



Hormones – Nuts and Bolts

Ron Rothenberg MD

Founder, California HealthSpan Institute

Clinical Professor, Family and Preventive Medicine

UCSD School of Medicine



- Hormone Bio-Identical
- Delivery method
- Dose
- Symptoms Can vary
- Lab test Can help – 80% clinical
- Safety
- Side effects
- Follow-up Clinical, lab
- Dose adjustment
- Controversy Medical, legal, philosophical



Hormone: Testosterone

- Delivery method
 - T gel compounded
 - T gel commercial
 - T patches
 - T buccal
 - T pellets
 - T cypionate compounded
 - T cypionate commercial
 - HCG
 - HCG + T



T Dose Men

- Gel 50-200 mg/day
- Cypionate 50-150 mg IM/week
- Pellets 75 mg x 5-10 q 3 months
- HCG 1000-5000 units per week
 - Possible dosing:
 - 250 units per day
 - 1000 units twice a week
 - T cypionate 100 mg IM on day 1
 - HCG 250 units SC days 5 and 6



Testosterone The Symptoms

- Symptoms
 - Grumpy old men
 - Cognitive Dysfunction
 - Inflammation – Osteo, Rheumatoid Arthritis
 - Pain – lowered threshold
 - Frailty – less muscle and bone, more visceral abdominal fat
 - Atherosclerosis – coronary, carotid others
 - Insulin resistance
 - Sexual Dysfunction – less libido and decreased erectile function



Lab tests

- Conventional medicine
 - Only 3 possibilities: high, low, WNL
- Anti-aging medicine
 - Optimize to the youthful end of the spectrum

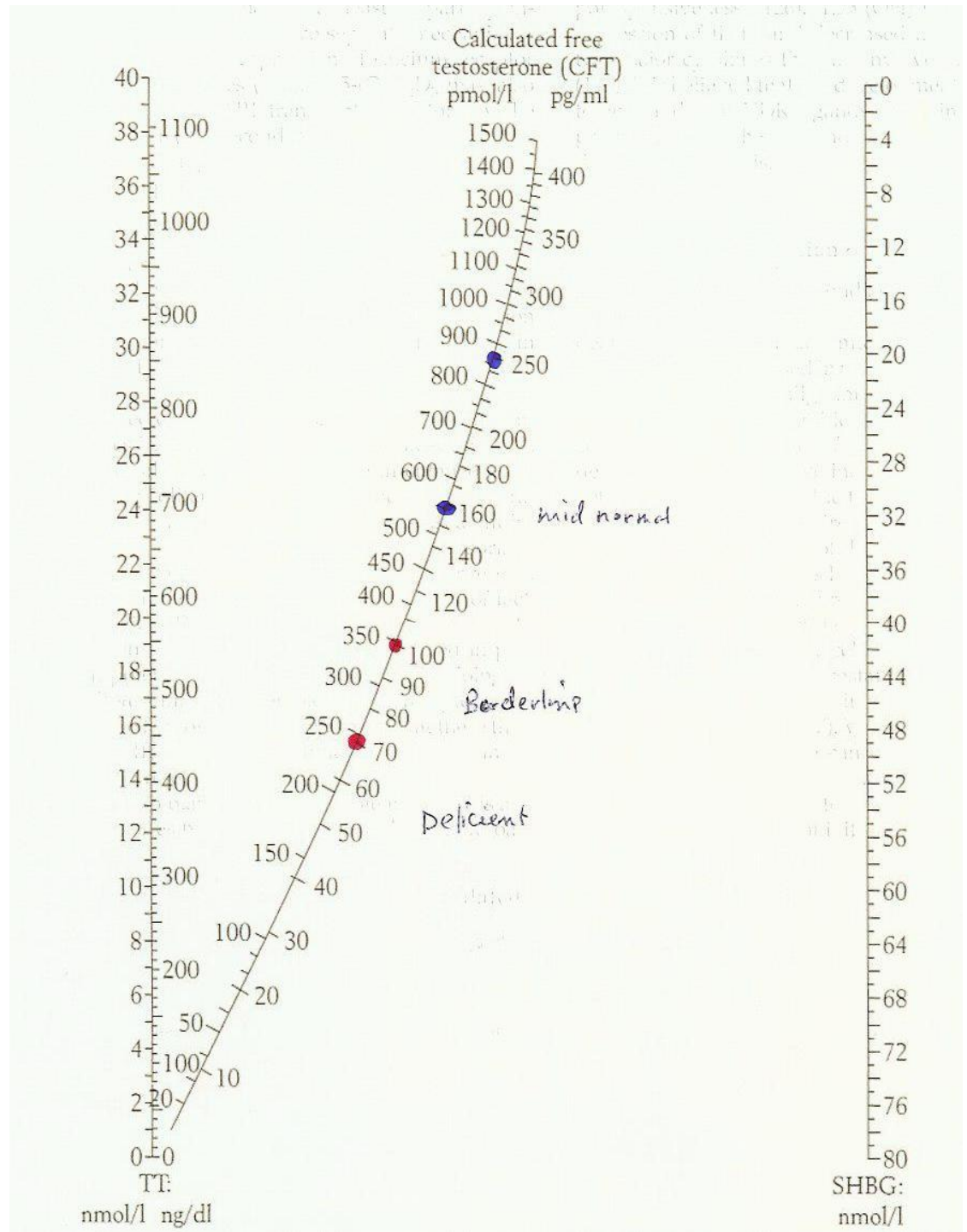


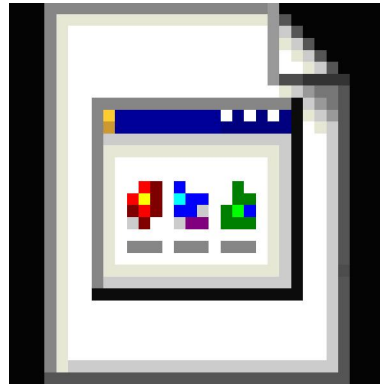
T Lab Tests male

- Total - doesn't consider SHBG
 - Optimal 700-1000 ng/dl
- Free – doesn't consider albumin
 - Optimal 18-24 ng/dl
- Bio-available – most useful
 - Free plus weakly bound to albumin
 - Optimal 300-500 ng/dl
- SHBG – E drives it up, T, GH drives it down
- Saliva – may be better for transdermal Rx
 - 30-142.5 pg/ml
 - Optimal 100-150 pg/ml
 - Therapy 230-350 pg/ml
- Urine



From "Androgen Deficiency in the Adult Male" by Dr. Malcolm Carruthers
Taylor & Francis 2004
Thanks to Eugene Shippen MD





A4M Test Calc Dec 2005.htm



T safety

- Prostate cancer screen
 - PSA < 4.0
 - PSA similar to baseline if prior values known
 - DRE – no suspicious findings of PC
- H and H baseline
 - Keep Hg < 18 by donating or discarding blood once or twice a year



T side effects

- Decreased sperm count
- Decreased testicle size
- No “roid rage”
- Possibly more assertive or aggressive
- More libido




T Metabolites

- E2, E1
- DHT
- To control or not to control?



E2 reduction and Aromatase inhibition

- Don't let E2 go to zero
- Just treat if symptoms or very high E2
- Flavanoids – Chrysin
- Grape seed extract
- Progesterone
- Calcium-d-glucarate 
 - inhibits beta-glucuronidase,
 - enzyme produced by colonic microflora
 - increase glucuronidation and excretion of potentially toxic compounds.
 - involved in Phase II liver detoxification.
 - Estrogen excreted instead of re-absorbed
 - 1500-3000 mg daily.
- Anastrozole?



5 alpha reductase

- Don't let DHT go to zero
- Just treat if symptoms or very high DHT
- Saw Palmetto
- Progesterone
- Finasteride?
- Dutasteride?



T safety issues

- PSA, PSA velocity, Free PSA
- DRE
- Active Prostate Cancer
- S/P Prostate Cancer, Radical Prostatectomy, PSA remains 0
- Follow H and H
- Follow E2

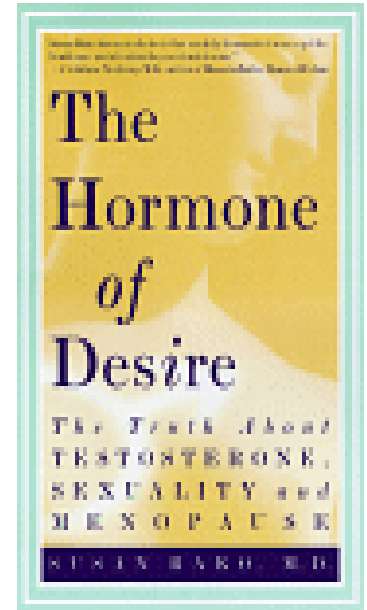


Controversies

- Prostate cancer
- BPH
- Heart disease
- “Roid rage”
- Testicular “atrophy”
- Sperm count



TRT in Women



- T needed for sense of well being
- Anxiety
- Lack of self confidence, motivation
- Fatigue
- Strength especially upper body
- Libido
- Nipple and clitoral sensitivity
- T usually decreased in perimenopausal and menopausal women
- Body composition, Bone density
- DHEA can increase T in women but not in men
- “Relative Androgen Deficiency” with normal levels



T in women

- Preparation
- Compounded gel
- 1% = 10 mg/gm
- 0.5% = 5 mg/gm
- Dose 2.5- 10 mg per day q AM
- T cypionate injections 20-40 mg/month



T Lab Tests Female

- Total - doesn't consider SHBG
 - Optimal 50-75 ng/dl
- Free – doesn't consider albumin
 - Optimal 5-8 pg/ml
- Bio-available – most useful 10-30 ng/dl
- SHBG – E drives it up, T, GH drives it down
- Saliva
 - 4.5-40 pg/ml reference range
 - Optimal 30-50 pg/ml
 - Therapy 30-60 pg/ml
- Urine



Testosterone dose in women

- Transdermal
- 0.5-1.0% ½ g -1 gm =
- 1.25-10 mg



T women safety

- No serious safety issues
- Control side effects
- Do not use if hirsutism present
- Questionable use in breast cancer due to conversion to E via aromatase
- Do not use if male pattern baldness present
- T is schedule III



T women side effects

- Decrease dose early in sequence so you do not go beyond skin
- Sequence:
- Oily skin
- Acne
- Increased facial hair
- Too much libido, aggressiveness
- Clitoral enlargement
- Deepening of voice



Follow up

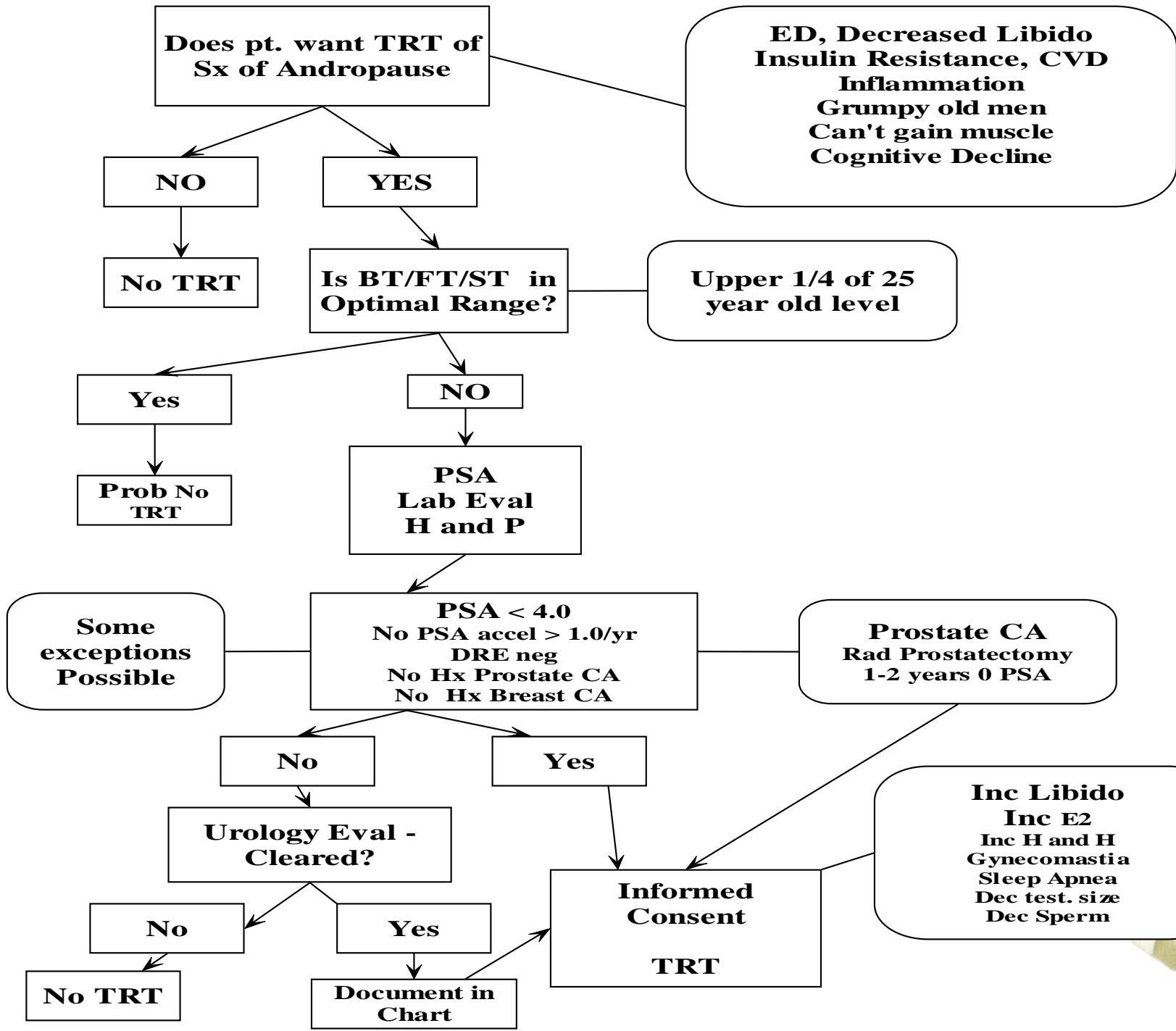
- Clinical
- Lab
- Decrease dose if side effects present
- Increase dose if benefits not seen up to dose of 10 mg
- Women are complex and sometimes still do not have libido even when T is high

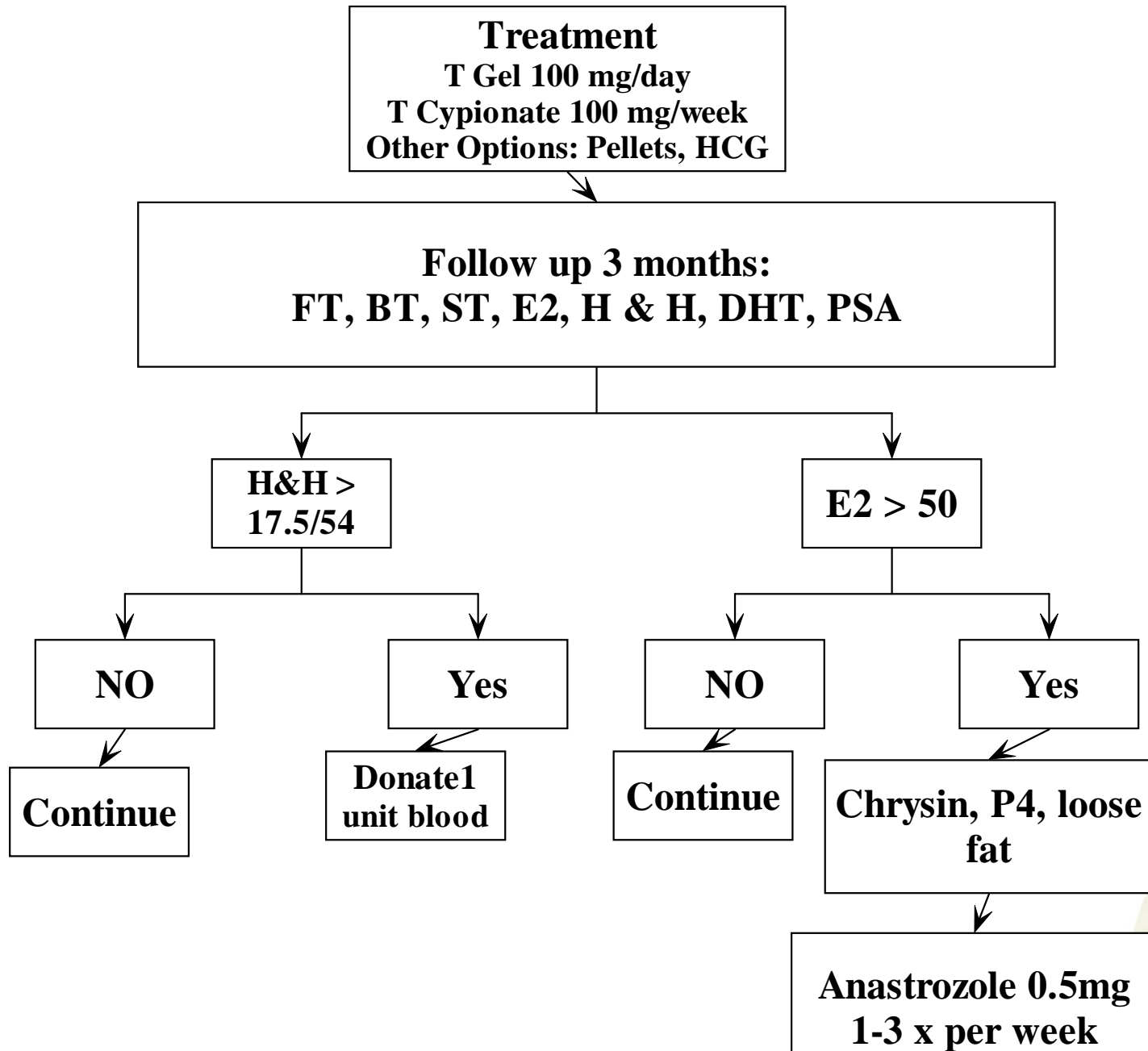


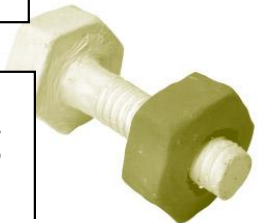
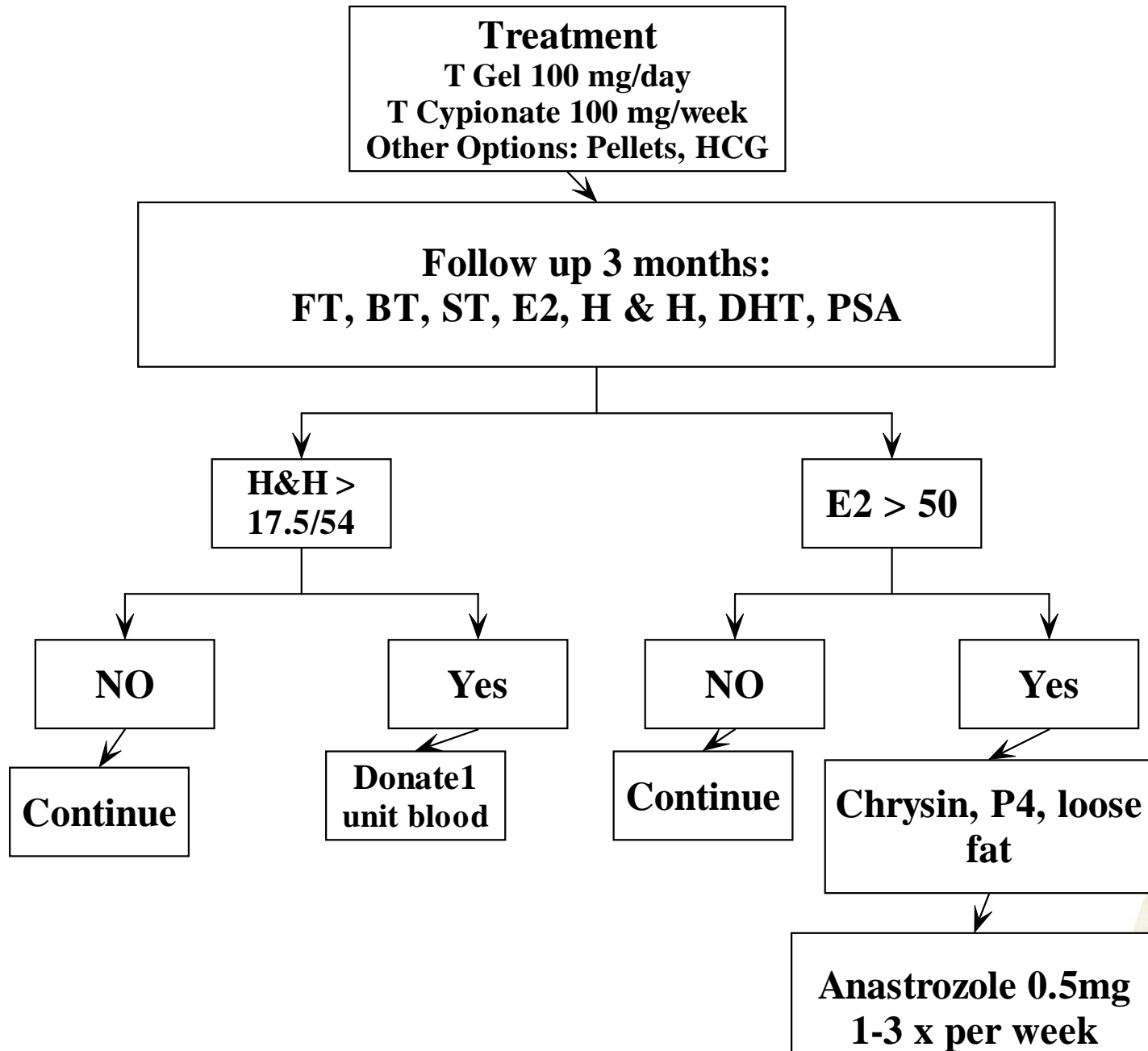
Controversies

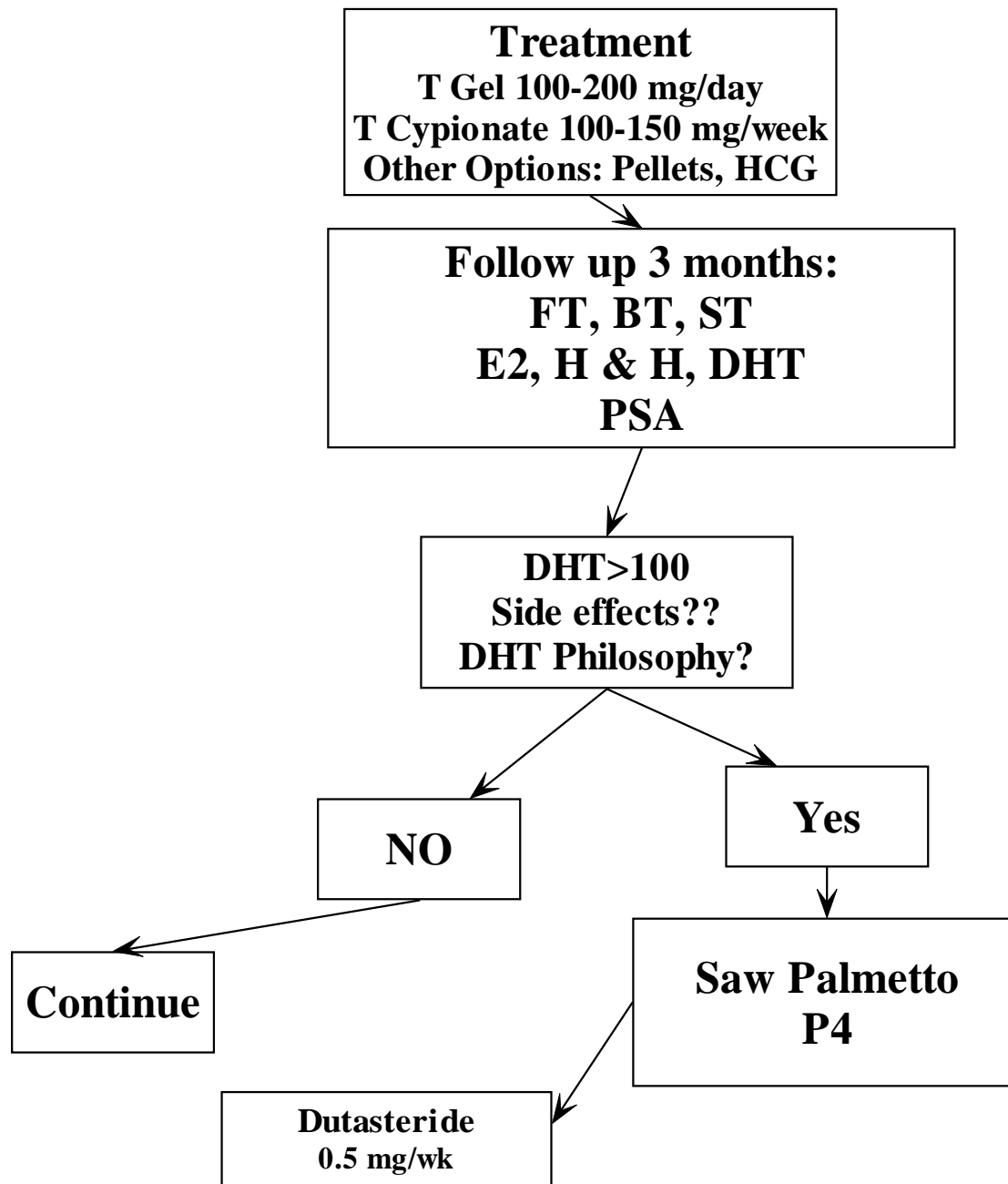
- Androgenic side effects?
- Should you treat a woman with low libido who has youthful range lab tests?
- Does T always work to restore libido?
- “My dog ate my Testosterone”

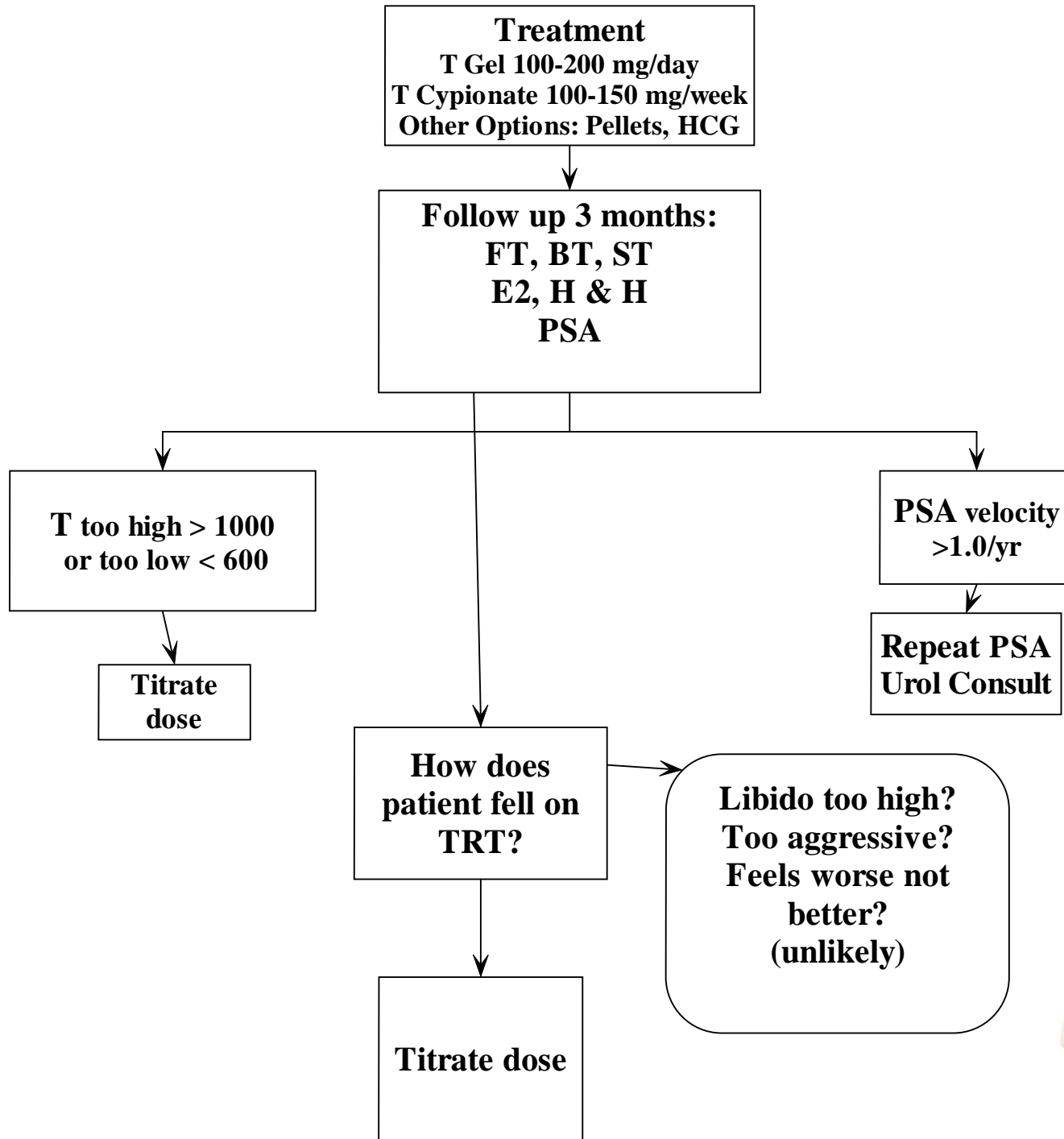


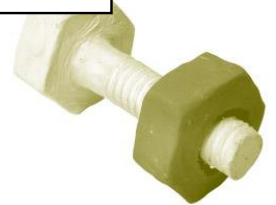
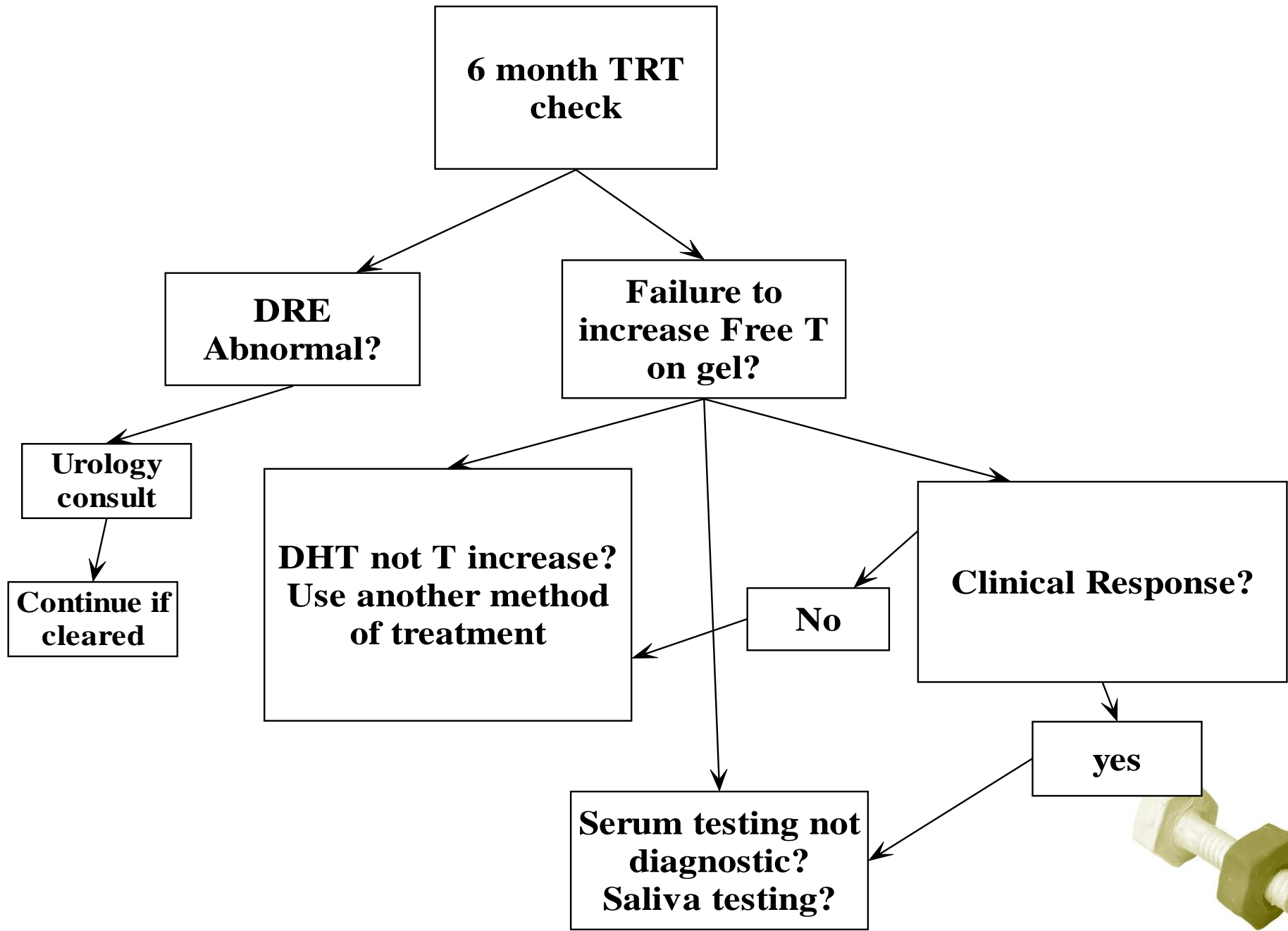


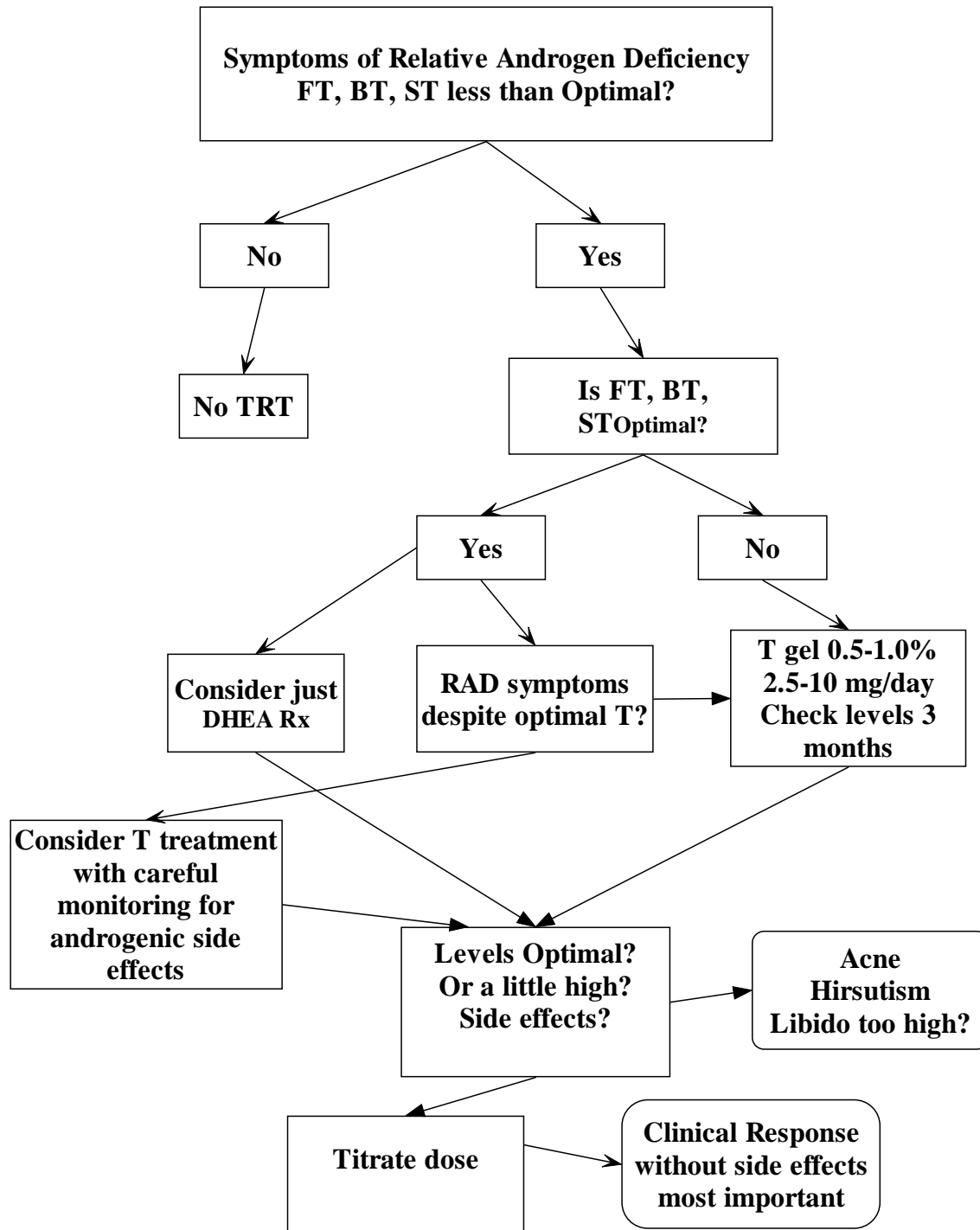












TRT Women



DHEA

- No unique symptoms of deficiency but...
- Low levels associated with
 - Obesity, Type 2 diabetes
 - Immune dysfunction
 - Autoimmune disease
 - Cancer
 - Hypertension
 - Cardiovascular disease
 - Depression and loss of well-being
 - Low libido, Erectile dysfunction
 - Osteoporosis



DHEA Anti-aging steroid

- **Anti-aging steroid**
- **Based on both in vitro and in vivo**
- **Stimulatory effect of immune system**
- **Anti-diabetes mellitus**
- **Anti-atherosclerosis**
- **Anti-dementia (neurosteroid)**
- **Anti-obesity**
- **Anti-osteoporosis**
- **Anti-cancer**
- **Nawata Het al. Mechanism of action of anti-aging DHEA-S and the replacement of DHEA-S.**
Mech Ageing Dev 2002 Apr 30;123(8):1101-6



Lab tests

- DHEAS not DHEA
 - Serum optimal
 - Men 400-600 micrograms/dl
 - Women 150-300 micrograms/dl
- DHEA Saliva optimal
 - Men 250 pg/ml
 - Women 200 pg/ml



Dose

- Men 25-100 mg
- Women 12.5-25 mg

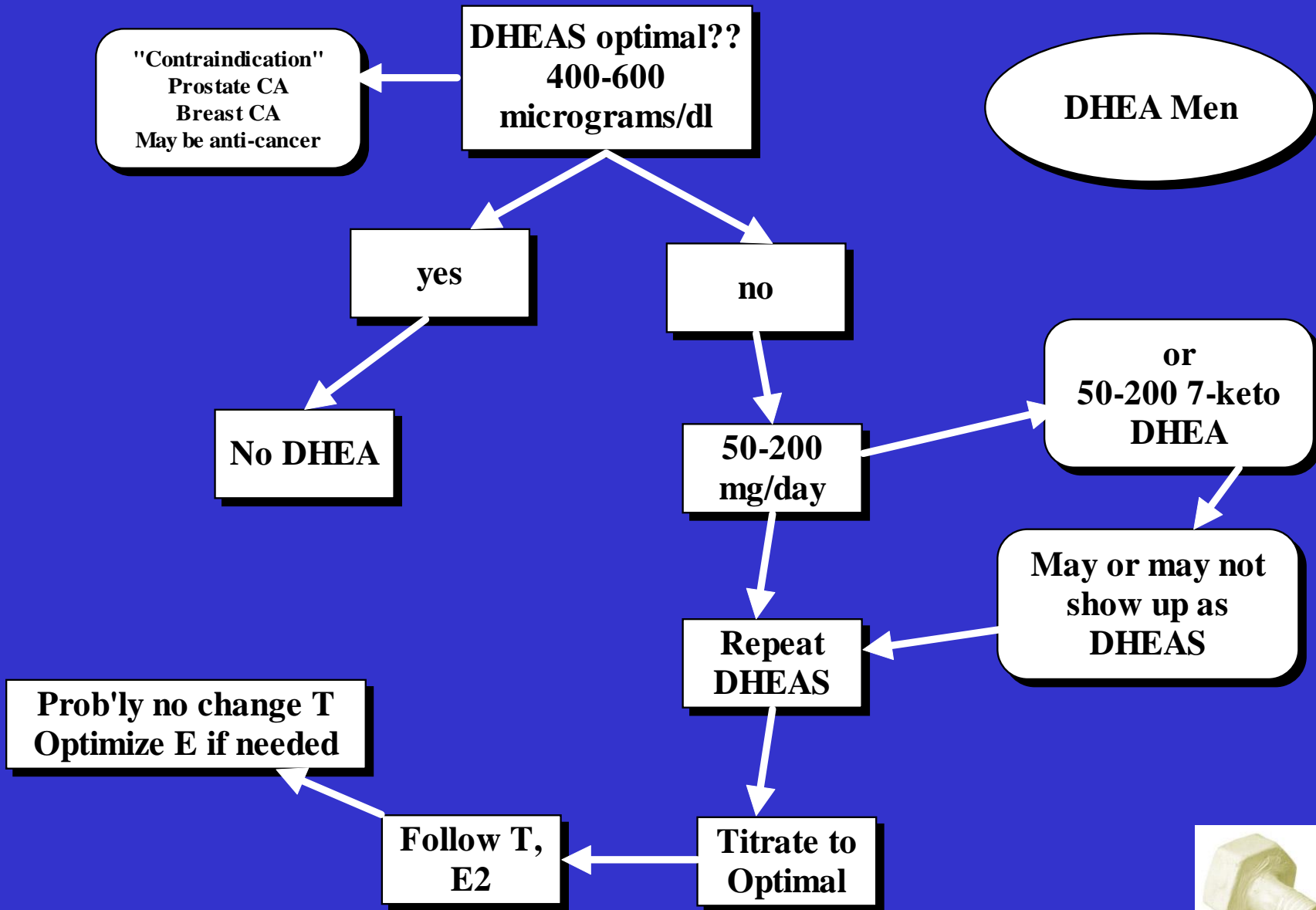
- 7-keto DHEA
 - No downstream metabolites
 - Probably the same benefits
 - More thermogenesis and weight loss
 - Men and women 25-200 mg



Controversies

- Use in Autoimmune disease
- Should every patient on corticosteroids be on DHEA?
- Since DHEA downstream metabolizes, can you treat all sex steroid deficiencies with DHEA?





DHEA Women

"Contraindication"
Breast CA
Reproductive CA
But may be anti-cancer

**DHEAS
Optimal?
150-300**

yes

no

**May not test
as DHEAS**

No T or E

No DHEA

**DHEA 10-50
mg/day**

**7-oxo DHEA
25-200 mg/day**

**Is BT/FT/ST
too high?**

**DHEAS
Optimal?**

**Titrate
Dose**

**Avoid
Androgenic Side
effects**

Acne, Hirsutism



Hypothyroidism – Symptoms/Signs

- Weight gain
 - Unable to metabolize calories
 - Too tired to exercise
- Lowered body temperature
 - May have heat intolerance as well as cold intolerance
- Lack of energy, tired
 - May also have adrenal component
- Cognitive dysfunction
- Fluid Retention
 - Periorbital, ankle edema, hypertension



- **Cold Intolerance**
- **Handshake test**
- **Fatigue**
- **Dry Skin**
- **Constipation**
- **Difficulty losing weight**
- **Eyebrow thinning lateral 1/3**



Lab tests - Optimal

- Free T3 in upper 1/3 of reference range
 - 3.5-4.2 ng/dl
- T4 is a pro hormone
- TSH < 1.9



Thyroid

- The Drug
- Combination of T3 and T4
- Armour = 39 T4 + 9 T3 per “grain” = 60 mg
- Can have compounded equivalent
- Short half life of T3 makes it difficult to use just T3
- Dose 1-4 grains
- Follow symptoms and Free T3



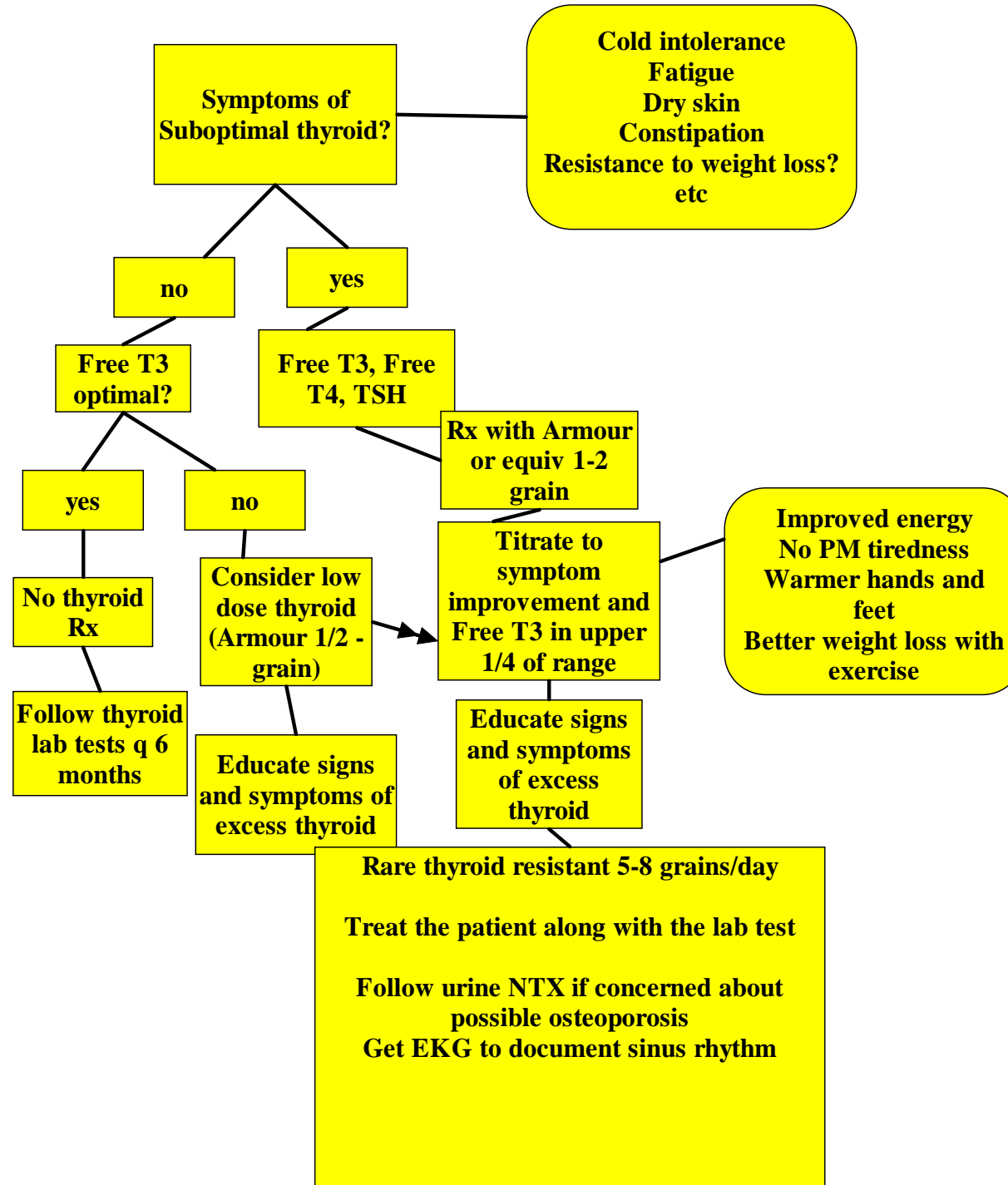
Controversies

- Is T3 plus T4 better than T4 alone
- Atrial Fib
- Osteoporosis
- Just look at the TSH, you do not need other testing
- Why test at all, just treat clinically no matter what the results
- “Type 2” Hypothyroidism?



Thyroid math





Female Hormones

- Estrogens
- Progesterone
- Testosterone

- “Delicate balance between E and P both antagonistic and complimentary”
- Thierry Hertoghe MD



Complimentary effects

- Feminization
- Libido



Progesterone deficiency symptoms

- Agitation
- Irritability, aggressiveness
- Anxiety, anger
- Weight gain
- Water retention
- Headaches
- Swollen or tender breasts



Progesterone deficiency symptoms

- Bloating
- Spotting or breakthrough bleeding
- Mood swings
- Poor sleep, insomnia
- Water retention
- Achy joints
- Excessive bleeding, menorrhagia
- Endometriosis
- Fibrocystic breasts



Dose

- Oral 50-200 mg HS
 - Sedating + metabolite is sedating
 - 5-allo-pregnenolone
- Transdermal is more bio-available, may be preferred if sedation is not an issue
- 50-100 mg
- Premenopausal – usually cycle days 14-25
 - Can use 2 or more steps eg 50 mg days 1-14
 - Can use daily if needed for mood stabilization
- Menopausal – continuous or cycle?



Controversy

- Provera is dangerous, why is progesterone better?
- Does she still need progesterone with no uterus?
- Can you give her too much P4?



Estrogens

- E1=**Estrone** Maybe more than she needs
- E2=**Estradiol** Effective Estrogen,
Catechol and methoxy metabolites are protective
- E3=**Estriol** cancer protective, weak



Estrogen deficiency

- Hot flashes
- Night sweats
- Fatigue
- Poor memory and Foggy thinking
- Low energy



Estrogen deficiency

- Depressed mood
- Decreased concentration
- Decreased sexual desire or libido
- Vaginal dryness
- Excessive daytime sleepiness
- Stress incontinence and UTI's
- Osteoporosis, Cardiovascular disease, Dementia



Estradiol Lab tests

- Serum Day 21 150 ng/ml optimal
- Saliva (better if on transdermals)
- Day 21 premenopausal 15 pg/ml
- Menopausal on E2 10-20 pg/ml



Dose

- Biest = E3 + E2 usually 80/20
- 1.25-5.0 mg per gram
- Once per day or BID
- eg 1 gram 80/20 Biest 2.5 mg/gm =
2.0 mg E3 + 0.5 mg E2
- Pellets, IM E2
- E2 patches



Safety Issues and Testing

- Breast Imaging
- Thermography
- Pap smear once a year
- Ultrasonography: breast ovaries uterus



Excess Estrogen

- Agitated
- Anxiety
- Weight gain
- Water retention
- Headaches
- Swollen or tender breasts
- Bloating
- Spotting or breakthrough bleeding
- Mood swings
- Poor sleep
- Achy joints
- Excessive bleeding



Controversies

- Do all women need E?
- Does Bio-identical E increase rates of breast cancer and cardiovascular disease?
- Lab tests vs. clinical picture to treat initially.
- Does transdermal work on all women?
- Why not use bio-identical oral E?



Cortisol Deficiency

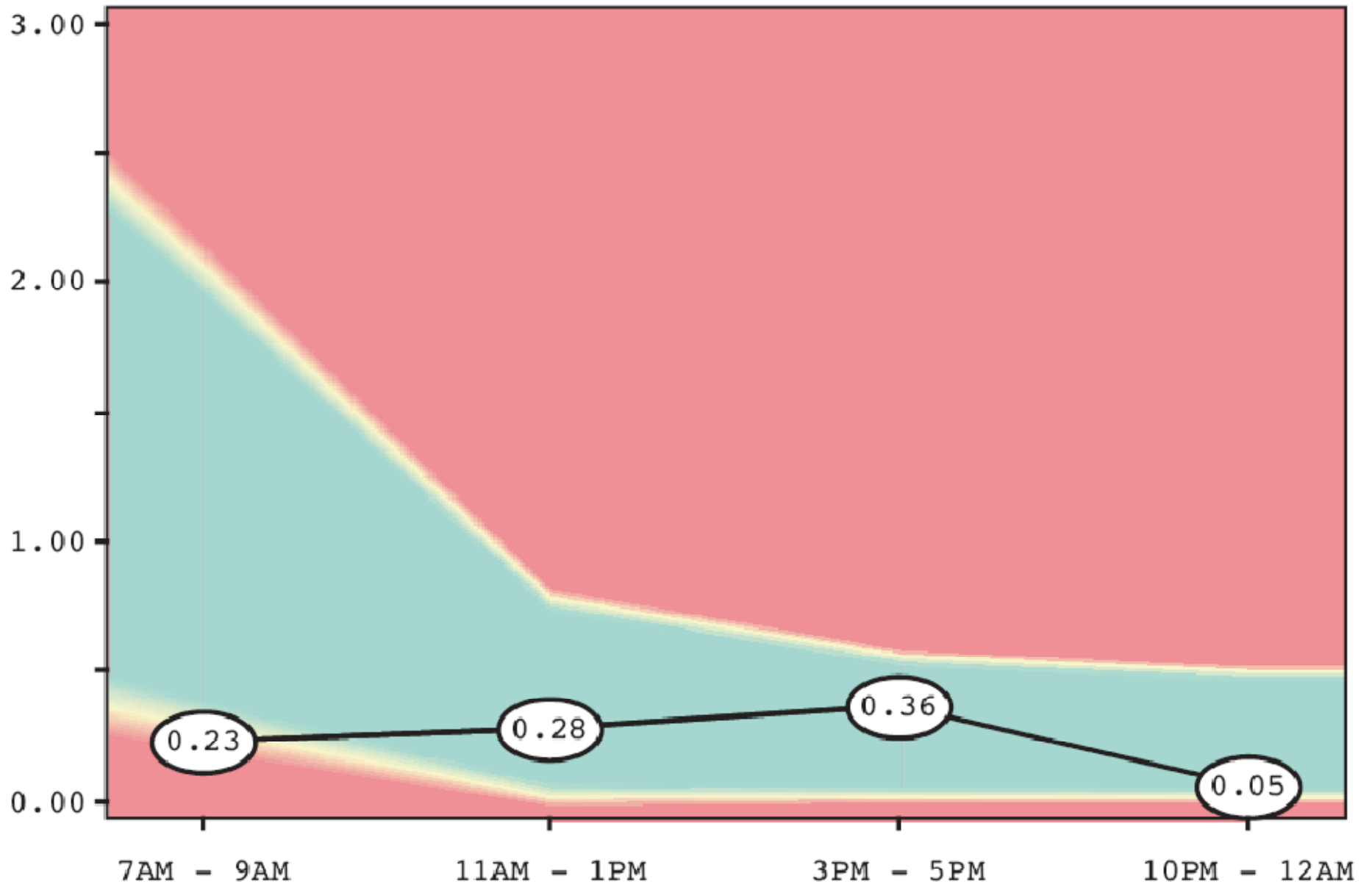
- Fatigue
- Anxious, nervous
- Poor stress tolerance
- Hypersensitivity to environment
- Absent-minded, Forgetful
- Feeling spacey, confused
- Depression
- Paranoid feelings
- Irritable / hostile
- Concentration problems



Lab test

- AM cortisol – only one data point
- Salivary cortisol – draws curve
- Can be high
- Can be low – adrenal fatigue





Treatment

- High
 - Lifestyle
 - Eliminate stress
 - Meditation
- Low
 - Adrenal support
 - Bio-identical cortisol
 - Compounded cortisol
 - 5-30 mg per day divided BID



Controversies

- What? You are treating a patient with corticosteroids.
- Do precursors work?
- How useful are lab tests?



Growth Hormone

- Big Pharma brands
- Compounded



Symptoms

- Decreased quality of life
- Sarcopenia (Loss of Muscle Mass)
- Loss of exercise capacity
- Osteopenia
- Loss of strength
- Increased total and intra-abdominal fat



- Glucose intolerance
- Dyslipidemia
- Increased fragility of skin and blood vessels
- Decreased skin thickness
- Decreased muscle tone, increased droopiness
- Decreased confidence and optimism
- Decreased immune function



Lab tests

- Stimulation tests
- IGF-1
 - Low values correlated with AGHD
 - Can have normal values and be deficient
 - Typically increases 100 ng/dl with 0.33 mg per day treatment
- 24 hour urine
- Spot urine



Dose

- Ramp up
- 0.2 mg per day
- 0.4 mg
- 0.6 mg
- Women need more than men
- Not effective in women taking oral estrogens (transdermal OK)



Followup

- 4 possible side effects
- Edema
- Arthralgias
- Paresthesias
- Glucose insulin getting worse instead of better



Controversies

- Unique legal status of GH
- Cancer?
- Side effects too prevalent?
- Diabetes?
- Dosage schedule?
- Do “secretagogues” work?



