TESTOSTERONE REPLACEMENT THERAPY:
A Recipe for Success

John Crisler, DO
www.DrJohnCrisler.com
Superior Age Management PLLC
All Things Male Center for Men's Health
MSU-COM Dept of Family & Community Medicine

INTERVENTIONAL ENDOCRINOLOGY DEMANDS A REVOLUTION IN THE WAY WE THINK ABOUT HORMONES.

ENDOCRINOLOGY ONLY AREA OF MEDICINE WHERE:

- “Normal Range” is found through purely statistical means
- “Normal Range” has absolutely nothing to do with health and/or happiness
- The t ½ (half-life) of the drug is not considered
- There is a strong bias against what is natural, in favor of that which is synthetic
- Physicians practice via the names of studies
- The top Thought Leaders are PCP’s

WHAT “NORMAL RANGE” IS…

…and is NOT

Higher Death Risk in Men With Lower Testosterone Levels

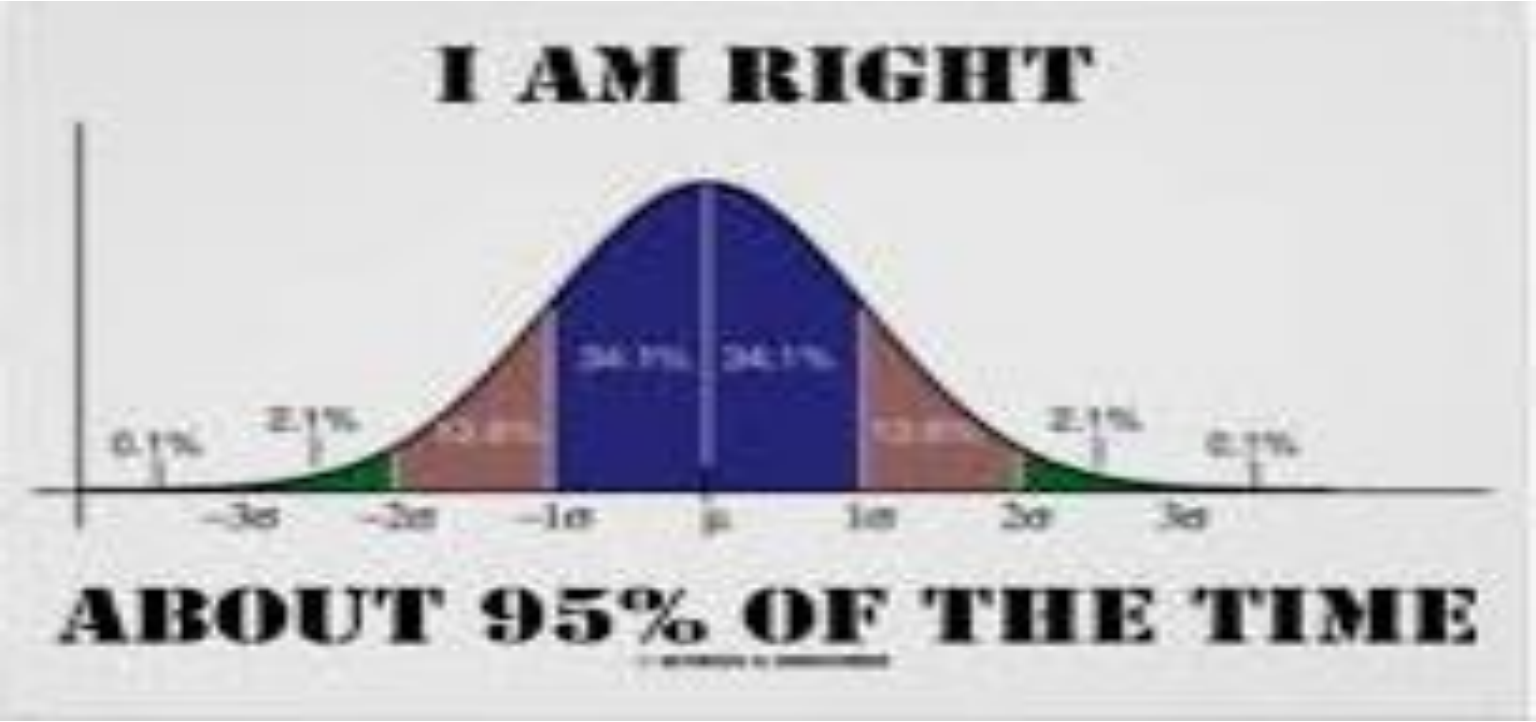
Circulation, Dec. 4, 2007; vol 116, Kay-Tee Shaw, MBBCh, professor of clinical gerontology, University of Cambridge, England. Robert Davis, MD, professor of urology, University of Rochester, N.Y.

Compared to lowest quartile WITHIN NORMAL RANGE:

- **Men in the second lowest quartile (Q2) were 25% less likely to die.**
- **Men in the second highest quartile (Q3) were 38% less likely to die.**
- **Men in the highest quartile (Q4) were 41% less likely to die.**

How is “Normal Range” determined?

It's a bell shaped world.



"What epidemiology cannot do is define the individual differences in specific endocrine aspects that every doctor sees in every patient sitting before them."

--Dr. Eugene Shippen

From the Foreword to "Testosterone Replacement Therapy: A Recipe for Success", by Dr. John Crisler

“Laboratory tests are for doctors who do not know what they are doing”

--Ol’ Osteopathic Proverb

Wide variability in laboratory reference values for serum testosterone.

Morgantaler, et al.

J Sex Med. 2006 Nov;3(6):1085-9.

“Laboratory reference values for testosterone vary widely, and are established without clinical considerations.”

Lazarou S, Morhantaler, et al.

J Sex Med. 2006 Nov;3(6):1085-9

“Normal Range”

- Includes many who are sick
  --K+ example in dialysis patients
- Wide due to daily variability
  --the only way to tell for sure is 24h urine
  --”Let’s draw two and take the highest”
- Partitioning due to age differences
  --are we willing to accept that?
- Requirements for morning draw
  --when do we need our T?
- 2.5% of men will live normally at >1000
  --500 is only half of what they are built for

If Range is (250-1000)
500 is not “midrange”

…it’s 1/3 from the bottom

ISSUES WITH LABORATORY EVALUATION

- Collection error
- Laboratory error
- Insufficient laboratory methodology
- Pulsatile release of hormones
- Timing of sample collection
- Type of TRT being administered
- Different sample matrixes
- LAB TESTS ARE ONLY ESTIMATIONS

ISSUES WITH LABORATORY EVALUATION—Sample matrixes

- Serum—Common, insurance, but snapshot only
- Urine—Total daily production (AUC), but limited tests, compliance in collection
- Saliva—bogus for all but cortisol

Effects exceed the half-life of the medication.

They can extend for days, even months, after exposure.

The shape of the androgen profile—not just the peaks and nadirs—but the frequency, the shape, the intervals, are ALL part of the information being transmitted by the hormones.
The curve trumps half-life.

“In all chaos there is a cosmos, in all disorder a secret order.”

--Dr. Carl Jung

“Entropy is part and parcel of youth.”

--John Crisler DO

So how do we diagnose hormonal deficiencies?

The taking of thorough and proper Medical History is 80% of the diagnosis

Show me a laboratory test for depression, that warrants administration of powerful drugs which are completely foreign to the body

A.D.A.M Questionnaire

1. Do you have a decrease in sex drive?
2. Do you have a lack of energy?
3. Do you have a decrease in strength and/or endurance?
4. Have you lost height?
5. Have you noticed a decreased enjoyment of life?

A.D.A.M. Questionnaire (con't)

6. Are you sad and/or grumpy?
7. Are your erections less strong?
8. Has it been more difficult to maintain your erection throughout sexual intercourse?
9. Are you falling asleep after dinner?
10. Has your work performance deteriorated recently?

WHAT ARE THE SYMPTOMS OF LOW TESTOSTERONE?

- TAT Syndrome
- Fatigue
- USTA Syndrome
- Loss of muscle mass
- Fat gain
- Poor recovery
- Pain/Inflammation
- Irritability
- Depression
- Decreased memory
- Loss of Libido
- Erectile Dysfunction

WHAT IS TESTOSTERONE REPLACEMENT THERAPY (TRT)?

TRT: Restoration of Testosterone to HEALTHY physiologic levels.

TRT is NOT:

- Total T > normal range
- Steroids
- Viagra

INITIAL HYPOGONADISM PANEL

- Total Testosterone
- Bioavailable/Free T
- SHBG
- DHT (?)
- LH/FSH
- DHEA-S
- Estradiol
- Prolactin
- Cortisol
- Thyroid Panel (TSH, FT4, FT3, rT3)
- Comp Metabolic Panel
- CBC
- Lipid Panel
- PSA (if over 40)

TT vs. FT vs. BAT

Which is better?

Total T vs. Free T vs. BioT

- TT is all that is produced/absorbed

  --can show clearance when compared to time of administration
- About 2% of T is active as FT

  --about 60% attached to SHBG

  --the rest to albumin
- Bioavailable T “Gold Standard”…

  --but issues with formula

T SAMPLE PREPARATION (SERUM)

- Refrigerated, no additive serum preferred (Plain, Red Top tube)
- Heparanized serum less acceptable (green-top)
- NO Serum Separator Tubes (SST)

Prolactin

- Significant cause of hypogonadism
- May signal tumor presence
- Health benefits
- Must be maintained within normal range
- Ref Range (3.0-18.0 ng/mL)
- >300= tumor
- FASTED: elevated by eating, sex (<30)

HYPERPROLACTINEMIA CAUSES

- Pituitary tumor
- Stalk compression
- Primary hypothyroidism
- Chronic renal failure
- Cirrhosis
- Opiates
- Tri-cyclics
- D2 antagonists
- Metoclopramide
- Verapamil
- Chest wall trauma

Luteinizing Hormone (LH)

- Produced by pituitary
- Stimulates T production at Leydig cells
- Pulsatile production by pituitary gland
- Short half-life
- Acute phase reactant
- Must be careful in its interpretation
- Use to determine Low T cause, or follow Clomiphene Tx

Follicle Stimulating Hormone (FSH)

- Produced by pituitary
- Spermatogenesis
- 180-240 minute half-life
- Inhibited by estrogen too
- Add to increase fertility
- Available by select Compounders

Sex Hormone Binding Globulin (SHBG)

SHBG

- Made by liver (and other tissues)
- Assayed level in blood made by liver
- Difficult test to run
- Powerfully binds sex hormones
- Binds Androgens>Estrogen
- Variable “stickiness”
- “Normal Range”≤ 56, not 77
- The centerpiece of every sex hormone evaluation

High(er) SHBG

- Higher means less Free T….and E
- High(er) has big effect on Bioavailable level
- Elevated by Estrogen(s), Thyroid RT, etc
- MAY need higher doses to overcome
- Can lower with Danazol 50mg PO QD

  --I’ve found no benefit
- In intact systems (no TRT), lowering SHBG has no net positive effect
- Numerous positive actions of SHBG in body

Low(er) SHBG

- Lower means more Free T….and E
- Less SHBG to “buffer” Estrogen
- Lowered by Androgens, AI’s, GH, IGF-1, etc.
- Zinc knocks E off SHBG
- Inflammation, not insulin, ↓SHBG
- ↓SHBG ↑ urinary excretion of T

  …but not E

  --”Hyperexcreters”

Treating Low(er) SHBG

- Low SHBG ∞ ANXIETY
- Low SHBG → success w/ less variable TRT
- Injections > Transdermals
- Shots > BIW, TIW, QOD, QD
- NO WORKING OUT PRIOR TO LABS

  --falsely ↑SHBG

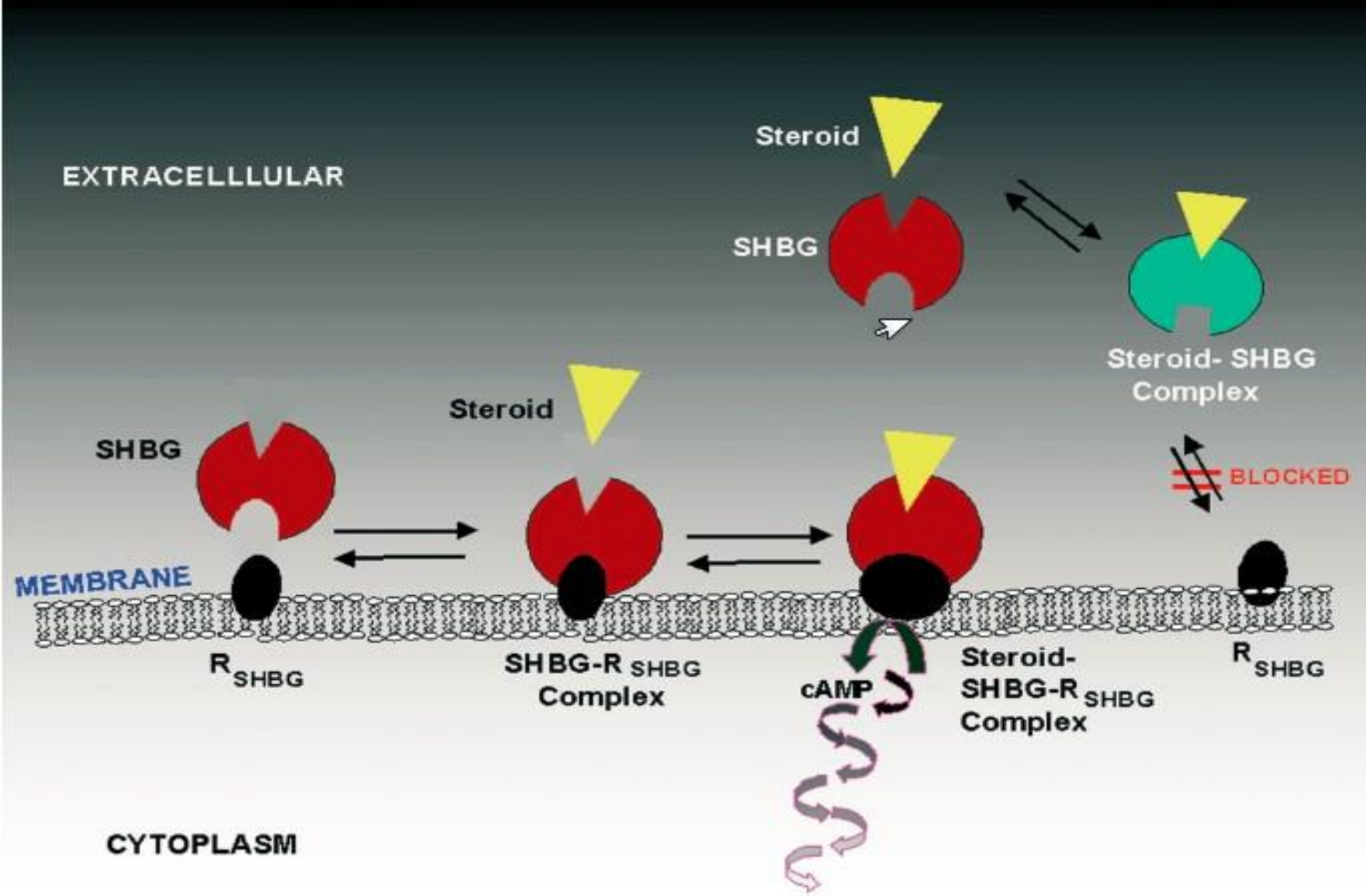


Figure 3 The SHBG signaling system. In its steroid-free configuration, SHBG binds to R_{SHBG} on cell membranes, forming a bipartite complex ($SHBG–R_{SHBG}$). SHBG, already bound to a steroid, non-competitively inhibits the binding of SHBG to R_{SHBG}. However, within minutes after exposure of $SHBG–R_{SHBG}$ to a steroid agonist, e.g. estradiol (Nakhla *et al.* 1990, 1994) or 5α-androstan,3α,17β-diol (Nakhla *et al.* 1995), a tripartite complex (steroid–$SHBG–R_{SHBG}$) forms that activates adenylyl cyclase, leading to the generation of the second messenger, cAMP.

Estrogen
and its
(mis)Management


I BEAT
ANOREXIA

NO ONE EVER SAID TO DRIVE ESTROGEN TOO LOW

Detriments of DECREASED Estrogen

- Damage to Lipid Profile
- CV system
- Brain health

  --brain makes its own E
- Bone demineralization

  --follow with urinary NTX
- Decreased sex drive
- Headache
- Multiple arthralgias

Detriments of ELEVATED Estrogen

- Suppresses HPTA
- Elevates SHBG
- Psychological morbidities
- Hot flashes
- Hypertension
- Water retention
- Increases clotting factors
- Prostate morbidity
- Cancers
- Female fat distribution
- Fx on thyroid function
- ↑ “Wimpy Factor”

SYMPTOMS OF ELEVATED ESTROGEN

- Water retention “sloshing”
- “Bloaty” feeling
- “Nipple issues”
- Sexual Dysfunction
- Excessive moodiness/Depression
- Fatigue

So what are we to do?

To treat, or not to treat

IF THE MALE PATIENT DOES NOT HAVE THE SYMPTOMS OF ELEVATED ESTROGEN, I DO NOT TREAT

EVERYONE WHO HAS TREATED ELEVATED ESTROGEN HAS SEEN IT:

- Flush extra water out
- Decrease bloating
- End “nipple issues”
- Restore libido
- Restore “manliness”
- Increase energy

ESTROGEN BUILDS BECAUSE

1). Increased T>E conversion

--increased TRT dose

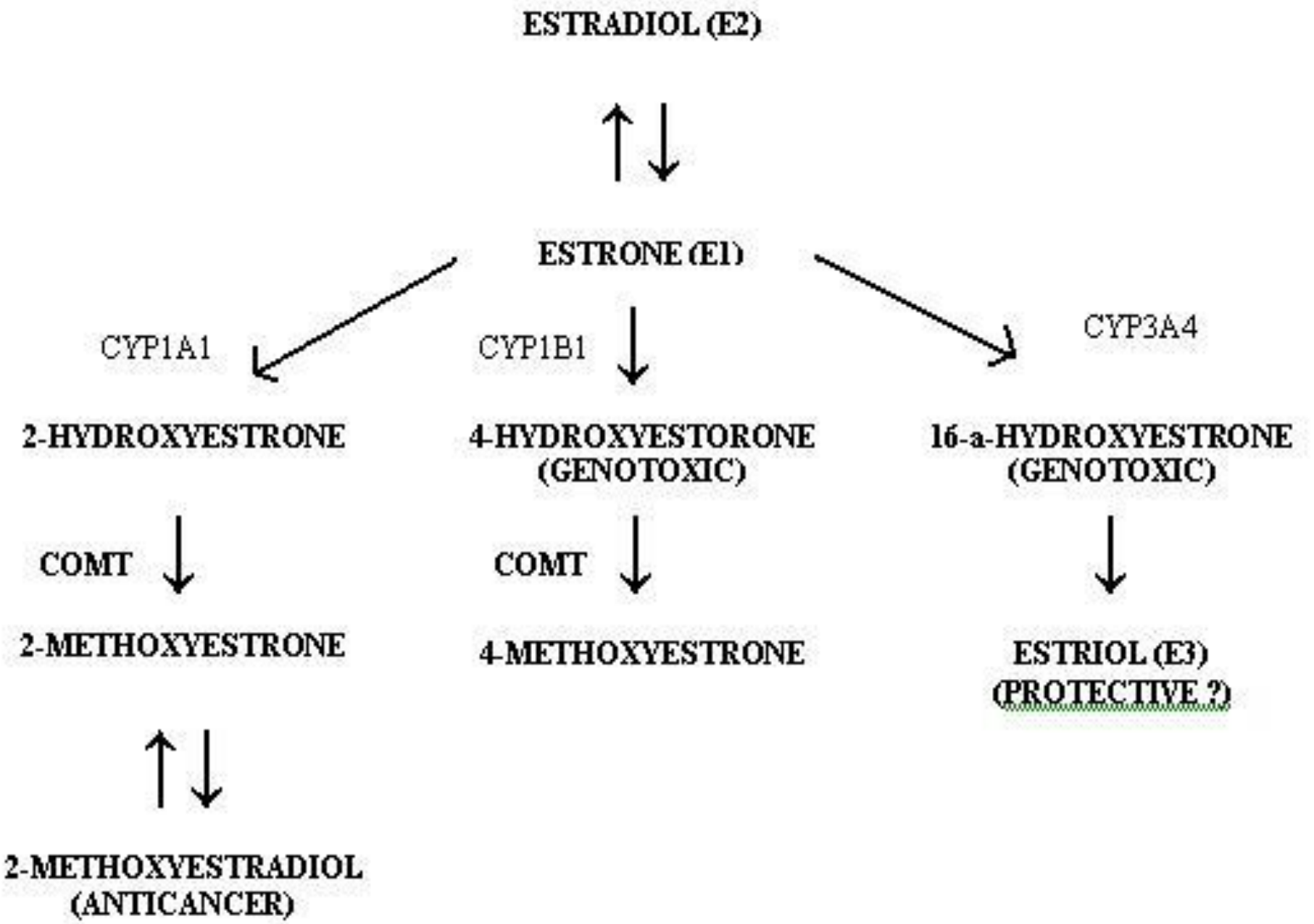
--increased Aromatase activity

2). Decreased E metabolization

3). Addition of xenoestrogens

4). Combinations of the above

Some Important Estrogen Metabolites



ESTROGEN MGM'T FACTS

- If you are only giving 60 mg of Test cyp QW, there is ↓chance of elev E
- If you are giving appropriate doses of HCG, there is ↓chance of elev E, compared to higher doses
- Using high dose Zinc to lower E:

  --STILL trying to lower E!

  --be careful of too much +2 cation?

  --must add copper ≈25/1

High-Sensitivity Tandem Mass Spectrometry Assay for Serum Estrone and Estradiol

Kushnir, et al. Am J Clin Pathol
2008;129:530-539

Comparisons of Immunoassay and Mass Spectrometry Measurements of Serum Estradiol Levels and Their Influence on Clinical Association Studies in Men

Ohlsson, et al. JCEM. Vol 98, issue 6.
March 27, 2013

False Prophets of E2 on Immunoassay (can overestimate actual value)

- CRP
- CRP-associated factor
- **Irreversible ("suicide") steroidal inhibitors**, such as exemestane
- NOT Nonsteroidal **inhibitors**, such as anastrozole and letrozole
- SERMS
- Progesterone

ALL THE STUDIES USING IMMUNOASSAY LABORATORY METHODOLOGY MUST BE THROWN OUT!

SHOW ME ONE PROPER STUDY WHERE AN APPROPRIATE DOSE OF AN AROMATASE INHIBITOR CAUSED NEGATIVE SIDE EFFECTS

SHOW ME ONE PROPER STUDY WHERE THEY ADMINISTERED AN APPROPRIATE DOSE OF AN AROMATASE INHIBITOR

LifeExtension®
National Diagnostics, Inc.

BLOOD TEST

5990 North Federal Highway, Ft. Lauderdale, FL 33308
1-800-208-3444 - LifeExtension.com

[redacted]

Tests	Result	Flag	Units	Reference Interval	Lab
Hemoglobin A1c					
Hemoglobin A1c	5.0		%	4.8-5.6	TA
	Pre-diabetes: 5.7 - 6.4 Diabetes: >6.4 Glycemic control for adults with diabetes: <7.0				
Thyroxine (T4) Free, Direct, S					
T4,Free(Direct)	1.58		ng/dL	0.82-1.77	TA
DHEA-Sulfate					
DHEA-Sulfate	**405.5**	**High**	ug/dL	48.9-344.2	TA
TSH					
TSH	1.870		uIU/mL	0.450-4.500	TA
Prolactin					
Prolactin	11.6		ng/mL	4.0-15.2	TA
Estradiol					
Estradiol	**93.9**	**High**	pg/mL	7.6-42.6	TA
	Roche ECLIA methodology				
IGF-1					
Insulin-Like Growth Factor I	**195**	**High**	ng/mL	54-194	BN
Reverse T3, Serum					
Reverse T3, Serum	**25.3**	**High**	ng/dL	9.2-24.1	BN
Vitamin D, 25-Hydroxy					
Vitamin D, 25-Hydroxy	41.6		ng/mL	30.0-100.0	TA
	Vitamin D deficiency has been defined by the Institute of Medicine and an Endocrine Society practice guideline as a level of serum 25-OH vitamin D less than 20 ng/mL (1,2). The Endocrine Society went on to further define vitamin D insufficiency as a level between 21 and 29 ng/ml (2). 1. IOM (Institute of Medicine). 2010. Dietary reference intakes for calcium and D. Washington DC: The National Academies Press. 2. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. JCEM. 2011 Jul;96(7):1911-30.				
C-Reactive Protein, Cardiac					
C-Reactive Protein, Cardiac	1.05		mg/L	0.00-3.00	TA
	Relative Risk for Future Cardiovascular Event Low <1.00 Average 1.00 - 3.00 High >3.00				
IGF-BP3					
IGF-BP3	3524		ug/L	2133-5711	BN
Estradiol, Sensitive					
Estradiol, Sensitive	20.0		pg/mL	8.0-35.0	BN
	This test was developed and its performance characteristics determined by LabCorp. It has not been cleared by the Food and Drug Administration. Methodology: Liquid chromatography tandem mass spectrometry(LC/MS/MS)				

FINAL REPORT

9/12/2017 7:02:51 AM

LIFE EXTENSION / NATIONAL DIAGNOSTICS, INC

This document contains private and confidential health information protected by state and federal law. If you have received this document in error, please call 800-208-3444.

ACCEPTABLE ESTROGEN TESTS

- Quest Diagnostics “Ultrasensitive Estradiol”
  --Code #30289
- LabCorp “Sensitive Estradiol”
  --Code # 140244
- Mayo Clinic “Enhanced Estradiol”
  --Code #EEST
- ARUP “TMS”
  --Code #93247

ESTROGEN ELEVATORS/MIMICS

- Age
- Obesity
- ETOH over-consumption (incl HOPS in beer!)
- Liver Dz
- Zinc deficiency (50mg Zn/2mg Cu QD)
- Vitamin C deficiency
- Excessive DHEA supplementation (100mg QD)
- Androstenedione supplementation
- Xenoestrogens (incl Vinyl IV bags!)

  --Lavender, Tea Tree Oil
- Liver Detoxification issues
- Soy
- Flax seed (lignans)
- Foods

Rescue from “Nipple Issues”

- Burning, itching, swelling, FREAKING
- Occurs with mere changes in hormone levels, even within physiological range, so…
- DO NOT treat in first month (get F/U labs)
- 20mg BID tamoxifen until gone, then taper

  --cut dose ½ Q5D
- Hold Growth Hormone (and peptides)

  --magnify E Fx
- Gynocomastia may be caused by progesterones

ANASTRAZOLE

- Aromatase Inhibitor (T>E)
- Other AI's available

  --Competitive Inhibitor >> "Suicide" Inhibitor
- #1 use of this med in world: Male TRT
- Concerns with Endocrine pathway disruption
- AI's as sole TRT is RARE (use very small dose)
- Does NOT lower GH production—if used right
- Does not harm Lipid Profile—if used right
- Does not cross Blood Brain Barrier

ANASTRAZOLE

- 2 day t½
- 0.25mg QOD, 0.5mg Q2-3D (usually)
- Titrate from there
- On shot day(s), i.e. QW, BIW etc.
- Allow 4 weeks prior to F/U labs
- Remember SHBG may lower, so E may need to be lower, b/c Free E is higher

HCG

HCG

- Mimic of LH—create physiologic doses
- Standard Tx for Secondary Low T
- Helps prevent testicular atrophy
- Helps preserve spermatogenesis
- Binds to LH receptors all over the body
- LH receptors in emotional centers of brain
- Increase libido, sense of well-being
- 100iu SQ QD> 500iu SQ BIW
- Not more than 500iu at a time

DHEA

DHEA

- “The Mother of All Sex Hormones”
- Cognitive, immune, sexual function
- Cardiovascular health
- SL is best administration

  --↑ (Free DHEA⁄DHEA-S)
- TD is great, but absorption issues
- When you add TRT, DHEA ↓
- No such thing as “too high” DHEA level

  --as long as E in males not a problem

  --as long as androgenicity in women not problem

DHEA

- Should be taken BID

  --(-S) is cleaved from DHEA intracellularly

  --EXCEPT saliva glands

  --evening dose will ↑ GH
- Male: 25mg SL/PO BID and ↑

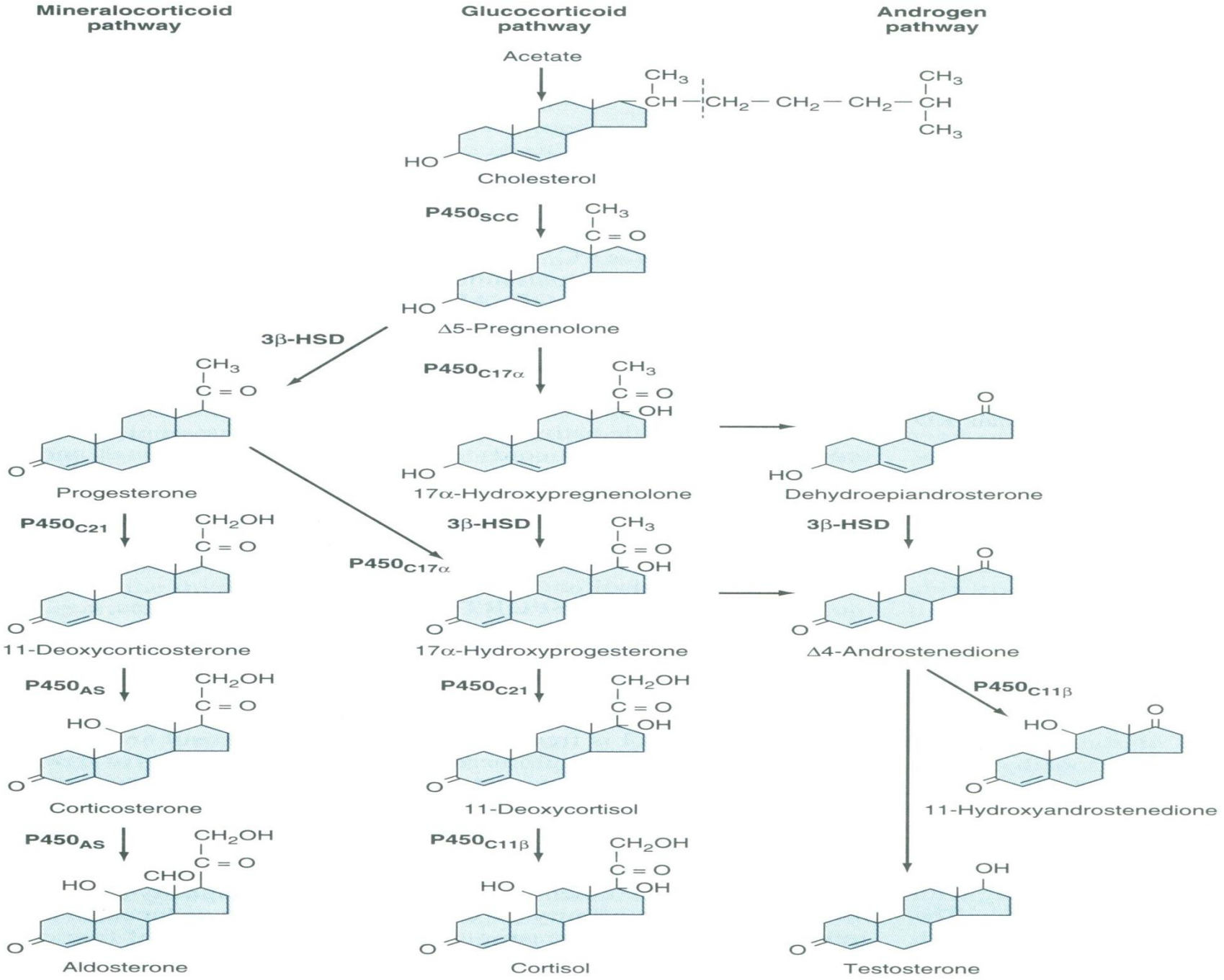
  --excess converts to Estrogen

  >E1…..E2↔E1, push toward E1

  --if on an Aromatase Inhibitor you can take more
- Female: 5mg SL/PO BID and ↑

  --excess converts to Testosterone

“BACKFILLING THE PATHWAYS”


Mineralocorticoid pathway
Glucocorticoid pathway
Androgen pathway
Acetate
Cholesterol
P450SCC
Δ5-Pregnenolone
3β-HSD
P450C17α
Progesterone
17α-Hydroxypregnenolone
Dehydroepiandrosterone
P450C21
3β-HSD
P450C17α
3β-HSD
11-Deoxycorticosterone
17α-Hydroxyprogesterone
Δ4-Androstenedione
P450AS
P450C21
P450C11β
Corticosterone
11-Deoxycortisol
11-Hydroxyandrostenedione
P450AS
P450C11β
Aldosterone
Cortisol
Testosterone

Androgen supplementation during aging: development of a physiologically appropriate protocol.

Urbanski HF1, et al. Rejuvenation Res. 2014 Apr;17(2):150-3. doi: 10.1089/rej.2013.1518. Epub 2014 Apr 8.

- Old male rhesus monkeys
- Given oral testosterone in evening
- Given DHEA in the morning
- “…a noninvasive androgen supplementation paradigm that restores youthful circulating levels in old male primates.”
- “…preserves natural circulating circadian hormone patterns…will produce fewer adverse side effects….”

"BACKFILLING THE PATHWAYS"

- HCG

  --TRT induces secondary hypogonadism

  --this lowers CHOL>PREG

  --LH analog incr P450scc enzyme activity ↑PREG

  --↑ CHOL transport across inner mitochondrial membrane

- DHEA

  --TD 50-100mg QD in gel

  --25mg BID oral/SL

  --100mg PO QD can elevate E1

  --TD>PO SR>standard oral preparation

- Pregnenolone

  --50-300mg TD/PO QD (higher dose with anxiety)

LD CLOMID Tx

Clomiphene Tx

- The most “Quantum” of all TRT Tx’s
- Originally created for female fertility
  ….then for male fertility
  ….then for male Secondary Hypogonadism
- Challenge Test OR long-term use
- Original dose: 50mg QD
- Half estrogen antagonist: Enclomiphene
- Half ESTROGEN agonist: Zuclomiphene
  --“weak estrogen” is still ESTROGEN
  -- why soy/flax seeds are bad for men

LD Clomiphene Tx

- New starting dose: 12.5mg PO QD
- F/U in three weeks
- Labs: TT, FT, SHBG, LH, FSH, E2
- Pt subjective and objective responses my not correlate
- SHBG may rise
- Estrogen may rise
- Counteracting “BroScience”

LD Clomiphene Tx

- SHBG may elevate. Use TT/FT, or assay
- Add Aromatase Inhibition if necessary

  --Control E or it will cause negative Fx AND suppress Gn production
- Aid estrogen metabolism:

  --DIM 100mg BID

  --Calcium d-glucarate 500mg BID

SUBCUTANEOUS TESTOSTERONE INJECTING

SubQ Testosterone Injecting

- No holes in muscles
- Smaller needles
- Decreased risk of infection, bleeding
- Seeing DECREASED Estrogen
- Increases libido
- May decrease total weekly dose
- Better for those with lower SHBG
- May take a little time to come on

NO TRT “CYCLING”

- Historically “borrowed” from AAS use.
- No evidence of benefit
- Does not do what is claimed
- Leaves substantial periods of letdown
- The body thrives on regularity

IT’S ALL ABOUT BALANCE

LESS CAN BE MORE

FIND THAT “SWEET SPOT”

When you miss your shot, do you miss your shot?

RATIOS

RATIOS

- Hormonal effects are not linear
  --cross reactivities
  --Binding Globulin influences
- It's a bell curve world!
  --even when the "bell" is upside down
  --slopes are important
- The direction of movement is important
  …there is an acceleration
  --men feel objectively the direction of acceleration
- Each hormone is but one part of a much greater "symphony"
  …all must be considered

T/E ratio

- Measure of system performance

  -- ratio does have importance, but…

  -- absolute values of hormones are much more important

  -- cannot elevate E without consequence, even when T is proportionately high

  --at low SHBG, E may be more challenging
- Used to explain pathophysiology:

  Low T→ higher proportionate E →morbidity
- Desirable ratio changes over [conc] changes
- Desirable ratio changes over [SHBG] changes
- NOT a treatment goal

The Meat and Potatoes of TRT

TESTOSTERONE DELIVERY SYSTEMS

- Gels and Creams
- Patches
- Implantable Pellets
- IM
- Orals

ALL Testosterone
is
“Bioidentical”

Gels and Creams

- Ease of application
- May be more convenient—OR NOT
- Stable across week, not day
- “Pulsing” [T] is beneficial
- Quickly attains stable serum levels
- Boosts DHT
- May elevate estrogens more
- Risk of accidental transfer
- Be mindful of application method
- Avoid antecubital fossa—looks like AAS use
- EXTREMELY variable absorption…dry weather
- …if poor→ thyroid evaluation

Gels and Creams (con't)

- "Big Pharma" products:
  --MUCH more expensive
  --support physician education ("The Cause")
  --covered by insurance
  --vouchers
  --1-2% concentration
  --be mindful of application technique
  --permeability enhancers

Gels and Creams (con't)

- Compounded gels/creams
  --various bases
  --1%, 5%, 10, 20%
  --higher conc. → less E, DHT conversion
  --yam-based T's
  --creams slow absorption, but more stable
  --Chrysin does not work
  --MUCH less expensive

T GEL APPLICATION

- Jars with measuring spoons
- Plastic capped syringes
- Metered Dose Pumps (my favorite)
- 1% apply to outer arms, shoulders, flanks
- 5%, 10%, 20% applied to forearms
- Scrotal application (cream only!) in rare cases

Testosterone Patches

- Convenient—MAYBE!
- No risk of accidental transfer
- Stable serum androgen levels
- Little DHT, E boost
- Scrotal patches available
- 2/3’s--Contact Dermatitis

IMPLANTABLE PELLETS

- Provide long half-life
- Some patients consider them convenient
- Billable office procedure
- Extrusion risk is technique dependent
- Increased risk of scarring, pain
- No one knows the PK's of T pellets
- Are NOT physiologic

Testosterone Injection

- Convenient—MAYBE!
- MUST be injected ≤ weekly
- Stable across day, not week
- Ease of dose titration
- Injection risks
- Most popular form of TRT

NEEDLE SIZES

- Glutes: 22ga 1 ½”
- Thighs: 25ga 1”
- SubC: 27, 28, 29ga 3/8”, ½”

RELATIVE CONTRAINDICATIONS:

- Prostate-Specific Antigen (PSA) >4.0 or acceleration >0.75/year
- H/H> 18/55 ERYTHROCYTOSIS --not Polycythemia!
- Sleep Apnea
- Cardiac, Hepatic, Renal Dz

POTENTIAL RISKS (listed)

- Increased risk of bladder outlet symptoms due to increase in prostate volume
- Edema in patients with preexisting cardiac, renal, or hepatic disease
- Erythrocytosis
- Gynecomastia
- Acne
- Decreased sperm production
- Stimulation of growth in previously undiagnosed prostate cancer

DRUG INTERACTIONS:

- Diabetic Medications
- Propranolol
- Oxyphenbutazone

FOLLOW-UP LABS

- Total T
- Free T
- LH/FSH (especially with Clomid Tx)
- SHBG
- Estradiol
- CBC
- Comp. Metabolic Panel
- PSA (if over 40)

FOLLOW UP LABS (con't)

- Initial F/U at 2 weeks with TD (transdermal)
  --stable serum T levels quickly attained
  --logistical consideration of 30-day dose

- Initial F/U at 4 weeks with IM
  --takes that long to equilibrate
  --interpret by PK's of T ester (48-72 hour peak)
  --cypionate/enanthate t½ 5-8 days

- F/U at 4 weeks S/P dosage change or estrogen control s/p HPTA-suppression

FOLLOW-UP LABS (con't)

- Once dose is titrated:
  --q 6 months or yearly
  --Include PSA
  --Digital Rectal Exam (DRE)

TIMING OF LABS FOR SHOTS

- Cypionate, Enanthate esters peak at 48-72 hours s/p IM injection
- Decline thereafter
- T½ = 5-8 days
- No lab draw on injection day
- Use these facts to interpret labs

TIMING OF LABS FOR TD's

- Apply at same time each day
- Always ask patient when they apply (lifestyle)
- Split dose?
- Allow at least 2 hours prior to draw
- Above no consequence with 24 hour urines
- Appreciate daily variability of TD's

KEEP THE BIG PICTURE IN MIND

- Every-body is different. Customize.
- Things move in circles
- “Start Low—Go Slow”
- Make sure they know why you are doing it
- Think about how they are going to interact with their conventional doctor
- NEVER be surprised by ANYTHING
- Remain a man/woman of science

LABS<GLANDS<SYSTEMS…
<SYMPTOMS…
<HEALTH and HAPPINESS

CONTROL:

UPSTREAM>>DOWNSTREAM

When you raise hormones, you also increase nutritional needs.

WHAT IS THE FUTURE OF TRT?

- Elevating T to healthy, happy levels
- Estrogen metabolism
- Actions at the androgen, estrogen receptors
- Restoring endocrine pathways
- Bringing “conventional medicine” to evidence-based medicine

THE GOAL?

"The ultimate goal of TRT medicine is to optimize health and happiness in our patients, which means producing an environment where we have elevated testosterone to sufficient levels, with the body responding as if unaware of the exogenous manipulations."

--John Crisler, DO

CASE STUDY

42yo male presents with Hx of c/o depression, fatigue, muscle loss, fat gain, “brain fog”, lack of libido and ED

Previous physician placed him on Testosterone Cypionate 200mg/mL, 1mL IM QOW

Pt reports he feels GREAT the first few days after his shot, but with nipple tenderness, and water retention, and “a bit jacked up”.

“By the middle of the second week I feel terrible”

LABS [Day 13]

- Total T: 213 (241-916)
- Estradiol LC/MS: 9 (<35)
- SHBG 11 (<56)

TRT regimen changed to:
Test Cyp 50mg SQ BIW
HCG 100iu SQ QD (Pt agreed to 500iu BIW, day before test cyp shots)

ONE MONTH LABS [Day 3]

- Total T: 625 (241-916)
- Estradiol LC/MS: 29 (<35)
- SHBG: 11 (<56)

Pt reports “I feel MUCH better, much more consistent”
But c/o “itchy nipples”, and “bloaty” feeling, and “my libido just isn’t where it should be”

Add Anastrozole 0.25mg BIW, taken with each shot of Test cyp

ONE MONTH LABS

- Total T 737 (241-916)
- Estradiol LC/MS: 17 (<35)
- SHBG 13 (<56)

Pt reports “I love you”

…”my wife loves you, too.”

