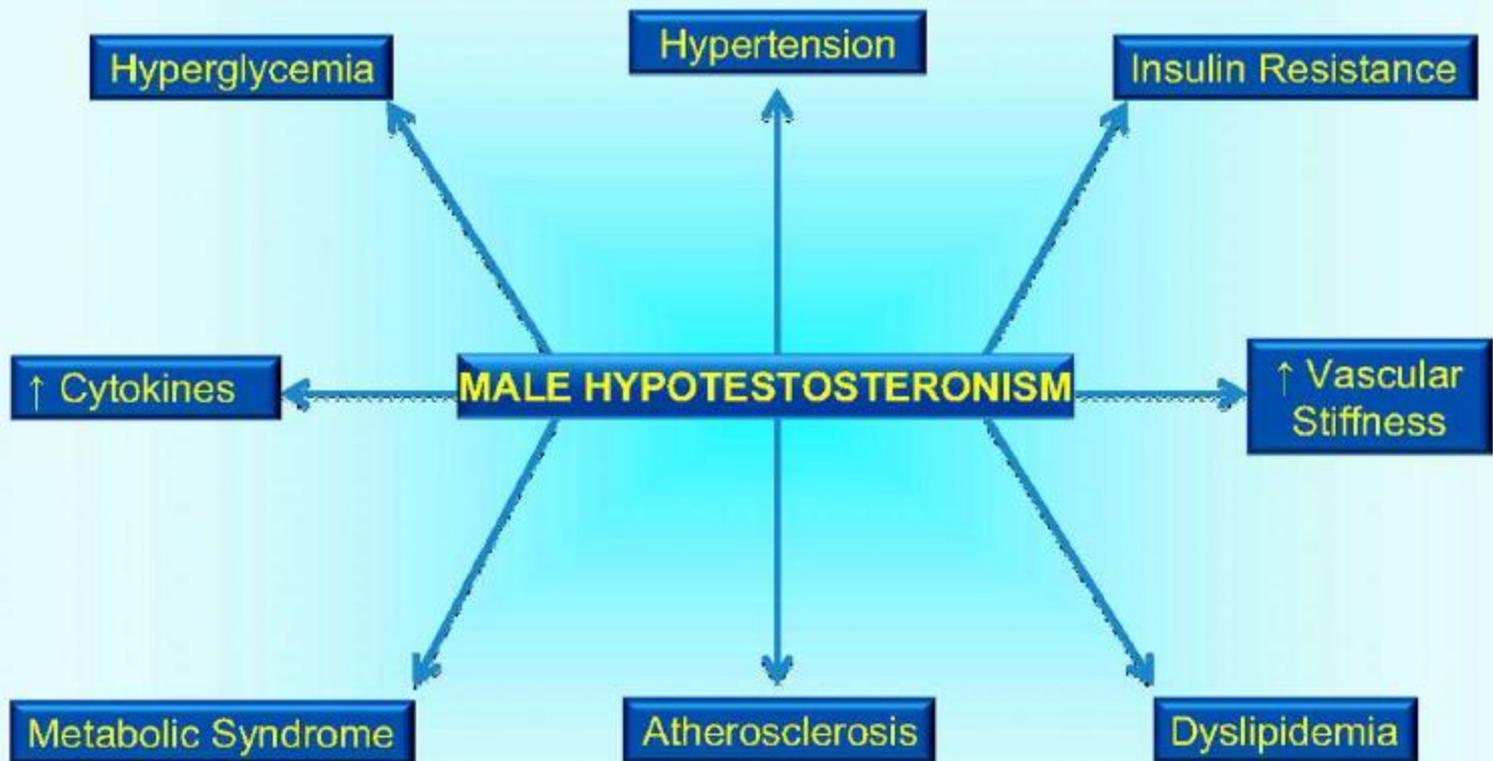
# High endogenous T = Low Mortality *cv disease and prostate cancer*

- 10 year prospective study
- 11,606 men – 40-79 years old
  - This study was of endogenous T not treatmentHigh T =
    - no increase in Prostate Cancer
    - low mortality from CV disease and cancer
  - Low T = high mortality from CV disease

# High endogenous T = Low Mortality

- 41% decrease in chance of dying in men with serum T >564 compared to 350
- For each increase in 173, chance of dying went down 14%
- Extrapolating:
  - Comparing T 300 to 1000
  - 57% decrease in chance of dying

*Khaw KT. et al. Endogenous testosterone and mortality due to all causes, cardiovascular disease, and cancer in men. Circulation. 2007;116:2694-2701*



From Dr Ron Rothenberg 2008

# Cardiac Data:

- *Heart Attacks/ stroke.* The cardiology and neurology literature is documenting at an increased rate the cardiovascular protective effects of testosterone in men.
- Men who maintain testosterone levels at the upper quartile of the range (800-1100 ng/dL) have much lower cardio and vascular mortality and morbidity.

# T Improves Cognitive Function

- T correlated with cognitive function and TRT improves it
  - *Alexander GM, Swerdloff RS, Wang C, et al. Androgen-behavior correlations in hypogonadal men and eugonadal men. II. Cognitive abilities. Hormones and Behavior 1998; 33(2):85-94.*
  - *Barrett-Connor E et al. Endogenous sex hormones and cognitive function in older men. J Clin Endocrinol Metab 1999 Oct;84(10):3681-5*
  - *J Clin Endocrinol Metab. 2002 Nov;87(11):5001-7 (memory)*

# T and Cognitive – Cerebral Blood Flow

- High Free T was associated with better performance on tests of memory, executive function, and spatial ability, and with a reduced risk for Alzheimer's disease.
- Improved cerebral blood flow
  - *Moffat SD, Resnick SM. Long-term measures of free testosterone predict regional cerebral blood flow patterns in elderly men. Neurobiology Aging. 2006 May 11*

# Testosterone improved memory in Alzheimer's

- Treated group improved over 1 year
- Control group deteriorated
  - *Tan RS A pilot study on the effects of testosterone in hypogonadal aging male patients with Alzheimer's disease. Aging Male. 2003 Mar;6(1):13-7.*
  - TRT prevents Alzheimer's peptide (beta- amyloid precursor protein) in men *Proc Natl Acad Sci USA 2000 Feb 1;97(3):1202-5*

# T Improves Depression

- TRT decreases depression in men with refractory depression and low testosterone
  - *Am J Psychiatry* 2003, Jan;160(1):105-111
  - *Am J Psychiatry* 157:1884, Nov 2000
- TRT increases sense of well-being and energy, many stop anti-depressant meds (SSRI)
  - *J Geriatr Psychiatry Neurology* 2000 Summer;13(2):93-101
- T works when psych drugs do not work in pts with low T
  - Cooper MA. *Testosterone Replacement Therapy for Anxiety Am J Psychiatry* 157:1884, November 2000

# T Increases Spontaneous Erections

- TRT increases nocturnal and spontaneous erections and improves mood
  - *Burris A et al. A long-term, prospective study of the physiologic and behavioral effects of hormone replacement in untreated hypogonadal men. J Androl 1992 Jul-Aug;13(4):297-304*

# Testosterone in Men-

## Indications:

- *Diabetes.* Testosterone is critical for the regulation of insulin and blood sugar. As testosterone is restored in diabetics, their need for insulin declines.

# Low T Correlates with Metabolic Syndrome

- Low T levels correlate with
  - increased central obesity
  - increased systolic BP
  - Diabetes and high HgbA1c
    - *Svartberg J. Epidemiology: testosterone and the metabolic syndrome. Int J Impot Res. 2006 Jul 20*

# T Improves Insulin Resistance and Diabetes

- Decreased Hgb A1c by 17%
- Decreased abdominal obesity
- Decreased FBS
  - Testosterone supplementation in men with type 2 diabetes, visceral obesity and partial androgen deficiency.
    - Boyanov MA, Boneva Z, Christov VG. *Boyanov MA, Aging Male* 2003 Mar;6(1):1-7

# Myth of Cancer

- If Testosterone causes cancer, why don't men get cancer at age 18?
- In fact, Low testosterone and low GH are associated with prostate cancer
  - *Tech Urol 2000 Sep;6(3):236-9 (Low IGF-1 assoc with prostate cancer)*

# NEJM Testosterone Review

- Reported that TRT associated with no increase in prostate cancer
  - *Rhoden EL, et al. Medical Progress: Risks of Testosterone replacement therapy and recommendations for monitoring N Engl J Med 2004; 350:482-492 Jan 29,2004*

# T & Prostate Cancer

- Low free T correlates with positive prostate biopsy and Gleason Score
- High T does not correlate with PSA or cancer stage
  - *J Urol* 2000 Mar;163(3):824-7 *Is low serum free testosterone a marker for high grade prostate cancer?* Hoffman MA, DeWolf WC, Morgentaler A.
- Declining androgens are a risk factor
  - *Eur Urol* 2002 feb;41(2):113-20 *Androgen replacement therapy and prostate safety.* Morales A.
  - *Cancer Res* 1999 Sep 1;59(17):4161-4 *On the prevention and therapy of prostate cancer by androgen administration.* Prehn RT.
  - *Prostate* 2001 Apr;47(1):52-8 *High-grade prostate cancer is associated with low serum testosterone levels.* Schatzl G et al. *Prostate.* (2001)
  - *Br J Urol* 1996 Ma;77(3):433-40 *Dihydrotestosterone and testosterone levels in men screened for prostate cancer: a study of a randomized population.* Gustafsson O, Norming U, Gustafsson S, Eneroth P, Aström G, Nyman CR.
- Increasing Estrogen is a risk factor
  - *Urology* 2001 Apr;57(4 Suppl 1):31-8

# High T : Lower Prostate Cancer

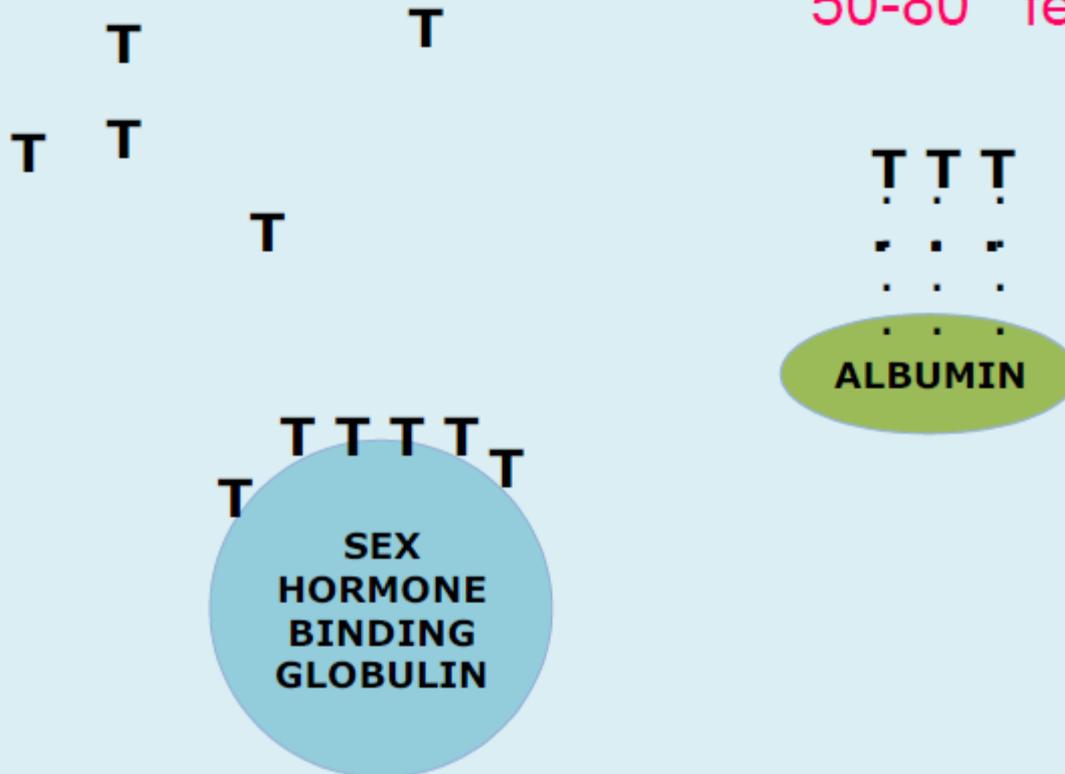
- Upper 1/4 of T levels have relative risk of 0.82 compared with lower levels
- Upper 1/4 of Free T levels had relative risk of 0.72
  - *Cancer Epid Biomarkers Prev* 2003 Dec;12(12):1410-6 no support
  - *Int J Cancer* 2004, Jan 20;108(3):418-24 *High levels of circulating testosterone are not associated with increased prostate cancer risk: a pooled prospective study.* Stattin P, Lumme S, Tenkanen L, Alfthan H, Jellum E, Hallmans G, Thoresen S, Hakulinen T, Luostarinen T, Lehtinen M, Dillner J, Stenman UH, Hakama M.

# Estrogen Estrone-E1 in Men

E1 and E2 levels increase as testosterone is converted in fat tissue. These are undesirable as they increase prostate cancer and cardiac risk.

# TOTAL TESTOSTERONE

T Optimal 750-1100 male  
50-80 female

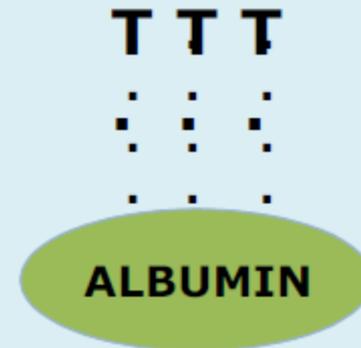
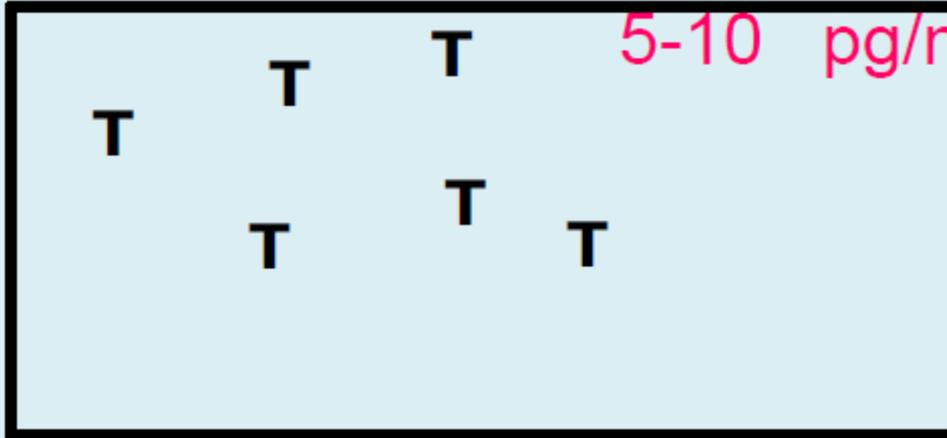


Dr Ron Rothenberg 2008

# FREE TESTOSTERONE

Optimal 20-35 pg/ml male

5-10 pg/ml female



Dr Ron Rothenberg 2008

# HCG injections

- Human chorionic gonadotropin (HCG)
- Polypeptide hormone produced by the human placenta
- Alpha and beta sub-unit.
- Alpha sub-unit is essentially identical to the alpha sub-units of LH and FSH
- Directly stimulates Leydig Cells (90% effective)

# HCG

- 2000-5000 units per week sub-q - divided
- No decrease in testicular size or sperm count
- Can use as TRT (measure free T to confirm success) or cycle with TRT every 6 months
  - *Zitzmann M Hormone substitution in male hypogonadism Mol Cell Endocrinol 2000 Mar 30;161(1-2):73-88*

# HCG in Men

- Start sc as HCG 250-500 IU sc M,W,F or daily in AM or bedtime. HCG Vial comes prediluted as 10,000 IU/10cc (=1000IU/cc), so .25cc=250IU
- May also rotate with 3 months on and 2-3 months off to avoid autoantibodies.
- Recheck levels in 3 weeks, the day after injection. May increase by 100 IU each time upwards to HCG 5000 IU per week (=700 IU per day), until desired effect reached. Some notice better result with smaller daily dose, i.e. 250 IU sc q day.

# Melatonin

- Melatonin is one of the most important anti-cancer hormones since it is critical for Natural Killer (NK) cell surveillance of cancerous cells.
- It is produced by the pineal gland.
- Melatonin levels reach 50% of normal by the 20's and near zero by age 40, therefore it is indicated in anyone over 40 regardless of whether they have a sleep issue or not..

# Melatonin

## Major Symptoms of Deficiency

- Insomnia
- Un-restful sleep
- Overactive mind during night
- Hot feet at night
- Difficulty recovering from jet leg
- Sudden night waking
- Depression/ anxiety
- Winter blues

# Melatonin Dosing

Melatonin can be raised by protein/carbohydrate (tryptophan/insulin) bedtime snack (i.e. milk, banana), darkness, drop in body temperature (as occurs after a hot bath).

- Dosing
  - Varies from 0.1 mg to 9.0 mg. Start low and slowly move upwards. For example start at 0.5 mg and move up until effect achieved. Sub-lingual works better than oral.
  - Can ask compounding pharmacy to compound at 5mg/cc, (=5 mg per 20 drops) 1 drop = 0.25mg, use 2-12 drops every night for 0.5-3 mg dose

# Somatopause

Growth Hormone Deficiency

# Growth Hormone

- Maintenance and repair of bones, joints, connective tissue, muscle
- Important to restore in anyone in late 60's-70's to prevent frailty and weakness.
- GH is made during **deep sleep** and causes loss of **deep sleep** (when low) which causes more loss of GH (chicken and egg scenario).

# Growth Hormones in Men & Women

- Growth hormone (GH) declines from mid thirties onwards. Assume about 50% activity around age 50
- GH is a major player in *all connective tissue maintenance and repair such as bone, muscle, fat, connective tissue, skin.*
- GH is a major player in **immune system** and activation of all other hormones
- Protects against *atherosclerosis*
- **Cancer**: There is concern that exogenous recombinant GH (HGH) can make cancer grow.

## **Secretagogues: An Alternative to Recombinant Human Growth Hormone**

*Mark L. Gordon M.D.\*, Erin F. Gordon, Alison M. Gordon,  
Rochelle H. Gordon, and Sidharth Anand*

*\* Clinical Professor, University of Southern California (USC) School of Medicine*

### **ABSTRACT**

**Objective:** To examine the efficacy of a compound of mixed amino acids, GABA, and *Mucuna pruriens* enveloped in a nanoliposomal delivery system to increase the production of growth hormone (GH), insulin-like growth factor 1 (IGF-1), and insulin-like growth factor binding protein 3 (IGFBP-3), in healthy individuals.

**Design and Method:** Within a private medical office, healthy individuals were screened for GH insufficiency (150-101 ng/ml IGF-1) and deficiency (less than 100 ng/ml IGF-1) prior to being given the secretagogue (Secretropin®). A morning dose of the preparation, 0.20 cc (600 mg) was placed under the tongue for 30 seconds prior to swallowing. A bedtime dose of 0.40 cc (1200 mg) was placed under the tongue for 30 seconds prior to swallowing. At both times the participant refrained from eating or drinking for at least 30 minutes prior to and after taking the secretagogue. Laboratory testing of at least IGF-1 and IGFBP-3 was performed prior to starting the secretagogue and at 1, 3, and 6 months.

**Results:** After a twelve-month testing period, the secretagogue was shown to increase patients' circulating levels of IGF-1 by 50-200% in 92% of the participants.

**Conclusion:** This nanoliposome delivered secretagogue was shown to be capable of elevating natural GH production and release in healthy individuals, as evident by elevated levels of IGF-1 and IGFBP-3.



## SECRETROPIN

Use to maintain healthy hormone levels\*

Sprays: 180 1 fl. oz. (30 ml)

Only available from your health care provider.

[www.secretropinrx.com](http://www.secretropinrx.com)

**Supplement Facts:**  
Serving Size 2 sprays

Amount Per Serving

Propylthiouracil 300 mg

Pyrogallolamine, L-Cysteine,

L-tyrosylserinephosphoryl

choline, Mucina pruriens,

L-arginine, serotone, &

alpha-keto-glutarate

\*Daily value not established.

**Other ingredients:** Cellulose

water, phospholipids, citric

acid, natural & artificial flavors

**Keeps:** To help maintain

healthy hormonal levels.\*

## SECRETROPIN™

Use to maintain healthy hormone levels\*

Sprays: 180 1 fl. oz. (30 ml)

Only available from your health care provider.

[www.secretropinrx.com](http://www.secretropinrx.com)

**Warning:** Not intended for use by anyone under the age of 18. Do not consume the product if you are pregnant or nursing. If you experience any adverse reaction immediately discontinue use and consult your physician. Keep out of reach of children. Do not use if seal is broken or missing.

**Directions:** Spray under tongue and swallow.

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91436. Made in USA.

\*These statements have not been evaluated by the FDA. This product is not intended to diagnose, treat, or cure or prevent any disease.