Testosterone:
The Highly Misunderstood Hormone in Women. How to navigate its importance during a women’s reproductive years into menopause

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20+ years in advanced BHRT therapy and hormone optimization, treated more than 20,000 patients
Disclosure Statement

• Dr. DeRosa is the founder and CEO of the Hormonal Health Institute and the Medical Director for Belmar Pharma Solutions.

• All of the relevant financial relationships listed for Dr. DeRosa have been mitigated.
Objectives

1) Learn the role of testosterone in women and how its abundant nature affects all organ systems in the body
2) Review how certain medications can cause significant clinically relevant testosterone deficiency
3) Understand the role of testosterone in breast health and review the evidence-based medicine related to testosterone in breast cancer patients
4) Discuss the role of testosterone replacement in women as they transition from peri-menopause into menopause
5) Explore the nature of gender bias in medicine and how hormonal therapies are influenced by this bias.
Let me tell you a story
27 Years Old and 2nd Year Resident

- Extreme Fatigue
- Insomnia
- Hot Flashes/Night Sweats
- Low Libido
- Anxiety/Depression
- Weight Gain
- Heart Palpitations, Pre-Syncope
The medical profession failed me...
...and I was part of the problem.

- Chronic illness and comorbidities
- More medications
- Skyrocketing cost
- Non-compliance
- Managing to illness
- Slow march to death
And there is...

Well-behaved women rarely make history.
Testosterone Overview
Life Expectancy and Menopause

J Am Geriatric Soc 1982;30:548
TSH versus FSH

TSH

100

FSH

F -
Ovarian Hormonal Secretion

- Estradiol: 100%
- Testosterone: 95%
Testosterone > Estradiol levels

Throughout the entire female lifespan

Dimitrakakis 02
Symptoms of Estrogen Deficiency

- Hot Flashes • PMS Worsening • Night Sweats
- Irritability • Dry Skin • Insomnia • Depression
- Mood Swings • Forgetfulness • Vaginal Dryness
- Heart Palpitations • Increased Allergies
Symptoms of Testosterone Deficiency

Low Libido • Weight Gain • Loss of Focus

Anxiety • Depression • Muscle Pain

Mood Swings • Memory Loss • Low Libido!!

Sugar Cravings • Fatigue • Belly Fat
Hormonal Peak to Decline

Estrogen $\rightarrow$ Cash and Savings
Testosterone $\rightarrow$ Cash Only

Testosterone Decline
Estrogen Decline
Special Consideration: Surgical Menopause

HYSTERECTOMY

With one ovary removed
  • Reduction in E2 & T1 levels by at least 50%

Without ovary removal
  • Increases risk for early E2 & T1 deficiency due to disruption of blood supply to ovaries from the surgery and decrease in blood flow after surgery
Oral Birth Control Pills and Testosterone
Current State of Affairs

- Birth control prevents pregnancy....DUH!
- OCPs are the “Go To”
- Not all are created equally
Oral Birth Control Pills

- Low constant levels of estrogen & progesterone (synthetic versions)
- Tricks the pituitary
- Shuts down the ovary
Ovarian Hormone Production

- Estradiol
- Progesterone
- Testosterone
What Does OCP Replace?

- Estradiol*
- Progesterone*
- Testosterone

*Synthetic version
Testosterone Production

95% of Testosterone

5% of Testosterone

SHBG
Oral Birth Control Pills

• Good estrogen to progesterone ratio (most)
• BUT...
All Oral Birth Control Causes
100% Deficiency of Testosterone
BUT WAIT, there's more!
Low Dose Estrogen OCPs

• Good for uterine bleeding but...
• *Estrogen/Progestin Ratio Flipped*
• *Still 100% testosterone deficiency*
• AXIS OF EVIL
LOW DOSE BIRTH CONTROL PILLS:

WORST IATROGENIC THING WE DO TO WOMEN!
Special Considerations

OCP increase SHBG which will affect thyroid levels
  • Lowers thyroid metabolism

Gender Bias
  • Men will never accept OCP due to testosterone deficiency state that is created
  • Women expected to accept this fact
KEEP CALM

There's Good News!
Intra-Uterine Devices (IUD)

- Low levels of uterine progesterone
- Uterine lining atrophy
- Hostile uterine environment
- Thick cervical mucus
Intra-Uterine Devices (IUD)

- Normal estrogen, progesterone & testosterone levels
- Contraceptive effect
- Long lasting
- Insurance coverage
Testosterone and the Breast
Androgens and the breast

Testosterone (T) has been used to treat breast cancer since 1937

Function of T at the androgen receptor (AR)

↓ Inflammation
↓ Proliferation/hyperplasia
↑ ER β – inhibits proliferation
↑ Increases cell death – Pro-apoptotic
↓ Invasive breast cancer (BCA) growth
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Aromatase (P450) – tissue-specific expression

T is aromatized to E2, which can stimulate ER + BCA
Aromatase activity/expression is increased in active BCA
T + Aromatase Inhibitor (AI)

Combination subcutaneous implant
  Anastrozole (T + A), Letrozole (T + L)
Simultaneous and continuous delivery of both active ingredients – 3 months
Avoids enterohepatic first pass effect
Beneficial effects of T
Avoids adverse effects of E2 in ER+ BCA
  • Estrogen-sensitive diseases
Tumor response and control of symptoms


Testosterone Implant Therapy in Women With and Without Breast Cancer: Rationale, Experience, Evidence

Rebecca Glaser\(^1,2,3\) and Constantine Dimitrakakis\(^3,4\)

Abstract
Testosterone (T) is the most abundant biologically active hormone in women. It has a direct effect at the androgen receptor in every major organ system. Local aromatization of T is a major source of bioavailable estradiol. Adequate amounts of bioavailable T are essential for optimal health, immune function, and disease prevention. More than 80% of bioavailable T in women is from the local intracellular production of T from the adrenal precursor androstenedione. Testosterone therapy (TT) may help prevent breast cancer events.

Breast Cancer Incidence Reduction in Women Treated with Subcutaneous Testosterone: Testosterone Therapy and Breast Cancer Incidence Study

Gary Donovitz\(^1,2\) and Mandy Cotten\(^1\)

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2. BioTE Medical, LLC, Irving, Texas, USA
3. Institute for Hormonal Balance, Arlington, Texas, USA

ABSTRACT
Objective: Testosterone (T) therapy has been shown to be breast protective in both pre- and post-menopausal patients. Additionally, estradiol (E) does not cause breast cancer (BC) in the majority of the world's literature. This study aimed to investigate the incidence of invasive BC (IBC) in pre- and post-menopausal women treated with T therapy and T in combination with E (T+E).

Materials and Methods: Since January 2010, a total of 2,377 pre- and post-menopausal women were treated with T or T+E implants. IBC rates were reported based on newly diagnosed IBC cases in the total study. Total cases divided by the total sample size and years in study was expressed as an incidence per 100,000 person-years (PY). The BC incidence was compared with age-specific Surveillance, Epidemiology and End Results (SEER) incidence rates.
Gender Bias in Medicine
Examples of Bias in Clinical Practice

• Cardiovascular disease/Acute MI
• Skin disorders
• ICU and life saving measures
• Psychoactive drugs
• Fibromyalgia
• Hormonal therapies
  • Lack of commercially available products for women
Hormonal Bias Origins

• Concept of sex hormones

• 1920-1940 Hormone Research Heyday
  • Identification of steroid hormones
    • Naming rights
    • Two sex characters and two sex hormones defining “maleness” and “femaleness”
    • Based on stereotypes ideas about gender
    • Caused lack of understanding and role of testosterone in women and estradiol in men
      • Caused a lack of perceived need for testosterone for women
Exclusion of Women in Medical Research

• Learnings of Clinical Trials
  • Very targeted study design with limited endpoints
  • Narrow indications increase the odds of approval by FDA
  • Limit Safety Risk Exposure
    • Reproductive Women are VERY HIGH RISK
      • Teratogenicity
      • Testosterone Category X
“This is why much of the research to date has focused on men with information extrapolated to women, even though this is physiologically and medically inappropriate.”
Patent Protections Affects Bias

• Why don’t compounded product makers obtain FDA approval of their most commonly made compounds?”
• Unique chemical structure or delivery mechanism
• Predominately affects women
  • Zero testosterone approved products
ENTER THE DARK SIDE
BIG PHARMA

• Started a well orchestrated attempt to eliminate compounded hormones
• Multifaceted attack
TROJAN HORSE: Clinical Guidelines

- Clinical guideline direct “standards of care”
- Big Pharma wants to protect the bottom line and status quo
- Provide significant financial support to organization that define the guidelines
- Testosterone International Consensus Statement
  - So called “experts”
- “There is no data to support”
  - True international experts consensus
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Checks indicate known flaws in the Testosterone Global Consensus Position Statement.
Testosterone Insufficiency and Treatment in Women: International Expert Consensus

Resolutions

Gary Donovitz, MD (Chairman), Erika Schwartz MD, Charles Miller MD Mickey Barber MD, Florence Comite MD, Ken Janson MD, Jeffrey Leake MD, Edwin Lee MD, Jeffry Life MD, Luis Martinez MD, Douglas Woodford MD
This is reminiscent of Galileo’s fight against orthodoxy, to make the sun the center of the solar system, the heliocentric view, rather than an immobile earth.
SAD TRUTH

• Women are predominately affected
  • Marked GENDER BIAS
• Lack of approved products or options
• Suggestions to use male products off label
• Doesn’t address the idiosyncratic nature of hormones which is more complex in women
• Would this be happening if men didn’t have access to their testosterone and ED products?
Men Get The Products They Need While Women Get Psych Drugs!!!
Feature Articles:

Angela DeRosa, DO, MBA, CPE
“I am Hot as Hell and Not Going to Take It Anymore: Part 1 and 2”
International Journal of Pharmaceutical Compounding
Vol. 24, No 6 Nov/Dec 2020
Vol. 25 No 7 Dec/Jan 2021

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