



Hormone Treatment (Testosterone) with Subcutaneous Pellet Implants

Rebecca L. Glaser, M.D., FACS



www.hormonebalance.org

Data

username: data

password: data

Testosterone... delivered by pellet implant



Testosterone pellet implants

- Testosterone, delivered by pellet implant is the most effective anti-aging, health promoting, disease preventative therapy available
- Safety profile
- Cost effective



Hormone Implants: Pellets

- Pellets made up of testosterone compressed into very small, solid cylinders
- 1972 'FDA approved' 75 mg testosterone pellet US
- 100 mg and 200 mg T pellets in Europe and Aus
- Other formulations and dosages need to be 'compounded' by trained pharmacists
- They come in sterile glass ampoules or vials



Simple procedure

- The insertion of pellets is a simple, 2-5 minute office procedure done under local anesthesia
- They are placed just under the skin of the upper buttocks or lower abdomen
- They completely dissolve over time
 - 3-4 months in women
 - 4-5 months in men



Data (evidence based medicine)



- History
 - Question the paradigm Women=Estrogen
- Clinical Data Men and Women
 - Bone health
 - Body composition
 - Cardiovascular health, lipids
 - Breast health
- Protocol
 - Testing
 - Dosing
- Current Research
- Procedure

Full text references

hormonebalance.org

DATA

username: data

password: data

History of hormone pellet implants



- Subcutaneous hormone implants have been used in Europe, US and Australia since 1938
- Superior to other methods of hormone delivery (oral, IM, topical)
- Deliver consistent, effective levels of physiologic hormones

Mishnell 41, Greenblatt 49, Thom 81, Stanczyk 88

Greenblatt 49 AJOG



- ...implantation of hard compressed pellets of crystalline steroids resulted in a slow and **more physiologic** absorption of the hormone...
- “Since the amount of hormone released to the organism is continuous though minute in quantity, it is conceivable that by this method the endogenous mechanism of hormonal secretion is more nearly approached and the physiologic action of the hormone more closely imitated.”



Greenblatt 49 AJOG



– Indications for Use of Testosterone Pellets

- Menopausal syndrome in whom estrogen therapy has proved unsatisfactory or is contraindicated
- In combination with estradiol pellets in patients with uteri who have severe menopausal symptoms, in order to **prevent the untoward bleeding** induced by estrogens
- Dysmenorrheic patient with **endometriosis** or small **fibroids**
- **Fibromyomata** for whom surgery is not feasible
- Nocturia of endocrine origin
- Increased libido is desired
- Palliative measure in patients with advanced **carcinoma of the breast**
- In combination with Desoxycorticosterone pellets for Addison's disease

Benefits



- Hormones (testosterone) delivered by subcutaneous implants, bypass the liver
 - Do **not** affect clotting factors
 - Do **not** increase the risk of thrombosis
- Bio-identical testosterone delivered by pellets is **cardiac protective**, unlike oral, synthetic testosterone
 - Do not negate the beneficial effects of estradiol on cardiac and lipid profiles
 - Notelovitz 87, Seed 00, Sands 97, Worboys 00

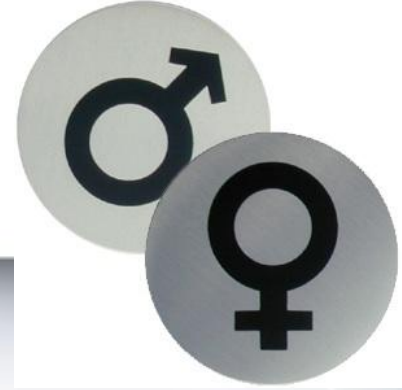


- Testosterone and estradiol delivered by pellet implantation **does not adversely affect**
 - Blood pressure
 - Lipid levels
 - Glucose
 - Lower glucose
 - Liver function



- Burger 84, Notelovitz 84, Barlow 86, Stanczyk 88, Davis 95, 00, Cravioto 01, Handelsman 96

Efficacy of Testosterone implants



- Increase energy
- Improve sleep
- Relief of migraine or menstrual headache
- Relief from depression, decrease anxiety
- Increased muscle mass and bone density
- Decreased soft fatty tissue
- Improved skin (increased collagen and elastin)
- Increased concentration and memory
- Decreased aches, pains, stiffness

Efficacy of testosterone pellet implants



- Improved libido and sexual satisfaction
- Improved sexual function in men
- No increased risk of strokes or blood clots
- Improve arterial vasodilation
- Extremely low incidence of side effects
 - Slight increase in facial hair (20-80%)
 - Mild acne (2-10%)

Staland 78, Thom 81, Brincat 84, Davis 95,00, Cravioto 01, Magos 83, Barlow 86, Cardoza 84, Ganger 89, Pirwany 02, Anderson 97, Sands 97, Seed 00, Montgomery 87, Worboys 00, Handelsman 96, Dunning 04

Hormone implants and breast cancer



- Testosterone delivered by pellet implant does not increase the risk of breast cancer unlike oral, synthetic methyl- testosterone
- Studies using testosterone implants have shown less stimulation of breast tissue and lower rates of breast cancer
- Treatment with testosterone and estradiol implants does not increase the risk of breast cancer, even in breast cancer survivors
 - Even high doses of estrogen/progestin therapy, when given with testosterone pellet implants, did not increase BC
- Davellar 91, Zhou 00, Dimitrakakis 03, 04, 06, Gambrell 06

Estradiol implants



- Increased incidence of breast cancer (Million Women's Study, Lancet 2003)
 - Continuous stimulation of breast tissue
- Cause prolonged uterine bleeding
 - Continuous stimulation of uterine tissue
 - Vaginal ultrasound, uterine biopsy
 - Progestin therapy
- Continuous estrogen is NOT physiologic

Testosterone and Breast Tissue



- Testosterone is the ‘antagonist of estrogen’ (1930’s)
- Testosterone action is **anti-proliferative** and pro-apoptotic (**increases cancer cell death**).
- It is mediated by the Androgen Receptor (**AR**)
 - AR pos tumors better prognosis, increased survival
- **Androgens** (testosterone, DHT) **inhibit** breast cancer in almost every breast cancer cell line
 - *Pharmacologic* doses (100X) of androgens can stimulate human breast cancer cells (MCF-7) in *vitro* via the Estrogen Receptor (**ER**)
 - In vitro (cell cultures in a petri dish) results are NOT necessarily clinically relevant in vivo (the human body)

Testosterone therapy for breast cancer

- Androgens, including testosterone implants, have been used to treat breast cancer patients



Testosterone and Breast Tissue



- Testosterone **inhibits** estrogen-induced mammary epithelial proliferation and suppresses estrogen receptor expression Zhou 00
 - Rhesus monkey, primate breast tissue
 - Estrogen alone increased mammary epithelial proliferation 6x and ER α by 50%
 - No change with progesterone
 - Testosterone decreased estrogen induced proliferation and totally abolished the increase in ER α
 - Tamoxifen increased proliferation 3x but decreased ER α



Testosterone and Breast Tissue cont.



- Endogenous androgens inhibit mammary epithelial hyperplasia. A physiologic dose of T to EP therapy attenuates the estrogen-induced mammary epithelial proliferation (MEP) Dimitrakakis 03
 - Rhesus monkeys
 - Treated with Androgen Receptor (AR) blockade, flutamide
 - 2x increase in MEP
 - Added testosterone to E & P therapy it **prevented** the estrogen induced MEP
 - Testosterone alone reduced ER α



Testosterone Implants and Breast Cancer

Dimitrakakis 04 Menopause



- 508 Post menopausal women referred for testosterone supplementation for emotional lability, fatigue, loss of concentration, breast tenderness, loss of libido, sleep disturbances and weakness despite ERT
- FH of BCa 29%
- 508 women T 50-150 mg every 5 month in addition to CHRT (161 E/T, 347 E/T/P), f/u 5.8 years

Dimitrakakis 04 Menopause



TABLE 2. *Breast cancer cases in women using testosterone compared with major studies*

	N	Age	Cases/100,000 woman-years	Years observed
Schairer et al ¹⁰ (E/P)	1,854	57.4 y	628	10.2
WHI ⁶ (E/P)	8,506	63.2 y	380	5.2
Million Woman ⁵ (E/P)	142,870	55.9 y	521	2.6
Million Woman ⁵ never-users	392,757	55.9 y	283	2.6
Adelaide (E/P/T)	347	57 y	293	5.9

Current E/P users are analyzed in comparison with never-users (from the Million Woman Study) and E/P/T users from Adelaide, South Australia. Citations refer to the "References" section at the end of the article. WHI, Women's Health Initiative; E/T, estrogen + testosterone; E/P/T, estrogen + progestin + testosterone.

Cases/100,000 woman years

- Adelaide E/P/T **293**
- WHI E/P **380**
- Million Woman
 - E/P **521**
 - Never users **283**
- Adelaide total **238**
- Adelaide E/T **115**

- The addition of **testosterone** to CHRT does not increase, and **may reduce the incidence of BCa**

Testosterone Pellet Implant Incidence of Breast Cancer

- Dimitrakakis, Glaser
- IRB approved 10 year, prospective trial looking at the incidence of breast cancer in women treated with testosterone implants
 - **Testosterone Pellet Implant**



Atrium Medical Center
Premier Health Partners

Pre-menopausal females



- Women may have deficient hormone levels as early as their early to mid thirties (premature ovarian failure)
- Indications for testosterone pellets
 - PMS (Anxiety, irritability)
 - Menstrual or migraine headaches
 - Sleep disorders
 - Depression, Post partum depression
 - Auto immune disease (MS)
 - Aches, pain, weakness, bone loss
- Must use birth control (consent)

Safety of maternal testosterone therapy during breast feeding

Rebecca Glaser, David Zava, Melanie Parsons, Mark Newman



- Dose and route of delivery
 - Vaginal Testosterone 0.5 mg daily
 - Sublingual Testosterone 1 mg BID
 - Testosterone pellet implant 100 mg SQ
- Results
 - Testosterone measurable in mothers blood
 - Absent from breast milk
 - Absent from infant blood
 - No adverse effects in infant (5 month FU testosterone pellet implants)

Abstract/poster presentation: International Congress on Hormonal Steroids and Hormones
& Cancer Sept 08

Andropause



Testosterone pellets in men

- There is no better way to deliver testosterone in men than with pellets.
 - Maintain **consistent** levels of testosterone while maintaining normal ratios of estrogen and DHT

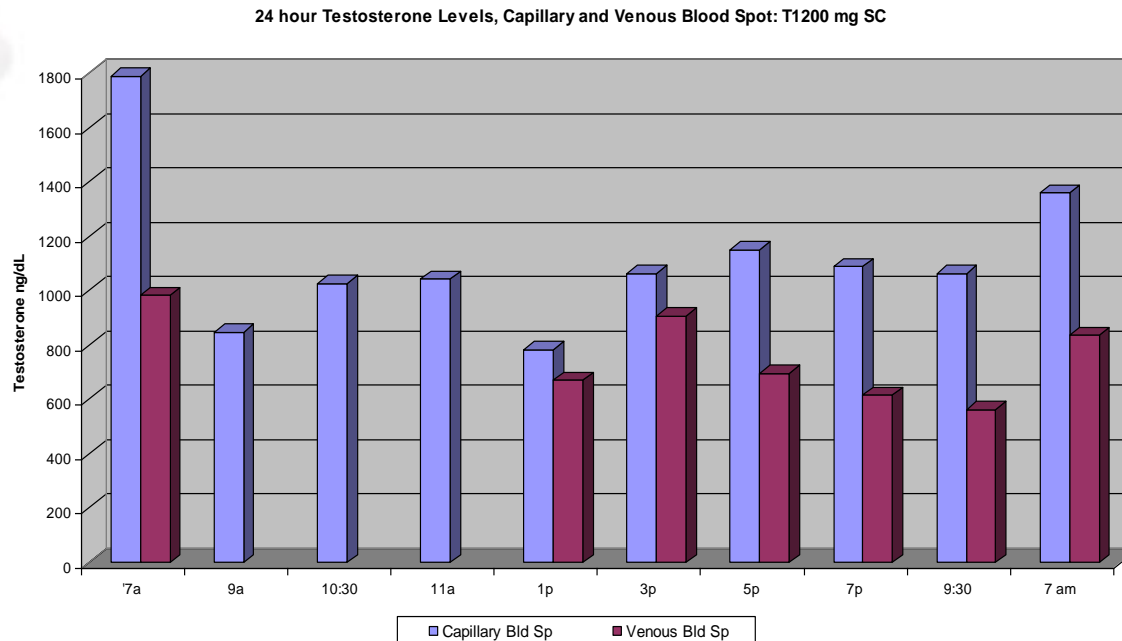


2008

Testosterone Pellets MEN



- Release rates from implants are known, consistent
- Is circadian release with testosterone implants
- Suppression of FSH and LH is dose dependent and correlates with clinical effects
 - Suppression of LH may cause the testicles to decrease in size



24h range
562-983 ng/dL

Testosterone Pellets MEN cont.



- Testosterone implants are able to maintain bmd long term
 - A single implantation with 1200 mg of testosterone was **more effective** in increasing bone density than oral or IM testosterone in men with primary hypogonadism
- Extrusion <1%-8%, minor bleeding 0-2%, minor infection 1-5%
 - Complication rate is related to operator skill
- Early physical activity is a predisposing factor for extrusion

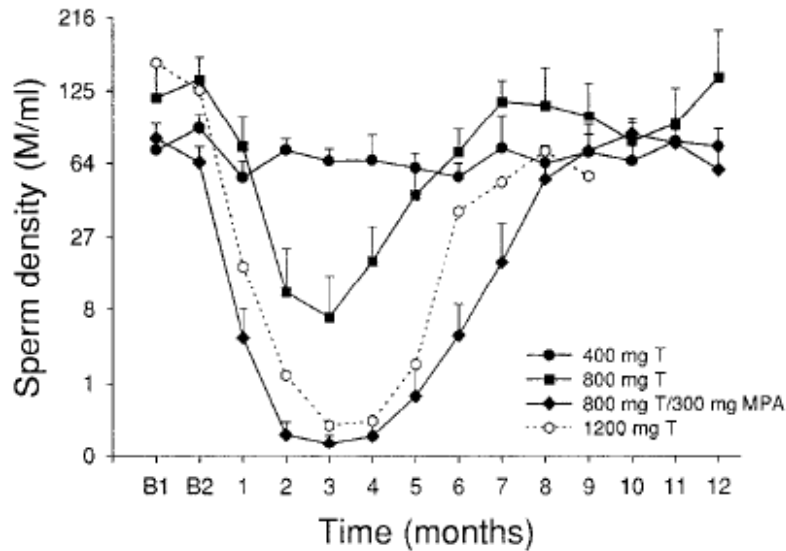
Testosterone Pellets MEN cont.



- No scarring to interfere with further implants
- Downside
 - Difficulty in reversing Testosterone effects (diagnosis of prostate Ca)
 - Treat with alternative method of TRT and recheck PSA 3 mos.
 - Minor *procedure* (5 minutes two to three times yearly)
 - Minimal discomfort
- Continuation rate of 93%
- Consistency, compliance, convenience

Handelsman 90,92,97, Kelleher 01, 04, Conway 88, Jockenhoeval 96,
Zacharin 03, Schubert 03

Handelsman 96 JCEM



- Sperm suppression is dose dependent
- 4, 200 mg testosterone pellets, delivering 6 mg per day, were inadequate to suppress spermatogenesis vs. 1200 mg of T or 800 mg & 300 DMPA
- **Metabolic Effects ***
 - No effect on PSA, cholesterol fractions, glucose, phosphate, LFT's, renal function tests or hematological variables. No evidence of hepatotoxicity.

Dunning 04

- “Testosterone replacement is safe and almost always successful by all methods, but implants are the most effective in maintaining sexual function and have fewer side effects.”



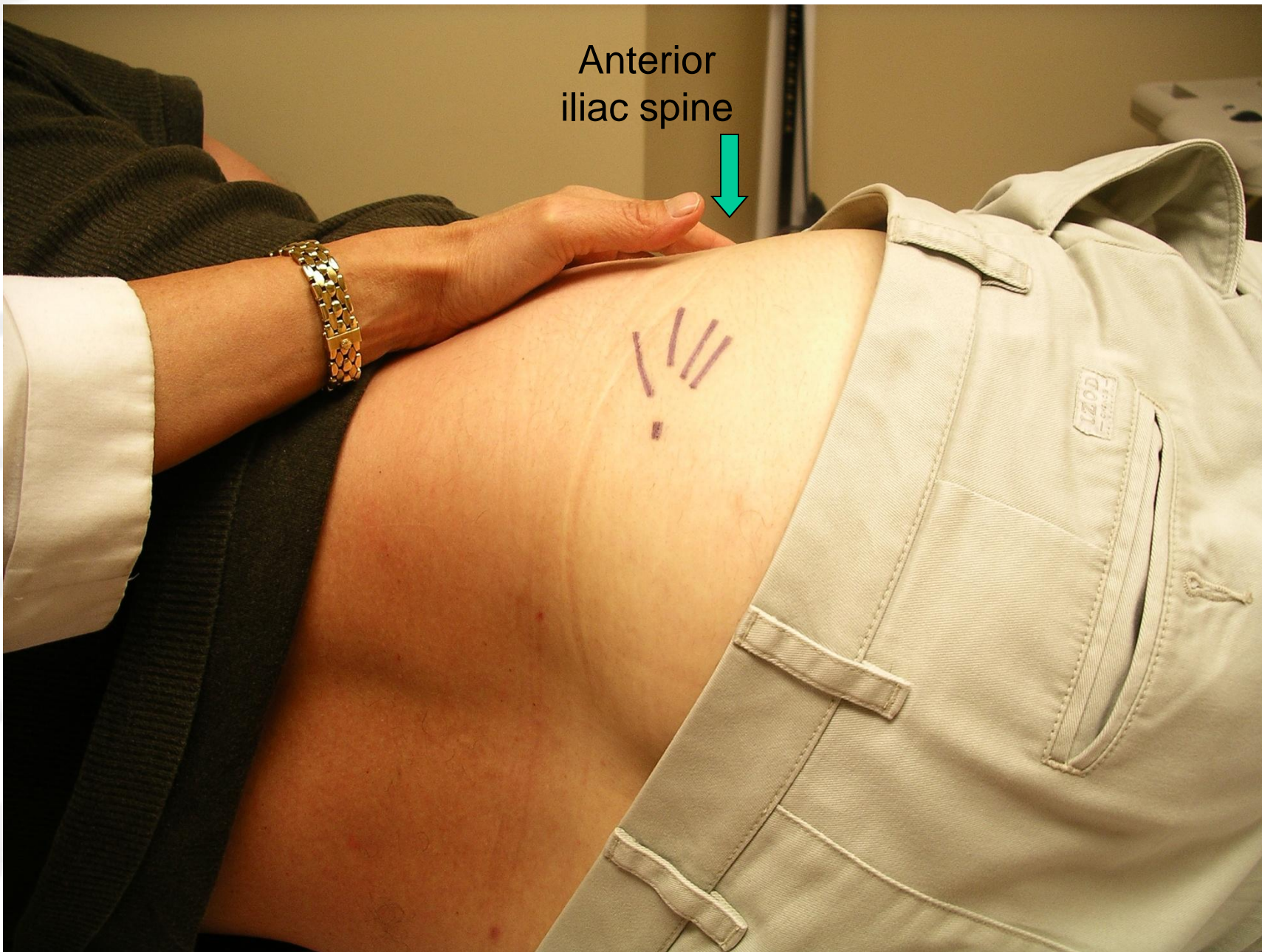
"...AND DO YOU, KATE, TAKE THIS MAN AS IS--
WITHOUT VIAGRA?"

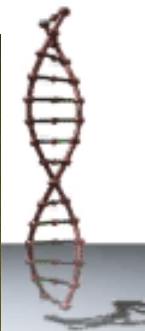
Simple Procedure





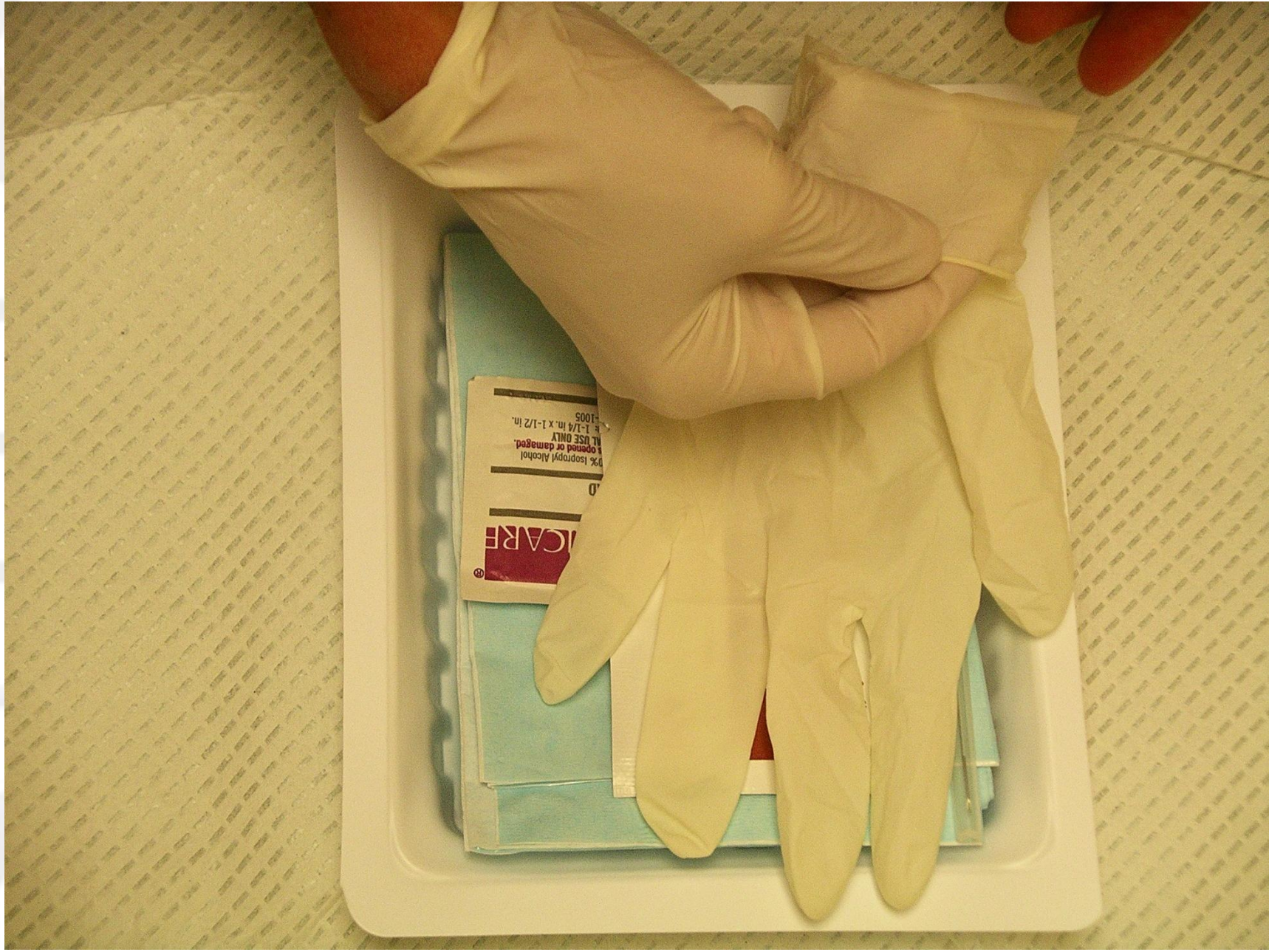
Anterior
iliac spine

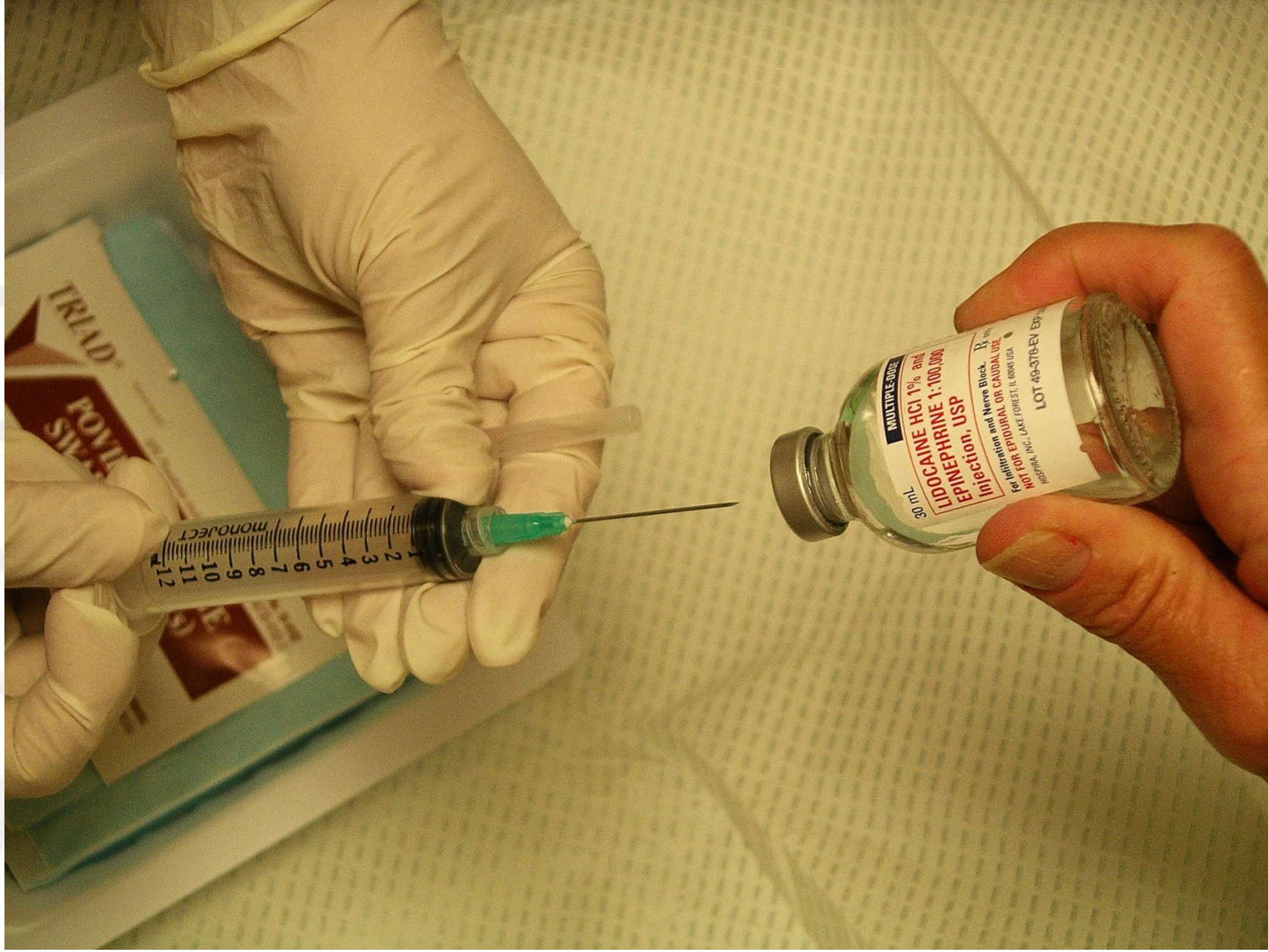










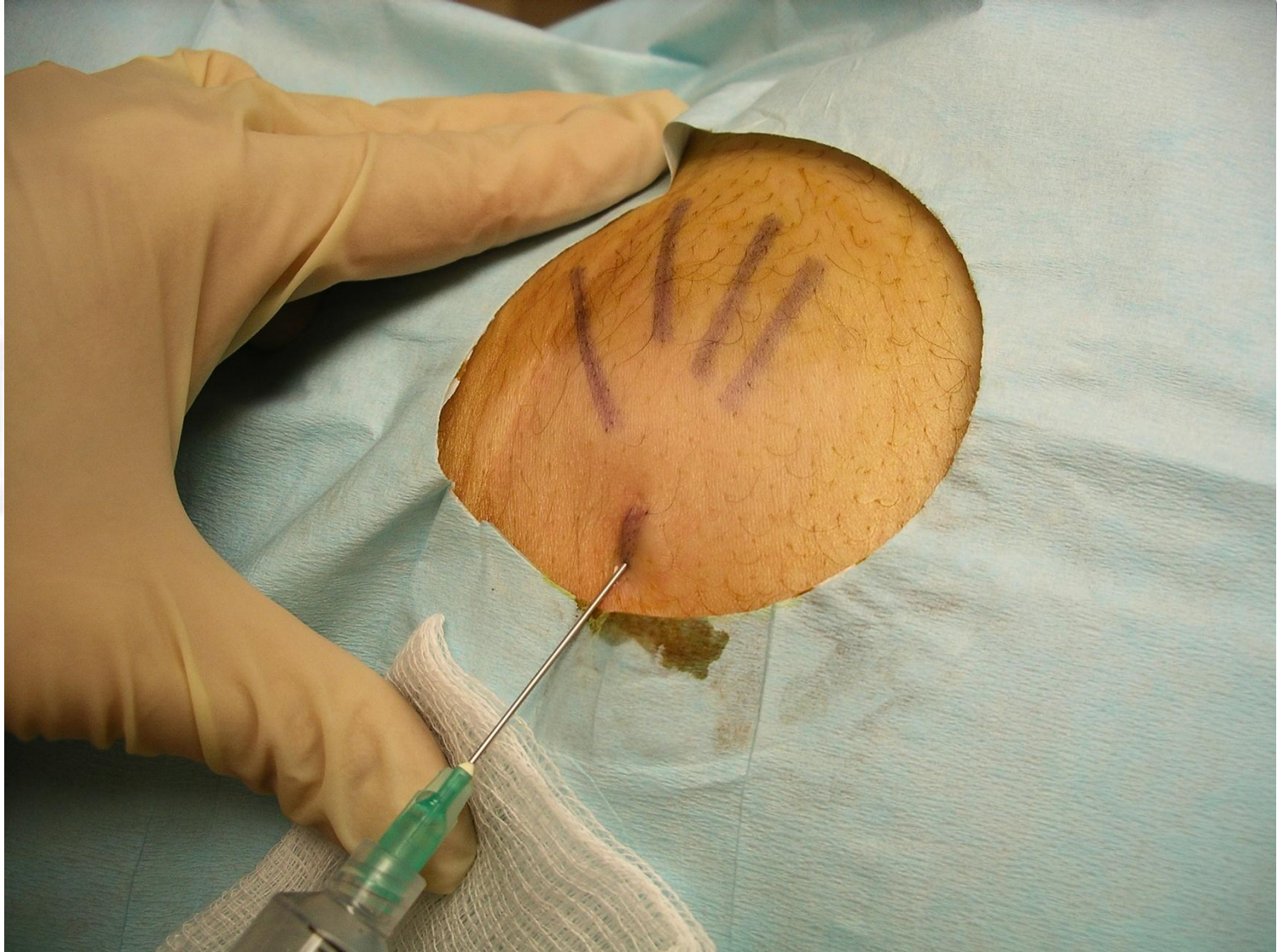


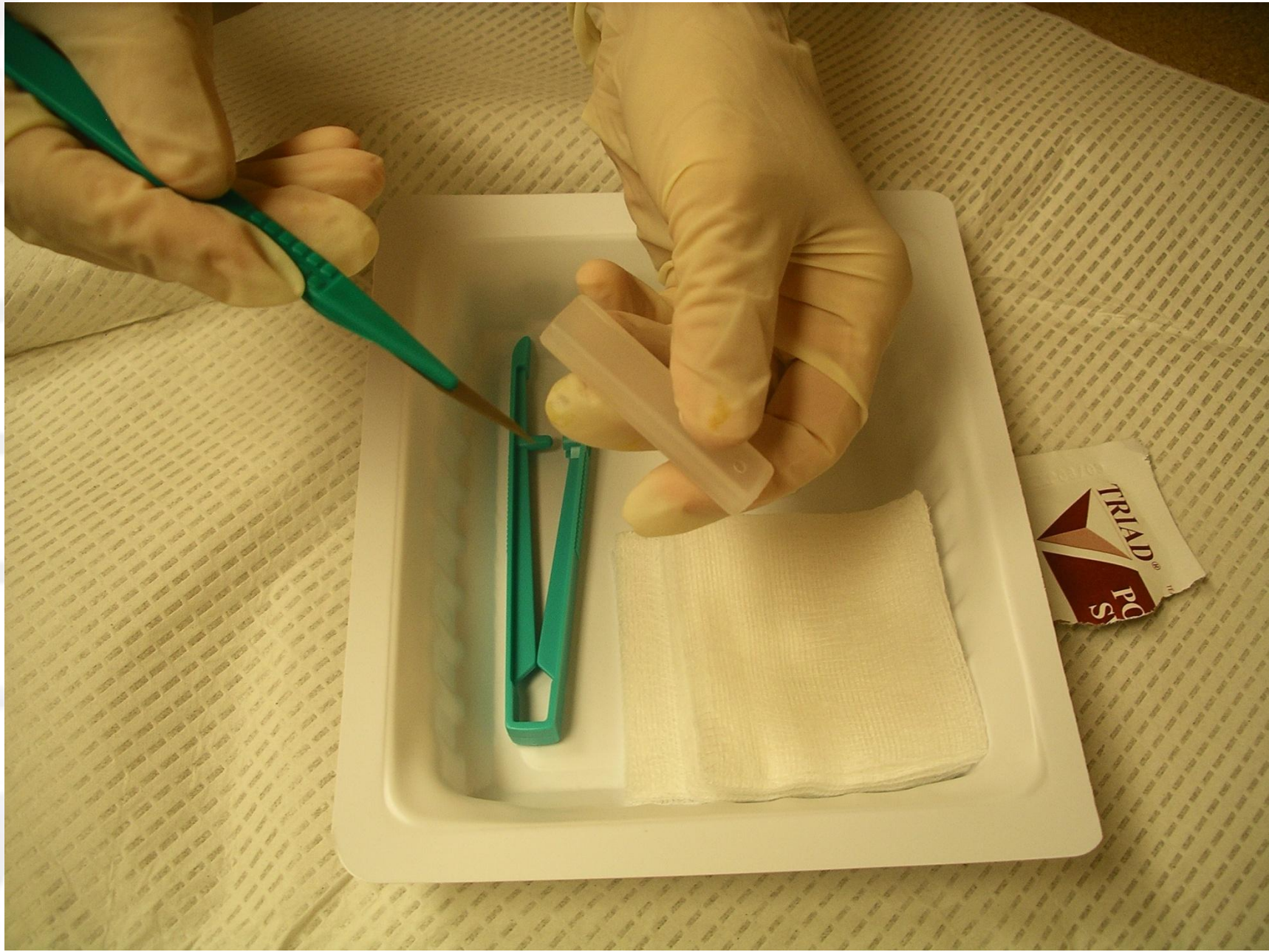






Men: 4cc 1% lido with epi, 4cc 1% without epi & 4cc Sodium Bicarb





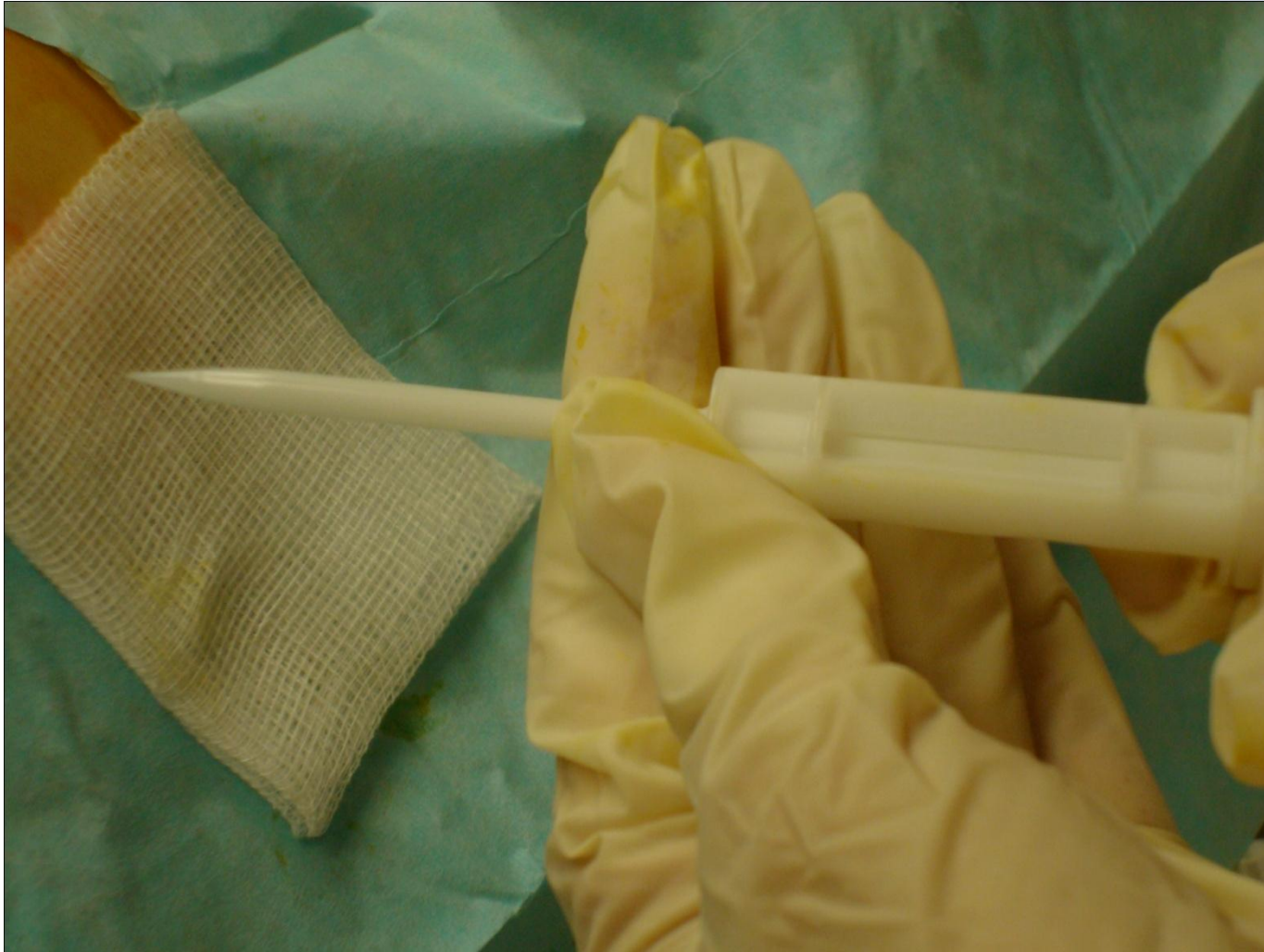
11 blade, 5 mm incision



Disposable 3 piece trocar set (fits 3.1 mm implant)



Sharp trocar & cannula inserted 5mm
in depth, tract parallel to the skin



3, 100 mg pellets per tract in men



Pellets are advanced with the blunt trocar. Rotate/reinsert cannula.

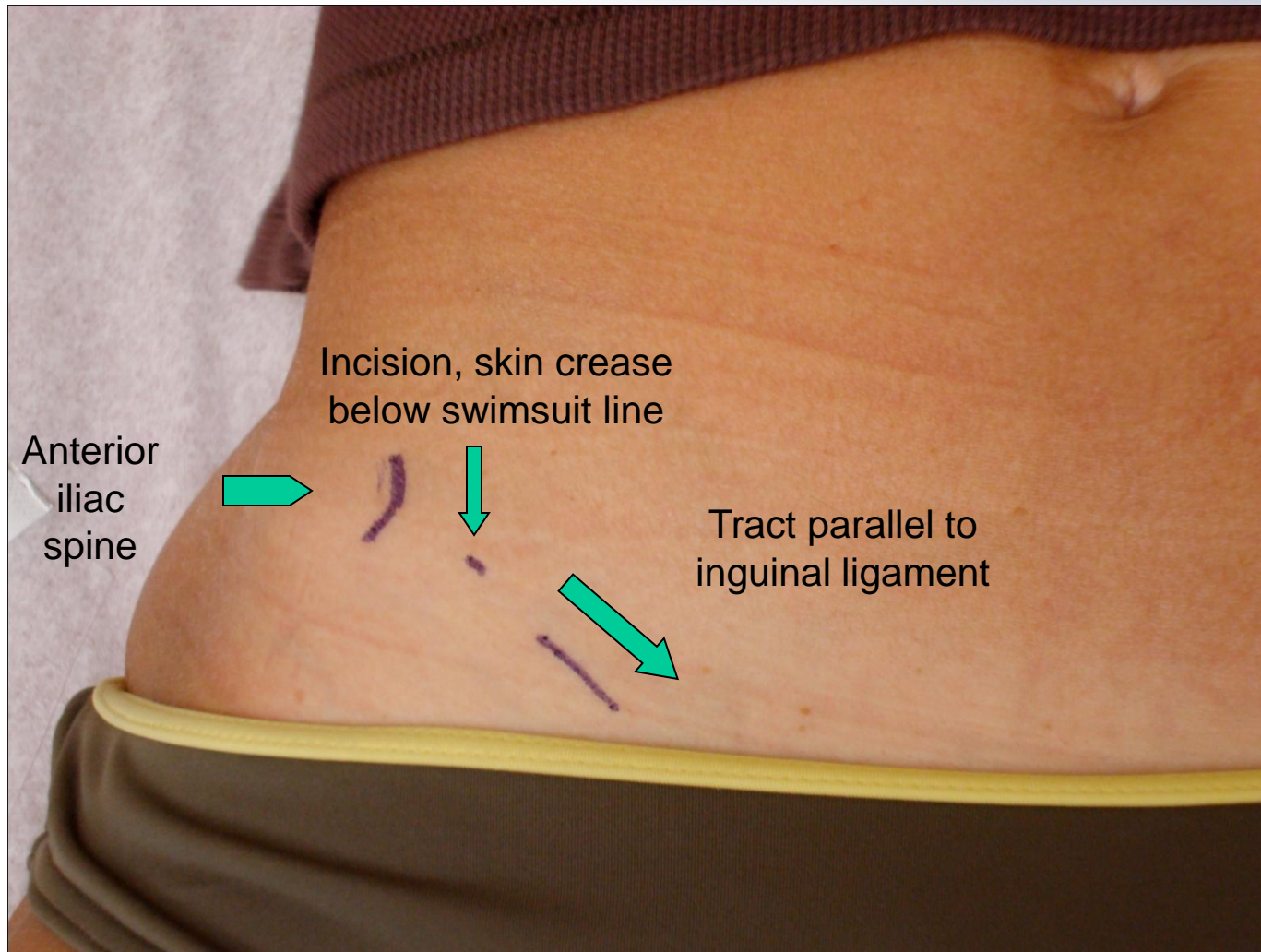




5-10 minutes of pressure (ice pack)



Landmarks abdomen



Treatment Protocol

- Testing
- Dosing
- Follow up



Women



#1 Testosterone delivered as a pellet implant

In the majority of pre and post menopausal women, almost all symptoms are relieved with a testosterone pellet implant **ALONE**

- Vaginal estrogen/progesterone therapy (10%)
 - Safety and efficacy (Glaser 08)
 - Vaginal estriol, \pm estradiol, progesterone 2-3 days per week
 - E3 0.5 mg, (E2 0.125 mg), P25 mg /DOSE
- Other systemic estrogen formulations (2%)
- Progesterone
 - Pellet implant, SL drops/troche, oral

Sherwin 85 AJOG



- Prospective, double blind, cross-over study
- Physical and Psychological symptoms
 - Estrogen-androgen
 - Estrogen alone
 - Testosterone alone
 - Placebo
- Testosterone alone was superior for relief of energy, well being, somatic symptom scores, psychological symptom scores
 - Associated with higher testosterone levels
- Worse symptom relief was estrogen alone and placebo

Efficacy Testosterone Pellet Implants

Glaser, York, Dimitrakakis



- Validated symptom survey (MRS)
- 300 patients, 1/3 Pre-menopausal
- Baseline rating compared to testosterone pellet implant (80-160 mg)
- Findings: statistically significant improvement in all 11 categories
 - $p < 0.0001$ Wilcoxon test for paired samples
- Effect was dose dependent

Menopause Rating Scale (MRS)

Which of the following symptoms apply to you at this time?

(X ONE Box For EACH Symptom) For Symptoms That Do Not Apply, Please Mark "None").

Symptoms:

		none	mild	moderate	severe	extremely severe
		-----	-----	-----	-----	-----
Score	=	0	1	2	3	4
1.	Hot flashes, sweating (episodes of sweating).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2.	Heart discomfort (unusual awareness of heart beat, heart skipping, heart racing, tightness).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.	Sleep problems (difficulty in falling asleep, difficulty in sleeping through the night, waking up early).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4.	Depressive mood (feeling down, sad, on the verge of tears, lack of drive, mood swings).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5.	Irritability (feeling nervous, inner tension, feeling aggressive)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6.	Anxiety (inner restlessness, feeling panicky)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7.	Physical and mental exhaustion (general decrease in performance, impaired memory, decrease in concentration, forgetfulness).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8.	Sexual problems (change in sexual desire, in sexual activity and satisfaction)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9.	Bladder problems (difficulty in urinating, increased need to urinate, bladder incontinence).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10.	Dryness of vagina (sensation of dryness or burning in the vagina, difficulty with sexual intercourse).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11.	Joint and muscular discomfort (pain in the joints, rheumatoid complaints)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



Beneficial effects of testosterone therapy in women measured by the validated Menopause Rating Scale (MRS)

Rebecca Glaser^{a,b,*}, Anne E. York^c, Constantine Dimitrakakis^{d,e}

Results: Pre-menopausal and post-menopausal females reported similar hormone deficiency symptoms. Both groups demonstrated similar improvement in total score, as well as psychological, somatic and urogenital subscale scores with testosterone therapy. Better effect was noted in women with more severe complaints. Higher doses of testosterone correlated with greater improvement in symptoms.

Conclusion: Continuous testosterone alone, delivered by subcutaneous implant, was effective for the relief of hormone deficiency symptoms in both pre- and post-menopausal patients. The validated, HRQOL questionnaire, Menopause Rating Scale (MRS), proved a valuable tool in the measurement of the beneficial effects of testosterone therapy in both cohorts.

Testosterone alone (continuous)

Effective & Safe hormone therapy



- Testosterone is the major substrate for estradiol in the brain, bone (osteoblasts, chondrocytes), vascular tissue, fat, breast tissue
- Uninterrupted sufficiency of circulating testosterone supports the production of estradiol by aromatase in E-dependent tissues and affords protection against estrogen deficiency
- Low circulating levels of estrogen in post-men women have no bearing on estrogen produced locally
 - 15 times mean plasma level of T:E2 in post men females

Testing females



- Free and total testosterone (inaccurate)
- Estradiol (no relation to end organ conversion of T to E2)
- FSH
- TSH
 - T4, T3, TPO later if indicated
- CBC (Hb & Hct) annually
- SHBG Optional
 - SHBG for calculated free androgen index (vs. free Testosterone)
 - Do not order a test if it will not change therapy

Testosterone Treatment: Female



- Dose Testosterone pellet
 - Weight
 - <100 lbs (45kg) 75 mg
 - 100-120 lbs (45-55 kg) 100-110 mg
 - 120-145 lbs (55-65 kg) 110-125 mg
 - 145-165 lbs (65-75 kg) 125-150 mg
 - >75 kg 150-225 mg
 - Increase the dose for symptom control (patient request)
 - Lower dose for acne and hair growth
 - There are rarely any other side effects
 - Anxiety is usually estrogen dominance, stress
 - Testosterone by pellet implant improves anxiety

Dosing Testosterone Implants Females



- End organ response, not serum ranges based on endogenous levels production
 - Relief from depression/anxiety
 - Increase bone density, muscle mass
 - Energy, sense of well being
 - Relief from aches and pains
 - Sex drive, libido
- Historical dosing: 50-225 mg (Burger, Gambrell, Natrajan, Studd, Jones, Saavas, Thom, Brincat , Glaser)
- 100-160 mg most common
 - Symptoms begin to return when testosterone levels reach the upper limits of normal
 - Side effects of androgen excess are minimal despite elevated serum levels

Routine FU Testing?



- Routine testing is not needed with testosterone alone
- Month one testosterone levels between 150-400 ng/dL
- FU data on 285 patients treated for > 1 year
 - Mean dose: 133.3 ± 26.8 mg
 - Mean interval of implantation: 13.8 ± 3.8 weeks
 - Mean serum testosterone level week 4: 299.4 ± 107.3 ng/dl
- Symptoms return when serum testosterone reaches the upper limits of normal (70-120 ng/dL)

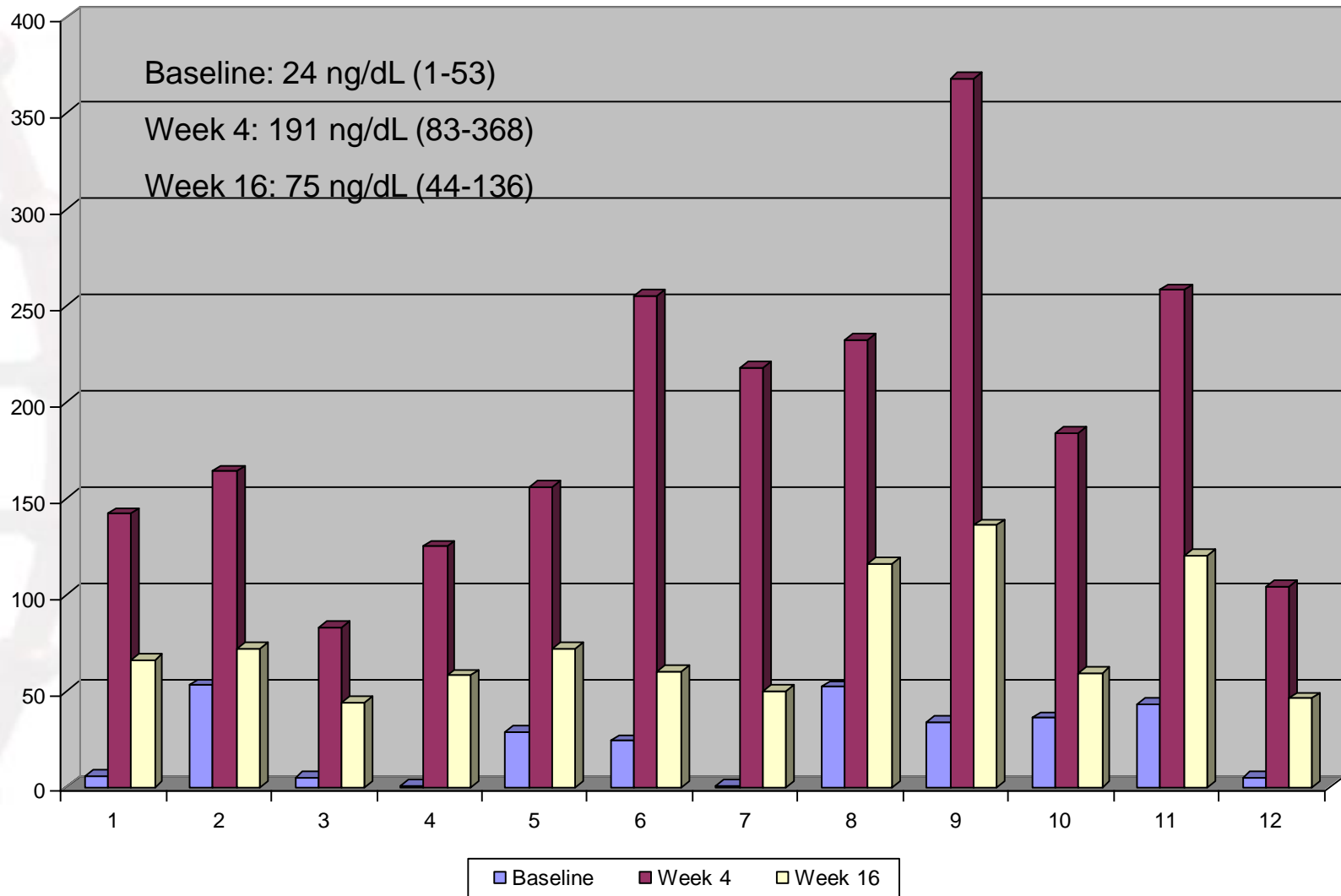
Is a single testosterone level meaningful?



- Individual variation
 - 12 patients treated with 100 mg of testosterone
 - Mean testosterone level 191 ± 80 ng/dl
 - Minimum 83 ng/dl, maximum 368 ng/dl
 - Salivary hormone levels normal
- Circadian variation
 - Serum testosterone level can vary over 200-500 ng/dl over a 24 hour period
- Other than increase in hair growth, symptoms of testosterone excess are extremely rare, despite elevated serum levels
- Higher levels do correlate with greater relief of symptoms

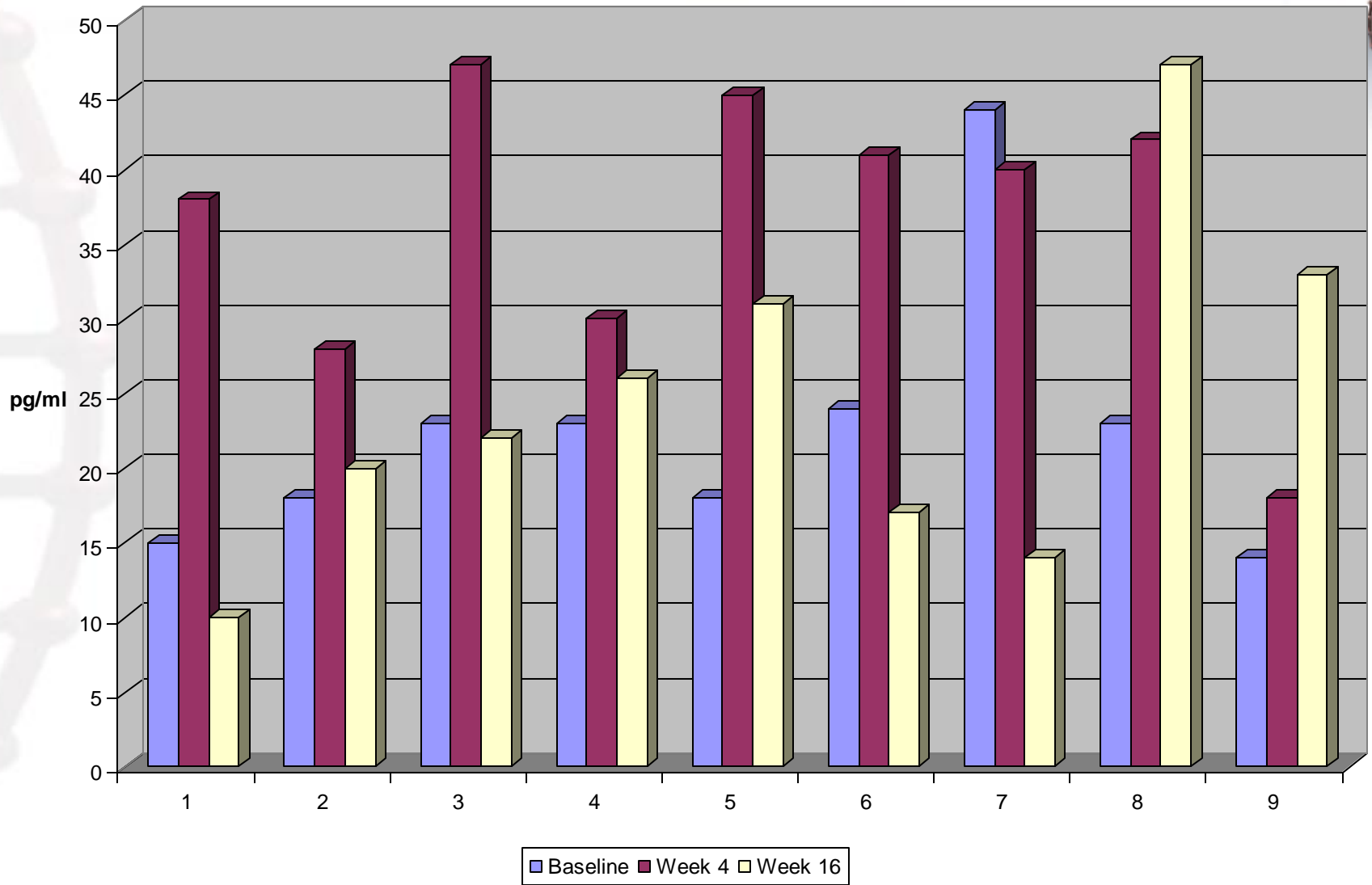


Serum Testosterone levels baseline, Wk 4, Wk 16: T100mg, E2 25 mg SC Implant



192 ± 91 ng/dL Burger 84

Salivary testosterone levels: T 100 mg SQ implant

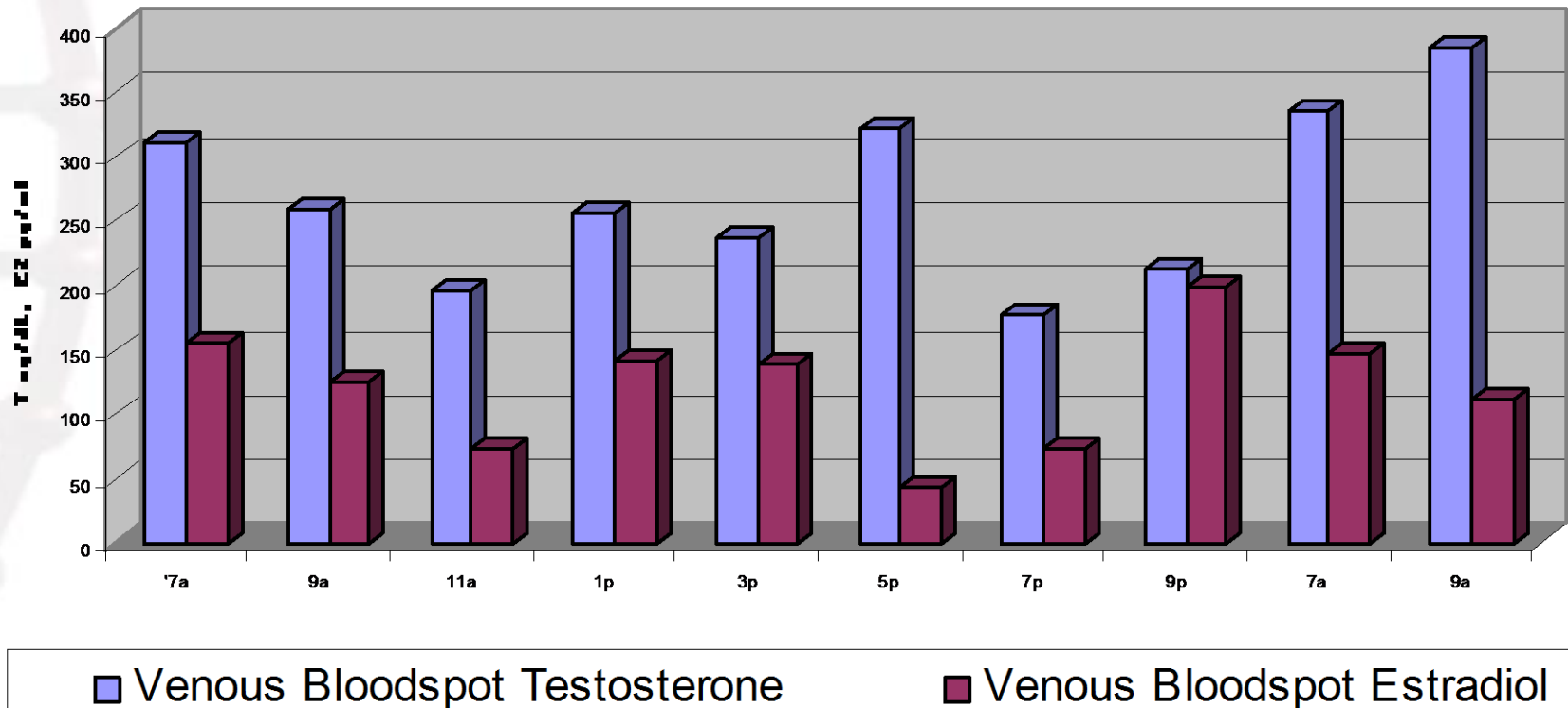


Venous blood spot testosterone and estradiol: T112.5 E2 50

Levels fluctuate throughout the day



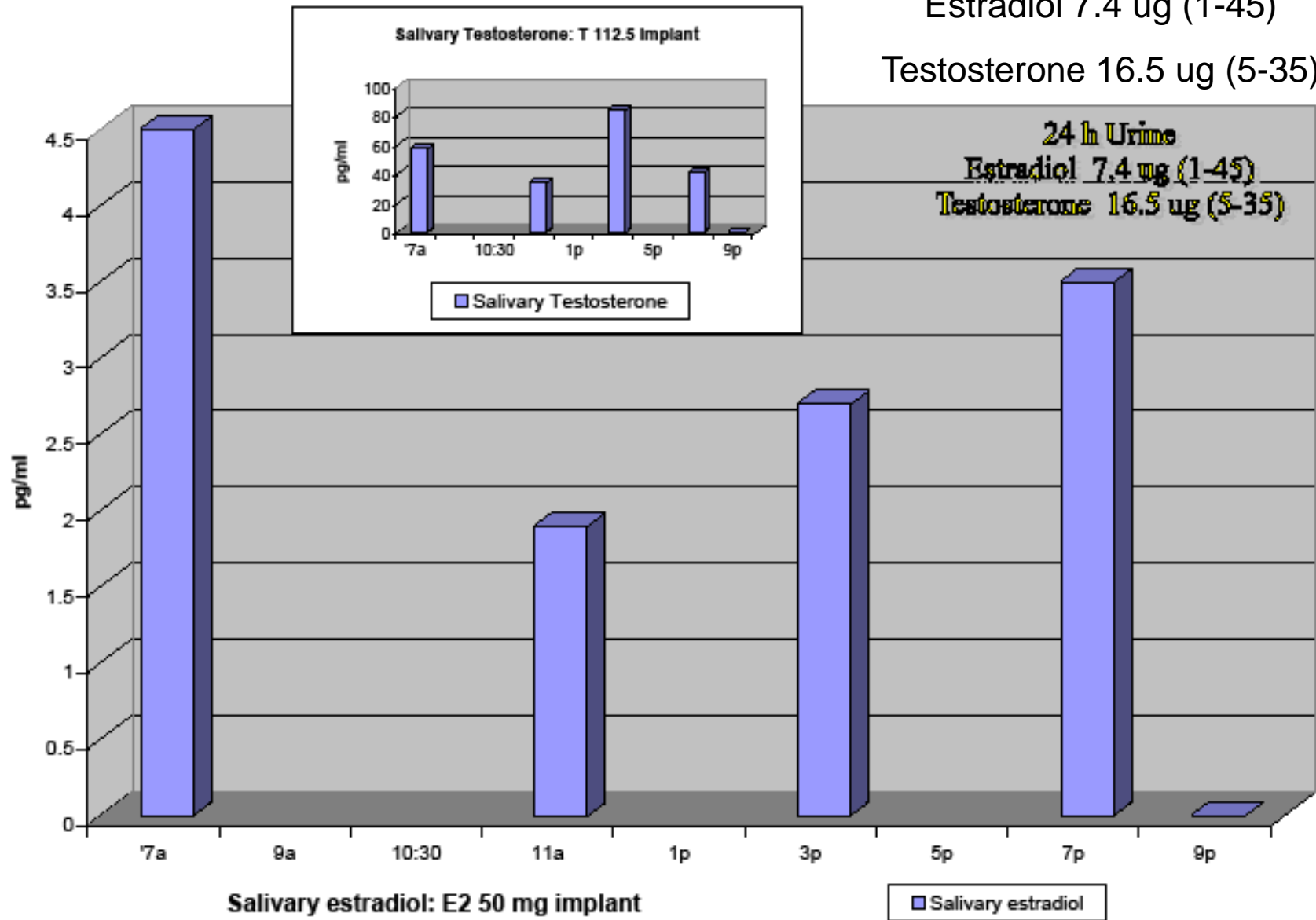
Venous Bloodspot Testosterone and Estradiol: T112.5 mg, E2 50 mg implants



24h urine

Estradiol 7.4 ug (1-45)

Testosterone 16.5 ug (5-35)



Lab tests males



- PSA
 - Less than 1.0
 - Stable PSA under 2.5 or negative biopsy
 - Approval from urologist
 - Trial of testosterone therapy with repeat PSA (stable)
- Testosterone (total, free)
 - Significant variation throughout the day (300 ng/dL)
- Sensitive estradiol
- CBC (Hb & Hct)
- Baseline liver panel* (statins and other drugs)
- TSH
- Optional: LH, SHBG

*Testosterone, delivered by pellet implant does not affect LFT's

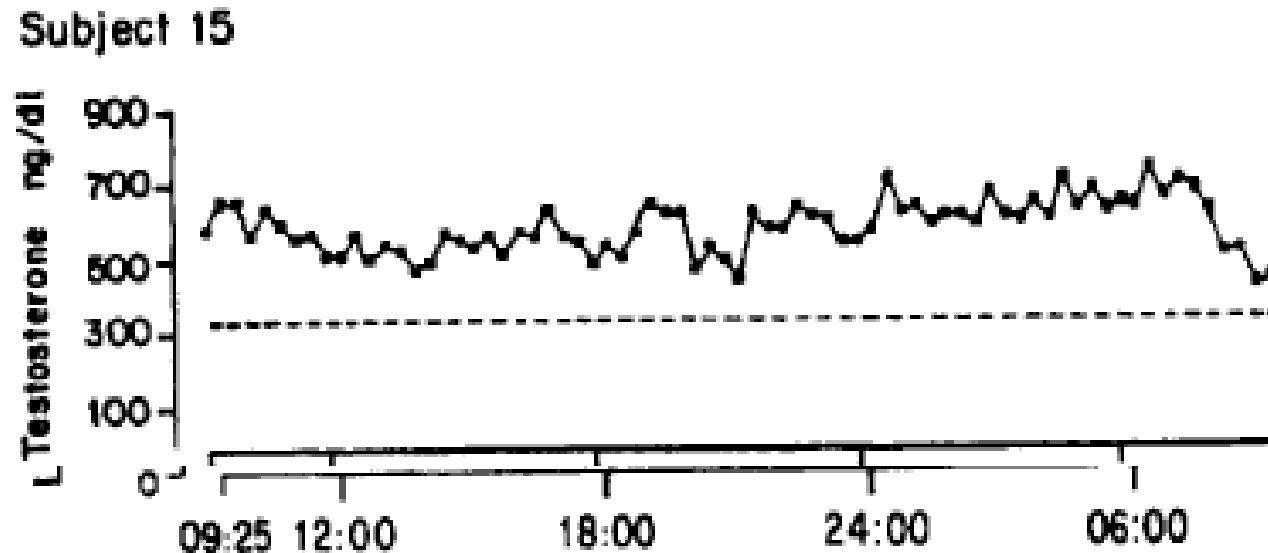
Carruther's 2008 (J Sex Med)



- Poor correlation between symptoms of androgen deficiency and testosterone levels
- Androgen Deficiency
 - Insufficient production
 - Increased androgen binding
 - Reduced tissue responsiveness
 - Resistance
 - Decreased Androgen Receptor activity
 - Impaired transcription and translation
- Document “TRIAL” of testosterone therapy
 - Use a validated survey

Spratt 88

serum testosterone levels men ages 18-37



- Testosterone levels vary significantly throughout the day
- Some groups report a diurnal rhythm, others do not
- Measured levels at 10-20 minute intervals
- Marked variation of testosterone secretion between subjects



am and pm testosterone

- am 4-10 am
- pm 4-8 pm
- Half of the testosterone levels were higher in the am, half were higher in the pm

Age, yr	AM T	PM T
37	819	829
31	933	420
19	582	588
22	680	488
29	634	762
26	656	656
18	470	239
24	1,014	332
37	1,184	903
35	509	625
29	1,220	1,316
29	891	619
32	753	855
26	823	982
29	506	470
31	525	278
22	712	551
24	698	1,032
34	828	647
32	637	732
28±6	754±214	672±270



Dosing Men



- **900-1200 mg** testosterone pellets
 - 1400-1600 mg larger men, chronic disease
 - 100 or 75 mg pellet implants with smaller trocar
- Most studies look at 600-1200 mg doses
- Complaints of anxiety/aggression with too high of dose (RARE)
 - Check Estradiol Levels
- If a patient is NOT doing well, no benefit
 - Check Estradiol Levels

Treatment levels men

- Restore testosterone to upper limits of normal for young men
 - 900-1100 ng/dL if you check at month one
 - Only check levels early if a patient has not responded
- Maintain testosterone over 600 ng/dL
 - Every individual has their own set point
- Symptoms are the best indicator of end organ response



FU Testing Males



- PSA prior to each insert for 2 years
- Testosterone
- Sensitive estradiol (none are accurate) until establish they do not convert T to E2
 - Re-check if needed before AI therapy
 - Diet, Lifestyle
 - Arimidex (anastrozole) 0.5 mg twice weekly
- Hb & Hct
 - Donate blood for Hb>18.5, Hct>53

PSA



- PSA < 1.0
 - Pellets
- PSA > 1.0
 - Treat the patient with IM, SL or topical testosterone
 - Re-check the PSA in 3 months (sooner for IM)
 - No elevation
 - Pellets
 - Elevation of PSA
 - Referral to urologist
- PSA > 1.0 and < 2.5 **AND** stable for 3 years
 - Pellets
- PSA > 2.5 and prior negative biopsy or clearance (in writing) from urologist

A new paradigm



Women
≠
Estrogen

Women \neq Estrogen



- 15-20 times more testosterone (ng/dl) than estradiol (pg/ml)
- Testosterone has been ignored except for it's role in sexual function and libido
- Androgen Receptors
 - Brain, bones, heart, blood vessels, nerves, muscles, skin breast, uterus, ovaries etc.
- Testosterone is the major substrate for estradiol

Testosterone Production in women

- Androgen production declines gradually with aging or precipitously with oophorectomy
 - A women at 40 has $\frac{1}{2}$ the testosterone as a 20 y.o.

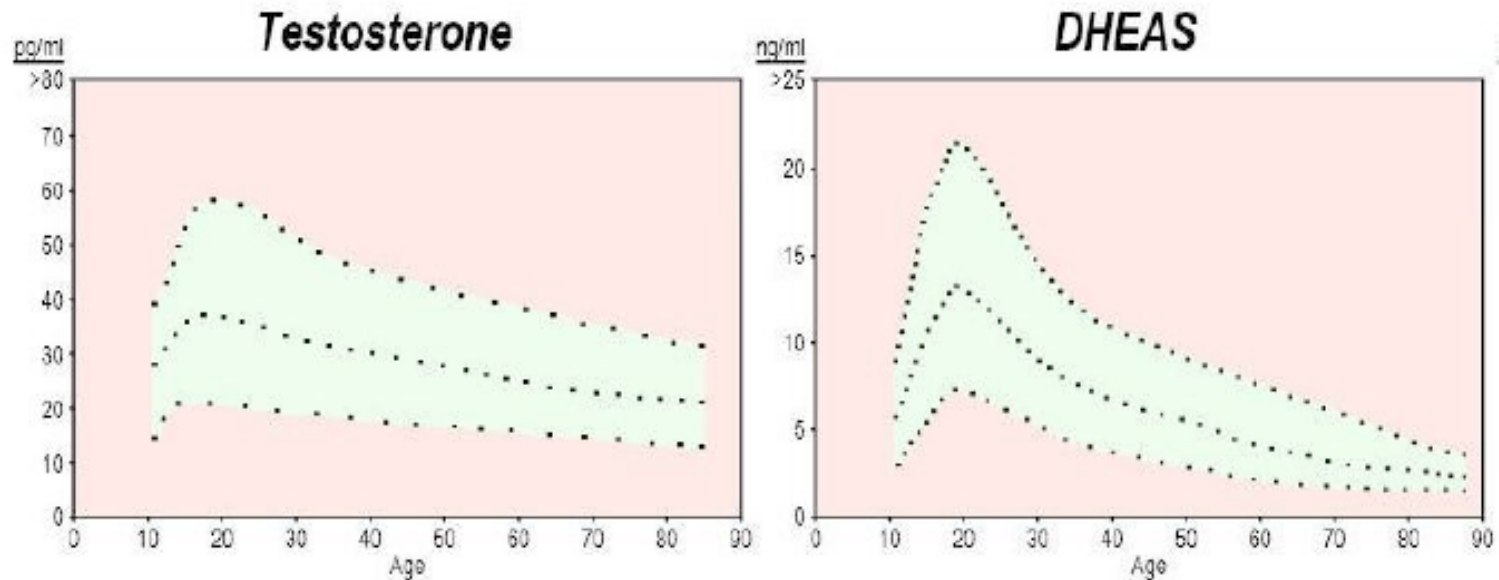


Figure 1. Salivary testosterone (pg/ml) and DHEAS (ng/ml) levels vs. age in 40,000 women tested between 2001-2007. The middle line represents the median, the upper line represents the 80th percentile and the lower line represents the 20th percentile.

ZRT laboratory, Beaverton, OR.

Balance



HORMONE THERAPY

≠

ESTROGEN THERAPY

Testosterone alone?

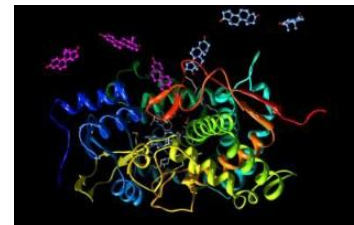
- How is that possible?
- What about balance?



Testosterone → estradiol

aromatase

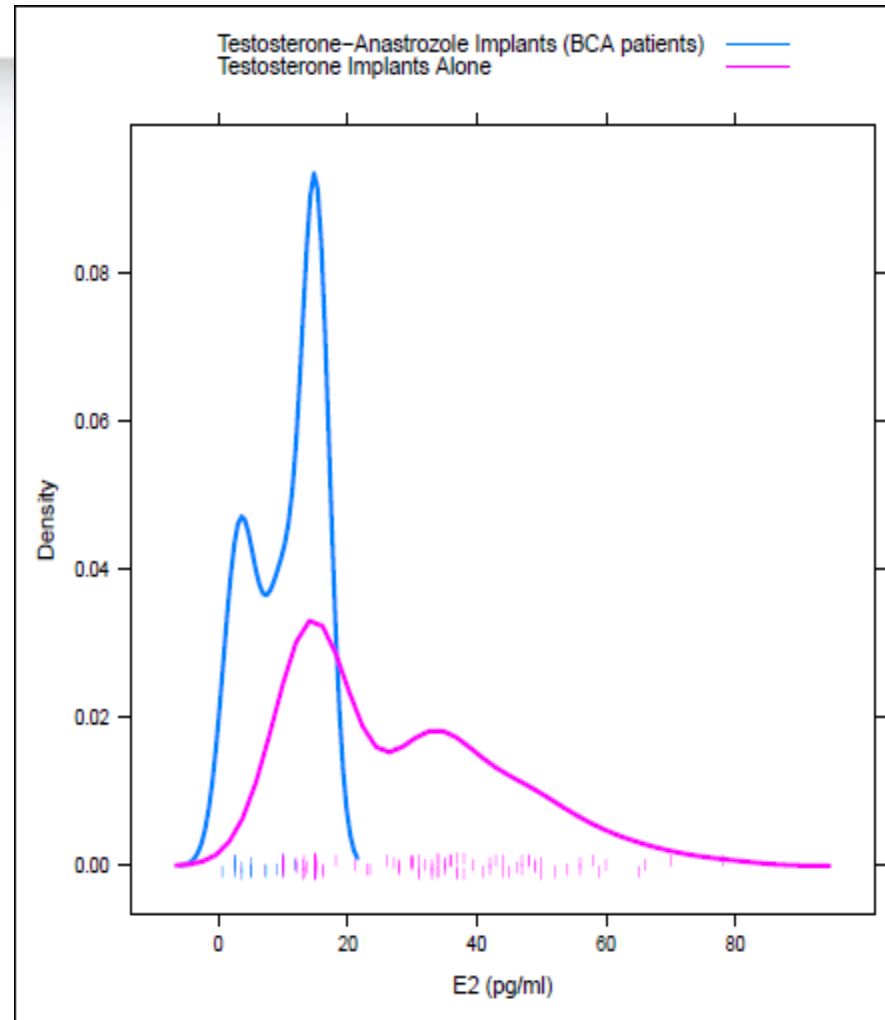
- Testosterone is the major substrate for estradiol in estrogen dependent peripheral tissues
 - Every cell that has estrogen receptors has the enzyme aromatase which converts testosterone to estrogen
 - Brain, bone, vascular tissue, breast, adipose tissue, endometrium
 - CONTINUOUS testosterone therapy *is* balanced estrogen therapy



Estradiol Density Plot

The levels of Estradiol (E2) in the group with the aromatase inhibitor is significantly less than in the group without it ($P < 0.0001$).

The separation of E2 in both groups is almost disjoint as illustrated by the kernel density plot.



Don't I need higher levels of estrogen?



- High levels of estrogen are needed for pregnancy
 - Estrogen and progesterone prepare the uterus for implantation of a fertilized egg
- Excess estrogen (estradiol): fluid retention, weight gain, PMS, anxiety, migraine headaches, increase in fatty tissue, insulin resistance, stimulates breast and uterine tissue
 - Most women feel best after they have their cycle when estrogen levels are lowest

Farmers

- ‘For increased rate of weight gain and improved feed efficiency’
 - Estradiol/Premarin
 - Increases growth rate by 10-20% in steers
 - Increases feed efficiency by up to 8%
 - Synthetic progestins
 - Increases growth rate and feed efficiency
- Diet: Take the fat out and increase whole grain



Trouble Shooting

- Refer to handout



Hot Flashes

- Refer to handout



It's your choice

- Refer to handout



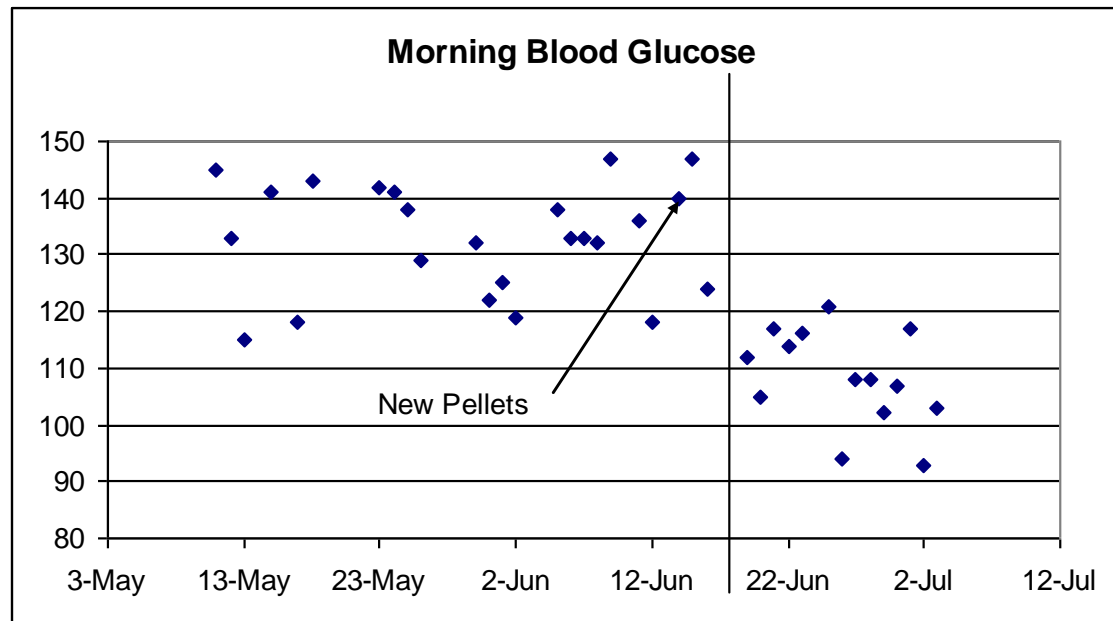
Healthy Hair (hair loss)

- Refer to handout

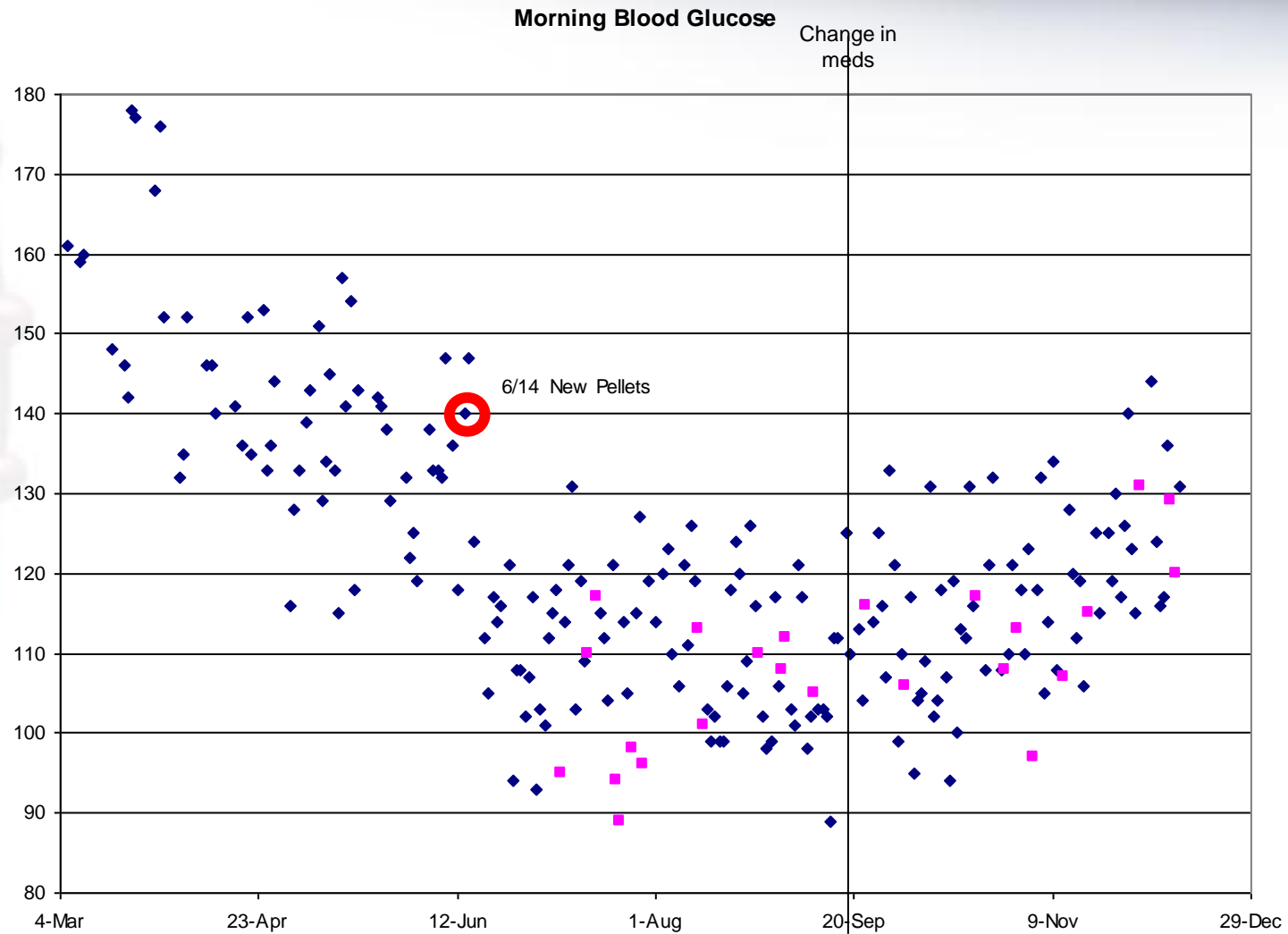


Blood Sugar (E.R.)

- 44 yo obese male with AODM and depression
- No energy, lack of motivation, central obesity, elevating cholesterol



ER cont.



Testosterone, delivered by pellet implant

- Common sense
- Simple
- It works

