

Primary Hormones

Testosterone Vehicles

Product	Dose	Lab Level	Comments
Clomid**	50mg 3-5x a week	2-3 months	Less than 40 years of age and prophylaxis.
AndroGel 1%	1-4 pumps/day	T(T)>350-750ng/dL	Apply to shoulder and upper arms only.
AndroGel 1.62%	1 x day	T(T)>350-750ng/dL	High DHT levels and Estradiol.
Testim 1% Gel	5-10g/day	T(T) 300-1000ng/dL	High DHT levels and Estradiol.
TestoCream 10%	½ - 1 gram/day	F(T)> 10-14ng/dL	Apply to flank if not in contact with other people.
Testosterone Cypionate IM	40-100mg/week-Male 10-30mg/week - Female	F(T)> 10-14ng/dL T(T)>300-1000ng/dL	Once weekly subcutaneous or IM injection.
Testosterone Pellets	Based upon weight.	F(T)> 10-14ng/dL T(T)>300-1000ng/dL	Initially high levels dropping over 4-6 months. Once implanted cannot remove.
Testosterone Lozenge (Troche)	Males: 25-50mg BID3x/wk Female:12.5-25mg.BID3x/wk	F(T)> 10-14ng/dL T(T)>300-1000ng/dL	Short half-life needing frequent dosing.
Testosome®	Males: 1cc Oral AM, Daily Females: 1cc Oral, TIW	Male: F(T)> 10-14ng/dL Female: F(T)> 2-4ng/dL	Short half-life with excellent absorption. CNS benefits include improved focus, concentration, decrease anxiety, improved depression, rise in libido and mental energy.¥
¥ - Based upon 3 months of testing with 10mg dose sampling.			

Clomiphene Citrate

- Three year study (2014-2016) on the use of Clomid in two groups: Less than 40 and greater than 40.
- 2016 study: Less than 40 with a Free T of 5-10 get one tablet every 3rd day. Blood work in 12 weeks.
- Older than 40 get UL-Testosterone protocol (20mg) every 3rd day with 25/50mg tablet of Clomid or no clomid. Blood work in 8-12 weeks.



Clomiphene Citrate

Telephone conversation

I reviewed test results.

Pituitary MRI is normal. Thyroid ultrasound is consistent with Hashimoto's thyroiditis without nodules.

We discussed treatment options for testosterone. I indicated that the clomiphene that he has used and has had success with it is not FDA approved for this purpose and we do not know the long-term effects. However it is available to him and maybe the most convenient thing to use. Also will likely preserve his fertility if that is currently intact. Exogenous testosterone will suppress his testosterone and spermatogenesis which doesn't mean it cannot recover in the future and be stimulated by hCG. These are all unknowns. Also is not a good idea for a young man his age to go without testosterone. Feels chronic fatigue and complete loss of libido.

I offered to get him another opinion with another endocrinologist or at another Medical Center. I also offered to send him to a urologist for subcutaneous testosterone implants and also consultation. He will consider his options and let me know.

Outcomes of Clomiphene Citrate Treatment in Young Hypogonadal Men.

Long-term follow-up of CC treatment for HG shows that it is a effective and safe alternative to testosterone supplementation in men wishing to preserve their fertility.

[Katz DJ1](#), [Nabulsi O](#), [Tal S](#), [Muthall JP](#).

[BJU Int](#). 2012 Aug;110(4):573-8. doi: 10.1111/j.1464-410X.2011.10702.x. Epub 2011 Nov 1.

Treatment Considerations

- ▶ **Human Chorionic Gonadotropin (HCG)**
- ▶ Produced in Human Placenta
- ▶ Stimulates testes to produce testosterone
- ▶ Does not affect sperm count or testicular volume
- ▶ Preferred if patient is under 40

Treatment Considerations

▶ **Human Chorionic Gonadotropin (HCG)**

▶ Dose to Preserve Size or Semen Volume:

▶ 250 IU SQ days 6 and 7 of weekly IM injection

▶ 250 IU SQ every 3rd day for Transdermal Gel

▶ Dose as Stand Alone Therapy:

▶ 3000 IU SQ q 2 wks (increases free T by 25%)

▶ Or

▶ 1000 IU SQ 2x/wk

Can develop antibody

▶ RX should be 2 months on, 1 month off.

Estrogens

- Estradiol leads to decrease production of:
 - Testosterone
 - DHEA
 - Progesterone
 - Pregnenolone
- E2 supplementation leads to transient increase in Cholesterol

Estrogen/Progesterone Ratio

- Optimal time to perform lab testing is days 19-21
- Measuring both Estrone (E1) and Estradiol (E2) with progesterone (PROG) will allow for the calculation of the EP Ratio.

E1+E2/P=E/P Ratio

- Estrogen Dominance as a comorbid factor to TBI can cause greater disturbance in neurochemistry especially with GABA.

- **If E1 is elevated, control w 7 Keto-DHEA**

Estrogen/Progesterone Ratio (Gordon, M. TBI, San Diego, 2015)

<i>Symptoms</i>	<250	250-1000	1000-5000	>5000
Headaches	Intermittent	Mild	Moderate	Severe
Sleep Issues	Intermittent	Mild	Moderate	Severe
Sleep Deprivation	NP	Intermittent	Mild	Moderate
Bloating	NP	NP	Mild	Moderate
Mood Swings	NP	Mild	Moderate	Severe
Anxiety	NP	Intermittent	Mild	Severe
Depression	NP	Intermittent	Mild	Severe
Panic Attacks	NP	Intermittent	Mild	Severe
Mastalgia	Intermittent	Mild	Severe	Severe

Progesterone/Estradiol Ratio

- **Alternative Measurement**

- ***Serum: $Pg \times 1000/E_2 = P/E_2$ Ratio***

- ***Saliva: $Pg/E_2 = Pg/E_2$ Ratio***

- **Results**

<100	=	Estrogen Dominant
100-500	=	Normal Ratio
>500	=	Progesterone Dominant

Female Hormone Treatment

(Gordon, M. TBI, San Diego, 2015)

	Estradiol	Estriol	Progesterone	Testosterone	Application
Starter	0.2mg	2.0 mg	100 mg	1 mg	Vaginal
Breast Tender	0.1 mg	2.0 mg	100 mg.	1 mg	Vaginal
Fatigue	0.2 mg	2.0 mg	50 mg.	1 mg	Vaginal
Libido	0.2 mg	2.0 mg	100 mg.	2 mg	Transdermal
Basic	0.2 mg	2.0 mg	100 mg.	No	Transdermal
Breast	0.1 mg	2.0 mg	100 mg.	No	Vaginal
Cancer	none	2.0 mg	100 mg.	1-2 mg.	Vaginal

Thyroid Dysfunction

HYPO THYROIDISM

DRY, COARSE HAIR

LOSS OF EYEBROW
HAIR

PUFFY FACE

ENLARGED THYROID
(GOITER)

SLOW HEARTBEAT

ARTHRITIS

COLD
INTOLERANCE

DEPRESSION

DRY SKIN

FATIGUE

FORGETFULNESS

HEAVY
MENSTRUAL
PERIODS

INFERTILITY

MUSCLE ACHES

WEIGHT GAIN

CONSTIPATION

BRITTLE NAILS

HYPER THYROIDISM

HAIR LOSS

BULGING EYES

SWEATING

ENLARGED THYROID
(GOITER)

RAPID HEARTBEAT

DIFFICULTY
SLEEPING

HEAT
INTOLERANCE

INFERTILITY

IRRITABILITY

MUSCLE
WEAKNESS

NERVOUSNESS

SCANT
MENSTRUAL
PERIODS

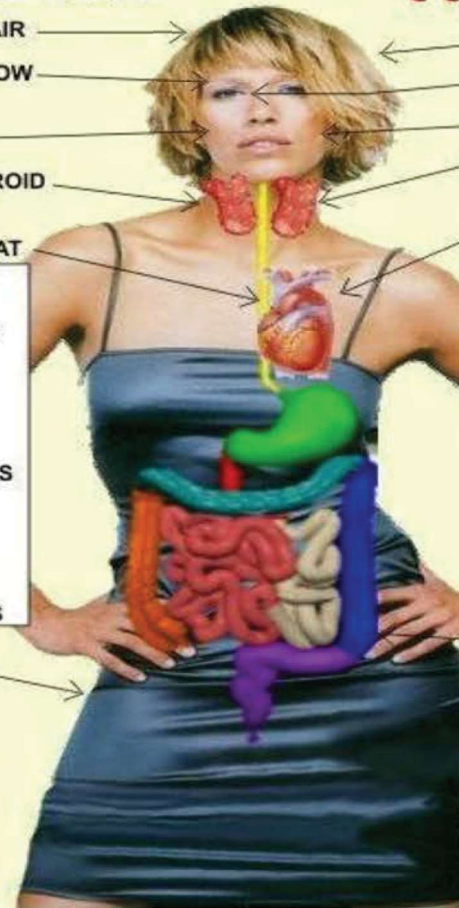
WEIGHT LOSS

FREQUENT
BOWEL
MOVEMENTS

WARM, MOIST
PALMS

TREMOR OF
FINGERS

SOFT NAILS



Treatment

- **Thyroid**

- The notable benefits of T3 and T4 on brain recovery and neurobehavior are clear.
- Controversy still exists between monotherapy with T4 and combination therapy with T3.
- If adequate levels of fT3 are obtained without the surreptitious presence of rT3, then neuroregeneration is possible.

Treatment

Serum TSH: Cut-off points within ref. range above which there is ↑ risks of disease		
mU/L	↑ Risks of disease	Reference
> 3.6		
> 3.3	↑ severe form of depression	Berlin I 1999 Nyrnes A 2006
> 2.6 (higher quartile)	↑ body mass index over 7 years	Nyrnes A 2006
	↑ waist circumfer., BMI, glucose, TG, systolic BP	Waterhouse DF 2007
> 3	↑ cardiac abnormalities (pat. + auto-immune thyroiditis)	Zoncu S 2005
	↑ post-partum hypothyroidism	Azizi F 2004
> 2.1	↑ stenoses, multi-vessel disease (angina patients)	Yun KH 2007
> 2	↑ homocysteine & CRP (patients + L-thyroxine)	Gursoy A 2006
≥ 2	↑ Familial predisposition to hypertension	Gumieniak O
≥ 2	↑ Hypercholesterolemia	(patients + auto-immune thyroid antibodies) Michalopoulou G 1998
	↑ Overt hypothyroidism	Geut KW 1993
3-1.99		
> 1.98	↑ aggravation of coronary heart disease	Auer J 2003
≥ 1.9	↑ systolic & diastolic blood pressures (men)	Iqbal A 2006
> 1.9	↑ auto-immune thyroid ATPO+ (pregnant women)	Sieiro Netto L 2004
≥ 1.8	↑ systolic & diastolic blood pressures (women)	Iqbal A 2006

The Case (for Adding T3)

Remyelination and Recovery.

- **Myelin repair-**T3 regulates the cell cycle of oligodendrocytes by either stopping their maturation from OLPC to terminal OL or by enhancing maturation for additional myelin production.
- **Inflammation-**
 - inhibits D1 synthesis (converts T4 to T3)
 - increases D3 which converts T4 to rT3.

LOW T3 IS STRONGEST INDEPENDENT PREDICTOR OF CARDIAC DEATH

- Low T3 < 3.1 Free T3
- Low-T3 syndrome is a strong predictor of death in cardiac patients and might be directly implicated in poor prognosis of cardiac patients.
- **Strongest independent predictor of death**
 > lipids or EF

• Lervasi, G et al. Low-T3 Syndrome, A Strong Prognostic Predictor of Death in Patients With Heart Disease *Circulation*. 2003;107:708

Doctor's Solution T4 Only

- Levothyroxine, Levoxyl, Synthroid

American Association of Clinical Endocrinologists and American Thyroid Association emphatically declared, in 2012, "Standard treatment is replacement with Levothyroxine. "

Garber, J., Cobin, R., Gharib, H., et al., Clinical Practice Guidelines For Hypothyroidism In Adults, Endocr Prac. 2012; 18(No.6) 989. Hollowell JG et al. J Clin Endocrinol Metab 2002 87(2)489-499

Any Treatment Other Than Desiccated T4 Is Outside Realm Of Medicine

Guarva, S., Hypothyroidism, "Science Based Medicine" <https://www.sciencebasedmedicine.org/hypothyroidism--facts--controversies-and--pseudoscience/>

T4 Only



Diet

Bone Broth-Helps restore gut barrier (i.e. heals the “leaky gut”)

Fermented Vegetables and Beverages (i.e. sauerkraut, kimchi, beet kvass, coconut water kefir, etc.). High in Probiotics

Fish and Shellfish-High in omega-3 fats. Eat at least one pound of cold-water, fatty fish per week EPA and DHA needs.

Organ Meats-Loaded micronutrients that promote healthy immune function.

Diet

- **Goitrogens**-Limit to 3-6 servings/week raw. Steaming/boiling reduces goitrogenic effect.
- **Eggs** (both whites and yolks)
- **Nightshades** (potatoes, tomatoes, sweet and hot peppers, eggplant, tomatillos, pepinos, pimentos, paprika and cayenne pepper)
- **Nuts**-30-day elimination if nut sensitive. Common allergen.

Limit Goitrogens (3-6 Servings/Week)

Cruciferous Vegetables

Bok Choy
Broccoli
Brussel Sprouts
Cabbage
Canola
Cauliflower
Chinese Cabbage

Collard Greens
Horseradish
Kale
Kohirabi
Mustard Greens
Radishes
Rutabaga
Turnips

Others

Soy
Pine Nuts, Peanuts
Millet
Strawberries
Pears, Peaches
Bamboo Shoots
Spinach
Sweet Potatoes

Immune Modulators

- Low Dose Naltrexone
- Plant Sterolins

Promote a balanced immune system

- Protects against negative stress responses
- Limits cortisol activity

Modulates the autoimmune response in Hashimoto's Thyroiditis.

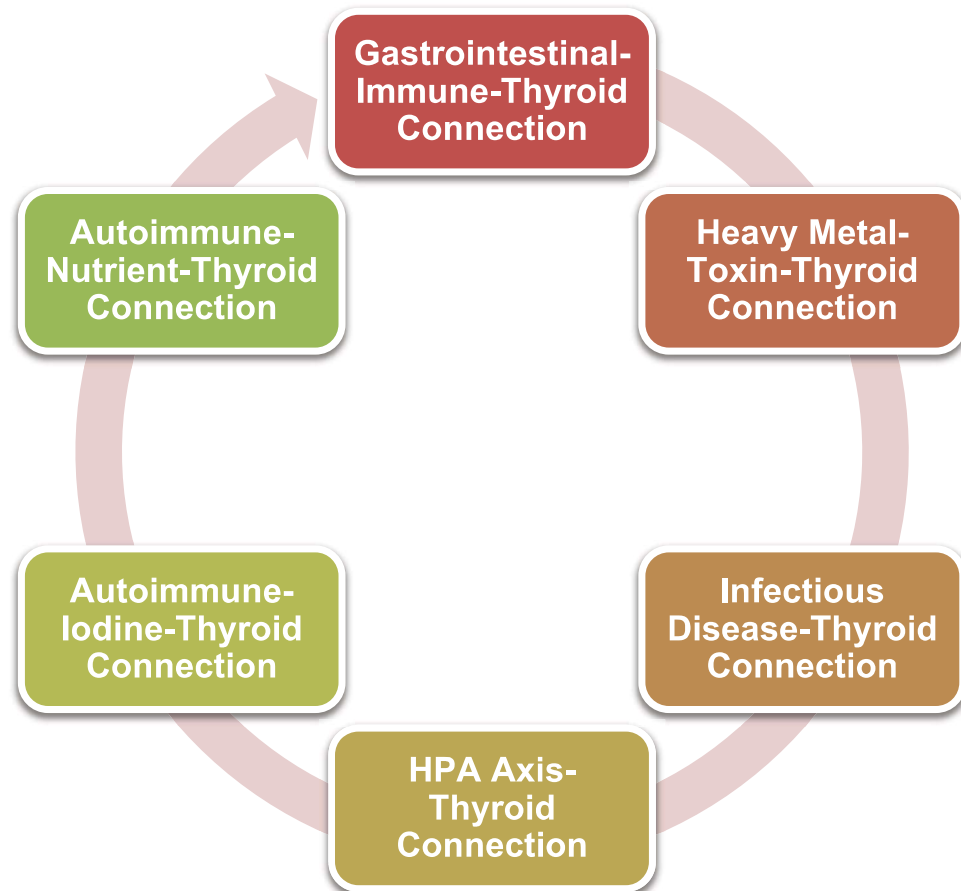
- Can decrease antibodies by 90%

Improves balance of T-helper 1 to T-helper 2 cells

Down Regulates overactive immune responses.*

- [Boaic P:1, Lamprecht JH.](#), Plant sterols and sterolins: a review of their immune-modulating properties. [Altern Med Rev.](#) 1999 Jun;4(3):170-7.
- Yamada H, Yoshino M, Matsumoto T, et al. Effects of phytosterols on anti-complementary activity. [Chem Pharm Bull.](#) 1987;35:4851-4855

*Shameless
Plug to
Invite Me
Back for
"The
Thyroid
Show"*



Growth Hormone Algorithm

+Lab Evaluation

Secretagogue (SRx) →

Retest 3 Mo. →

Increased → Continue 6 mo. then discontinue. Retest in 6 mo.

No Change or Decrease → Increase Dose; Retest 6 mo.

No Change or Decrease → Glucagon Stimulation Test or

→ Insulin Stimulation Test

→ If + Consider HGH

Secretagogue #1

- *Active Ingredients:* Pyroglutamine, L-Glutamine, L-Arginine, L-Lysine, L-Valine, L-Tyrosine, Alpha-ketoglutarate, L-Ornithine, L-alpha-glycerolphosphoryl-choline, Gamma Amino Butyric Acid (GABA), and Mucina pruriens.
- *Other Ingredients:* Deionized water, Lecithin, Phospholipids, Sodium citrate, Citric acid, Maltodextrin, Potassium sorbate, Artificial color and Flavor.

Secretagogue #2

Arnica Montana 6X, Deer Antler Velvet 8X, Hepar Bovinum 6X, HGH 24X, 30X, IGF 1 8X, Pituitary Bovinum 5C, 7C, 9C, Thuja Occidentalis 6X

Semorelean w GNRH 2 or 6

CJC 1295 w DAC

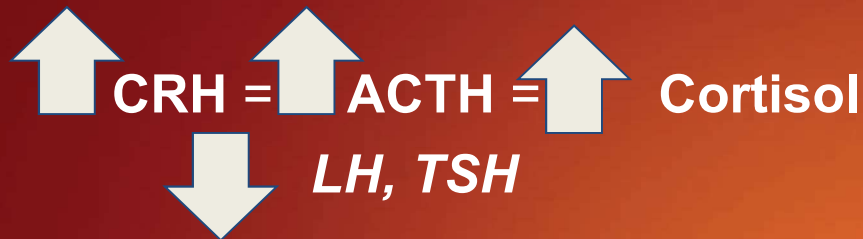
L-Dopa Raises Growth Hormone

- *Oral doses (0.5 g) caused a significant rise in plasma GH.*
- *The rise in plasma GH persisted for 120 minutes after the administration of the drug.*
- *The data suggest that a dopaminergic mechanism in the median eminence or a norepinephrine-sensitive site in the hypothalamus or limbic system may be involved in the regulation of growth-hormone secretion.*
- ***Parkinson's disease patients, on L-dopa therapy, enjoy an elevated plasma GH for a substantial part of the day***

Stimulation of Human-Growth-Hormone Secretion by L-Dopa. N Engl J Med 1970; 283:1425-1429 Dec. 24, 1970. A. E. Boyd, III, M.D., Harold E. Lebovitz, M.D., and John B. Pfeiffer, M.D. From the divisions of Endocrinology and Neurology, Department of Medicine, Duke University Medical Center

ACTH and Cortisol

- TBI =
 - **Acute increase** in the *Corticotropin Releasing Hormone (CRH)* from the Hypothalamus.



- ↑ Cortisol = ↑ production of rT3 from T4 with a corresponding
– ↓ free T3
- Not until Cortisol is corrected can there be an improvement in the production of T3.

ACTH and Cortisol

- 15% of Moderate to Severe TBI develop 1° or 2° Adrenal failure within 7-60 days.
- High Cortisol/DHEA Ratio=Active Depression
- Low Cortisol/DHEA Ratio=Depression Lessens

ACTH and Cortisol

Two peripheral systems for the regulation of Cortisol:

1. **Traditional:** CRH from the hypothalamus, inducing ACTH released from the pituitary causing an increase in adrenal cortical production and release of Cortisol.

2. **Non-Traditional:** Catecholamines stored in the splanchnic nerves can induce Cortisol production by release of dopamine, epinephrine, and norepinephrine and a wide variety of neuropeptides. (exercise and body trauma)

- **Due to the non-ACTH regulation of the adrenal cortex, you can have low levels of ACTH with high levels of Cortisol.**

Treatment

- Secondary Hormones
 - Pregnenolone
 - DHEA
 - Prolactin

Pregnenolone

A comparison of the pre- and postsynaptic effects of PS demonstrated that it was 100-fold more potent in inhibiting presynaptic GABAergic synaptic mechanisms than GABA_A receptors.

The net effect is a reduction in neurotransmission with potential clinical impact on anxiety, panic attacks, agitation, aggression, and insomnia.

- Social Phobias

A Presynaptic Action of the Neurosteroid Pregnenolone Sulfate on GABAergic Synaptic Transmission. *Mol Pharmacol* 64:857–864, 2003 Zakaria MT, CHEDLISH, VI, and Jaideep: Kapur, Department of Neurology, University of Virginia Health Sciences Center, Charlottesville, Virginia

Pregnenolone Steal Syndrome

- S/S Chronic fatigue and adrenal insufficiency.
- Pregnenolone is “stolen” from the Steroidogenic Cascade as the substrate for cortisol instead of your other hormones.
- Pregnenolone is normal or elevated; DHEA is low to low-normal or;
– *Pregnenolone and DHEA are low to low normal.*
- If stressed, the body uses Pregnenolone (and DHEA) to make Cortisol.
- W deficiency in Pregnenolone, Progesterone, or even 11 DOC, and DHEA will be reduced in production in favor of the adaptogenic Cortisol.

Pregnenolone Steal Syndrome

Pregnenolone levels can drop by:

- Statins
- Pregnenolone Steal Syndrome
- Rapid conversion to Cortisol (under stressors)

Benefits: Direct modulation of neurotransmission with stabilization of NMDA, GABA_A and Sigma-1 Receptors.

Dose: Lab <100 Rx 30mg
>100 RX 60mg

Pregnenolone Steal Syndrome

<i>Pregnenolone Steal</i>	<i>Result</i>	<i>Median</i>
Pregnenolone	131 ng/dL	110 ng/dL
Progesterone	2.1 ng/ml	0.8 ng/ml
ACTH	35.8 pg/ml	35 pg/ml
Cortisol	3.41 ug/dL	15 ug/dL
DHEA	106.2 ug/dL	245 ug/dL
free Testosterone	8.76 ng/ml	14 ng/ml

DHEA and DHEA-S

- **Stimulates oligodendrocytes to make myelin.**
- **Reduces Glia production of the inflammatory Cytokine IL-6.**
- **Protects the heart from Ischemic Heart Disease.**
- **Decreases cholesterol**
- **Decreases formation of fatty deposits**
- **Prevents blood clots**
- **Increases bone growth**

DHEA and DHEA-S

- Promotes weight loss
- Increases brain function
- Increases lean body mass
- Increases sense of well-being
- Helps one deal with stress
- Supports the immune system
- Helps the body repair itself and maintain tissues
- Decreases allergic reactions
- Lowers triglycerides

DHEA and DHEA-S

- Raises HGH production during the night.
- Has an antidepressant effects (1952).
- Improves wound healing.

Measure DHEA-S Female 200-250 ug/dl

Male 500-600 ug/Dl

Rx: (F) 10-25 mg/d (M) 25-100 mg/d

Deficiency and Excess S/S are similar to Testosterone

DHEA Post TBI

- Double Blind Crossover study =
- 67% men and 84% women experience increased strength, energy and psychological well being after 3 months .
- 50% reduction in depressive symptoms.
- Increases Pregnenolone (Negative Feedback)
 - ↑ Cortisol=
 - Mood elevation.
- Recommended Dose DHEA 25 mg with Pregnenolone 25 mg

Cortisol Treatment

1. Adaptogenic Herbs (See Supplements)

- Rhodiola,
- Ginseng,
- Cordyceps

2. DHEA

3. Pregnenolone

4. Adrenal Glandulars

or

1. Adaptogenic Herbs

2. Adrenal Glandulars

3. Cortef (Low Dose) 7.5 mg am, 5 mg noon, 2.5 mg 4 pm

Cortisol and TBI

- Cortisol levels and symptom severity is due to the augmenting effects of cortisol on dopamine activity.
- Elevation of Dopamine can increase symptoms of Anxiety and Panic Attacks.
- Elevated dopamine levels decrease Prolactin Production
 - (Tip Off to Rx. Resistant Anxiety)

- Cognitive Functioning, Cortisol Release, and Symptom Severity in Patients with Schizophrenia. BIOL PSYCHIATRY 2000;48:1121-1132. Deborah J. Walder, Elaine F. Walker, and Richard J. Lewine. Departments of Psychology and Psychiatry, Emory University, Atlanta, Georgia.

Prolactin

<25% of range (2.5-19 ng/ml) = (<5.375 ng/ml) =

Elevated Dopamine or GABA.

S/S = anxiety, panic attacks, restlessness, and fidgetiness.

(Treatment Resistant Anxiety Look for Low Prolactin)

> 75% = HP axis damage (16.125 ng/ml)

Increase Prolactin = ↓ LH = ↓ Testosterone

Loss of Dopamine or GABA =

Pituitary Adenoma or Prolactinoma.

Biological Psychiatry. Vol. 32, No.11, Dec. 1992, Pages 1004–1011

Prolactin

Elevation in Prolactin:

- Diminishes LH production and release
- Lowers testosterone
- Causes of elevation:
 - Hypothalamic dysregulation of pituitary
 - Adenoma

Decreases of Prolactin:

- Caused by elevation in Dopamine
 - Edginess
 - Agitation
 - Aggressiveness
 - Anxiety
 - Panic

Prescriptions

Amantadine-Facilitates dopamine release, blocks MAO-A, NMDA receptors
Reduces Parkinson's s/s, extrapyramidal syndromes, akathisia

Improves apathy, mental clarity

Dose 100mg/d x 28 d then 2x/d

Statins- *Dose: Atorvastatin 10 mg within 24 hours of TBI*

Cerebral Blood Flow :

Decrease: Thrombosis, Platelet activity, Inflammatory cytokines

Cerebral edema, microglial activity, oxidative stress, Apoptosis

Increases: **Neurogenesis, Angiogenesis**

Prescriptions

Bromocriptine- (Hyperprolactinemia)

Down regulates prolactin (Stimulates prolactin inhibiting factor)

Dopaminergic effect-

Improves cognition

Dose: 2.5 mg 2-3 x/d

Selegiline- (Apathy, Cognition) Dose: 5 mg 2x/d

MAO-B inhibitor

Immune booster

Anti-neurodegenerative effect; Protects against DNA damage

Increases: Growth Hormone, nitric oxide and anti-inflammatory interleukins

Release SOD-free radical production inhibitor

Prevents/reverses iron induced memory **loss**

Supplements

Vitamin D3

MVI

Methylated B6, B12, Folate

Phosphatidylserine

L Threonine

DL-Phenylalanine

Zinc Citrate

Omega 3 FA

Ribose

Glutathione

Tocopherols

Ascorbic Acid

Carnosine

Melatonin

Lipoic Acid

PQQ

Coenzyme Q 10

Quercetin

Supplements

Vitamin D3

(Measure 25 OH Vitamin D-Normal 30-100 ng/ml, goal 50-80 ng/ml)

↑ nerve growth in the brain

Planning, processing information, formation of new memories.

↓ vitamin D levels = poor brain function

Sun Exposure for 20 minutes adds 20,000 IU/d.

Supplementation: for every 1000 IU ↑ blood level by 8 ng/ml

Use at bedtime

Supplements

Methylated B6, B12, Folate-Synthesizes neurotransmitters.

Malfunction of the methylation cycle is due to diet deficient in B6, B12,
Folate

Lab: ↑ **homocysteine** (Goal <10)

Normal Homocysteine ensures proper metabolism of neurotransmitters

Balances mood

Cognition

Maintains Brain Volume

Mental fogginess and Memory Retention

Slows Brain Atrophy in Elderly

Peripheral Neuropathy

Supplements

Phosphatidylserine

- Major component of cell membranes
- Releases neurotransmitters and has role in synaptic activity
- Supports brain function
- Mental concentration, memory retention

- Dose: 100 mg 3x/d or 300 mg @ bedtime

L-Theanine

- Reduces anxiety
- Blocks excitatory stimuli at glutamate receptors in the brain
- Stimulates inhibitory, GABA.
- Relieves stress without drowsiness or impairing motor behavior.
- Improves alertness and attention.
- Supporting cognitive function and preventing cognitive loss
- Stroke prevention
- Schizophrenia s/s reduction
- **Dose: 250-400 mg @ bedtime**

Supplements

DL-Phenylalanine

- Essential amino acid DLP is a precursor to as dopamine, norepinephrine, epinephrine, and serotonin.
- Increases mental alertness, controls addictive substance abuse, promotes sexual arousal, and releases Ghrelin, an appetite curbing hormone.
- Breaks down opiate-like substances enkephalins in the brain.
- Modulates chronic pain.
- Supports emotional well being, memory and learning. Promotes endorphin release. Calms stressed joints and muscles.
- ***Think cravinas. substance withdrawal***

Supplements

Supplements

Zinc Citrate

- Deficiency associated with decreased Testosterone, increased Estradiol.
- Synthesizes and secretes LH and FSH
- Essential role in gonadal differentiation, testicular growth and development of seminiferous tubules, spermatogenesis, testicular steroidogenesis, androgen metabolism and interaction with steroid receptors.
- Zinc supplementation results in an increase in serum testosterone.
- Acts as Aromatase (Estradiol Synthetase Enzyme)
- **Dose: Zinc Citrate**
 - Zinc less than 50 mcg/dL; RX 30mg Zinc Citrate BID to TID
 - Zinc greater than 50 mcg/dL; 30 mg/Day.

Supplements

Diindolylmethane (DIM)

A metabolite of indole-3-carbinol (I3C) found in cruciferous vegetables such as; broccoli, kale and Brussels sprouts.

Anti-carcinogenic, anti-oxidant, anti atherogenic effects

3,3'-Diindolylmethane Inhibits Lipopolysaccharide-Induced **Microglial Hyperactivation** and Attenuates Brain Inflammation

Reduces TNF-alpha, IL-6, IL-Beta, NF-KB, *PGE2*

Think “Non Hormonal Relief of estrogen Deficiency Symptoms”

Dose: 100 mg 2-3 x/d

Supplements

Omega 3, Omega 6 Fatty Acids (Dose: 1000-4000 mg/d)

- Major constituent of the cell membrane
- Reduces irregular phospholipid metabolism during neuronal damage.
- Omega-3 FAs available:
 - Alpha Linolenic Acid (ALA), Eicosapentaenoic acid (EPA), and Docosahexaenoic acid (DHA).
- Arachidonic Acid, the primary N-6FA in the brain →
 - Cyclooxygenase (COX) and lipoxygenase (LOX) enzyme metabolism →
 - Pro-inflammatory O6/O9 that →
 - **increases cerebral edema, ischemia,**
 - **infiltration of leukocytes,**
 - **production of pro-inflammatory cytokines.**

Supplements

Ribose (Dose: 5 grams 3x/d)

- Phosphorylated to become ATP, in fact the backbone of all energy molecules. (Energy)
- Core of RNA, mRNA, tRNA and DNA.
- Transports inorganic phosphate into Oxidative Phosphorylation. (Energy - R-5-P)
- Poly (ADP-ribose) polymerase-1 (PARP-1), the DNA repair enzyme.
- “Think” Energy
- Approximately 66% of patients experienced significant improvement while on D-ribose, 45 % increase in energy.
- Average improvement in overall well-being of 30% (p < 0.0001).

The use of D-ribose in Chronic Fatigue Syndrome and Fibromyalgia: a pilot study. Journal of alternative and complementary medicine. Volume 12 number 9. pages 857-862. 2006.

Supplements

Glutathione

- Tripeptide (glu-cys-gly); most abundant non-protein thiol found in the brain.
- Glutathione acts as an antioxidant
 - Serves as a substrate for the enzyme glutathione peroxidase.
 - Mainly found in astrocytes.
- Functional impairment associated with glutathione deficiency

Dose: 50-100 mg 1-2 times/day in liposomal base or
600-1000 mg IV push (diluted in 3 cc NSS) over 5 minutes.

Note: Do not mix with Vitamin C

Supplements

N-Acetyl Cysteine (NAC)

Glutathione Precursor

Anti-oxidant, free radical capabilities against Superoxides, H₂O₂ and hydroxyl radicals.

Neurovascular-protective effects after TBI.

Early post-injury treatment with NAC reversed behavioral deficits associated with mTBI.

NAC + Vitamin E  **Nf KappaB**

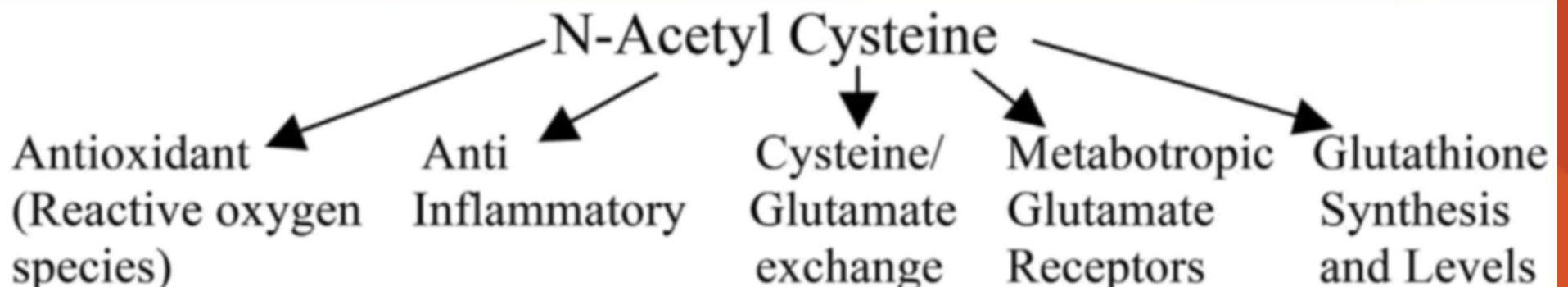
Efficacy of N-Acetylcysteine in Traumatic Brain Injury. PLOS ONE, April 2014, Vol 9,4 , Katherine Eakin L., Renana Baratz-Goldstein, Chiam G. Pick, Ofra Zindel, Carey D. Balaban, Michael E. Hoffer, Megan Lockwood¹, Jonathan Miller , Barry J. Hoffer , Dept of Neurosurgery, Case Western Reserve University School of Medicine, Cleveland, Ohio, USA, Dept of Anatomy and Anthropology, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel, Dept of ENT, Neurobiology, Communication Sciences and Disorders, and Bioengineering, U of P, PA, USA, Dept of ENT, Spatial Orientation Center, Naval Medical Center San Diego, San Diego, Ca, USA, Graduate Program in Neurodegeneration, Taipei Medical University, Taipei City, Taiwan

Supplements

N-Acetyl Cysteine (NAC)

A 4 gram loading dose was given followed by 2 grams twice a day, then reduced to 1.5grams BID after 4 days.

Early treatment with NAC resulted in a seven day symptom resolution rate of 86% as compared to 11% in those receiving placebo and began therapy between 24–72 hours after blast exposure.



Tocopherols and Tocotrienols

- **Vitamin E compounds**
 - **Tocopherols (alpha-, beta-, gamma-, and delta-)**
 - **Tocotrienols (alpha-, beta-, gamma-, and delta-).**
- **Vitamin E is a potent, lipid-soluble, antioxidant with neuroprotective benefits.**
- **Pre-traumatic supplementation with alpha-tocopherol reduces TBI-induced lipid peroxidation, oxidative injury, and impairment in spatial memory.**
- **Gamma-tocopherol most effective scavenging free radicals and reducing nitrogen oxygen species causing inflammation (RNS).**
- **Promotes nerve regeneration**

Dose: Mixed Tocopherols (Gamma 500 mg/ Alpha 400 mg) 1-3 times /day

Supplements

Ascorbic Acid

- Vitamin C is distributed throughout the brain
- Concentration in CSF is about tenfold higher than in plasma.
- Serves as a strong reducing agent
- Donates electrons directly neutralizing ROS
- Recycles the Tocopherol radical to its active reduced form.
- Dose: Ascorbyl palmitate form: 500-1000 mg 2x/d
 - IV 15-25 gm Vitamin C in 500 cc NSS over 1-2 hours 1/wk
 - (Do not use if G6PD deficient)

Supplements

L-Carnosine

- Dipeptide found in glial and neuronal cells throughout the brain.
- Acts as a chelator for divalent cations like Cu^{2+} and Zn^{2+}
- Suppresses amyloid-beta peptide toxicity
- Inhibits production of oxygen free-radicals, scavenges hydroxyl radicals and reactive aldehydes,
- Suppresses protein glycation.
- Carbonic acid activator (CA is decreased in Alzheimer's)
- Stimulates proteolysis, dissipates cross linkages, reduces inflammation

Dose: Stand alone-1000 mg/d

In combo w pregnenolone, quercetin, DHEA use 250 mg.

Supplements

Melatonin

- Produced in the pineal gland
 - Crosses the blood brain barrier; Enters neurons and glial cells.
 - Potent scavenger of peroxy and hydroxyl radicals
 - Prevents initiation and propagation of lipid peroxidation
 - Stimulates brain glutathione peroxidase.
- Acts as an antioxidant in both lipophilic and hydrophilic environments
- Inhibits nitric oxide synthase (NOS)
 - Prevents the toxic effect obtained after its interaction with superoxide radicals.

Dose: 0.5 mg/night 2 hours before bedtime. Every 7 nights increase 0.5 mg nightly until “hungover in am.” Then decrease by 0.5 mg until no longer foggy in am

ER form used for those unable to stay asleep

Supplements

Alpha Lipoic Acid-

Lipid peroxy radical (LOO•)
scavenger.

Neuroprotective

Regenerates other endogenous
electron-donating antioxidants:

- Vitamin E
- Glutathione
- Vitamin C.

Dose; 400-800 mg 1/d

Supplements


Curcumin

- Immune modulator, antioxidant, anti-inflammatory
- Reduces chemokines
- Reduces free radicals and improves cell viability in oxidative stress environment
 - Useful in Alzheimer's
- Anti-inflammatory, anti-carcinogenic, anti-infertility, anti-bacterial, anti-diabetic, anti-venom, anti-fibrotic, hypotensive activity.

Dose: 400-600 mg 2-3 times/d

Supplements

CoEnzyme Q 10

- Potent free radical scavenger in lipid and mitochondrial membranes.
- Increases cerebral cortex concentrations 
 - » increase in cerebral cortex mitochondrial concentrations of CoQ10.
- Exerts neuroprotective effects in neurodegenerative diseases associated with TBI.
- Preserves respiratory and cardiac mitochondrial function.

Dose: 100 mg./d + 100mg for every “risk” factor (Cardiac, respiratory, disease, statin therapy, neurologic compromise)

Use w/ PQQ

Coenzyme Q10 administration increases brain mitochondrial concentrations and exerts neuroprotective effects. Proc. Natl. Acad. Sci. USA Vol. 95, pp.8892–8897, July 1998 Medical Sciences Coenzyme. Russell T Matthews, L. Yang, S. Browne, M. Baik, F. Beal., Neurochemistry Laboratory, Neurology Service, Mass. General and Harvard Medical School, Boston, MA 02114

Supplements

PQQ

- Antioxidant, influences nerves
 - Maintains mitochondrial hemostasis
 - Promotes nerve growth factor
 - Supports intracellular neuronal response
 - Maintains NMDA receptor activity
 - Promotes learning and memory
- Dose: Use with CoEnzyme Q 10 20 mg PQQ and 100 mg Co Q 10

Supplements

Quercetin = Energy and Allergies

Similarity to resveratrol in generating mitochondrial biogenesis.

- Increases mRNA expression of: PGC-1 α , SIRT1, mtDNA, and cytochrome c concentrations.
-
- Increases production of ATP.
- Increases Glutathione Levels
- Effective (when combined w stinging nettle) in allergy relief.
- **Protects neuronal cells from oxidative stress-induced neurotoxicity.**

Protective Effect of Quercetin in Primary Neurons Against A β (1-42): Relevance to Alzheimer's Disease. Mubeen Ahmad Ansari, Hafiz Mohammad Abdul, Gururaj Joshi, Wycliffe O. Opii, and D. Allan Butterfield, Dept of Chemistry, Center of Membrane Sciences, Sanders-Brown Center on Aging, University of Kentucky, Lexington, KY 40536, USA

Supplements

Quercetin

- Cerebral metabolism has important consequences on motivation, mood, fatigue, anxiety, depression, and central motor drive from the cortex; **ATP dependent**.
- Within 7 days of introduction of Quercetin, mitochondrial biogenesis with increased oxidative phosphorylation by facilitating transcription, translation, and replication are recorded. = Energy
 - **Dose: 500 mg 2x/d**

Quercetin increases Brain and Muscle Mitochondrial biogenesis and exercise tolerance. Am J Physiol Regul Integr Comp Physiol 296: R1071–R1077, 2009. J. Mark Davis, E. Angela Murphy, Martin D. Carmichael, and Ben Davis. Div. of Applied Physiology, Dept of Exercise Science and Dept of Com. Science and Disorders, Arnold School of Public Health, U. of South Carolina, Columbia, South Carolina. USA.

Female Hormone Testing	Result	Range
Growth Hormone	0.6	5ng/ml*
Somatomedin C (IGF-1)	78	> 200 ng/ml
IGFBP-3	2950	>4000 ng/ml
DHEA-S	49.2	195 ug/dl*
Estrone (E1)	274	< 200 pg/ml*
Estradiol (E2)	191	90 pg/ml*
Progesterone	.06	5-7 ng/ml*
Pregnenolone	131	100 ng/dl*
EP Ratio	3457	< 250

DHT	23	< 30ng/Dl
SHBG	88	< 75 pg/ml
FSH	6.8	7 mIU/ml*
LH	5.0	5.1mIU/ml
Prolactin	7.2	14 ng/ml*
Zinc	89	95mcg/dL
Insulin	8	<30mIU/L
Vitamin D3	17	>60 ng/dl*
ACTH	35.6	35 pg/ml*
Cortisol	3.41	< 15 ug/dl

OLIVIA G.

Testosterone Free	0.8	2-4 pg/ml*
Testosterone Total	12.7	<44 ng/ml*

TSH	0.98	<2.5 mcu/ml*
T3, Free	3.6	> 2.5 pg/ml
T4, Free	1.8	> 1.5 ng/ml
rT3	168	80-250 pg/ml
T3/rT3 Ratio	2.14	>1.06
TPO	19	<35

FIXING OLIVIA G.

1. GH Deficiency
2. Estrogen Dominance
3. Hypoprolactinemia
4. Low Vitamin D3
5. Low Testosterone
6. Pregnenolone Steal

1. Secretagogue 2-3 Sprays at hs.
2. Progesterone
 - a. 1 gm @ hs 5% Cream nites 14-25 or 100 mg po
3. GABA/5 HTP
4. Vit. D3 q 1000 IU inc level 8 ng/dL
5. Zinc Citrate 50 mg
6. Pregnenolone 30 mg/DHEA 25 mg

Male Testing	Result	Range
Growth Hormone	4.7	5ng/ml*
Somatomedin C (IGF-1)	232	> 200 ng/ml
IGFBP-3	4182	>4000 ng/ml
DHEA-S	88	245 ug/dl*
Estrone (E1)	<5	< 60 pg/ml*
Estradiol (E2)	68	<25 pg/ml*
Progesterone	0.96	0.8 ng/ml*
Pregnenolone	121	110 ng/dl*
EP Ratio		< 250

DHT	33	< 55 ng/dl
SHBG	58	< 75 pg/ml
FSH	5.8	7 mIU/ml*
LH	8.9	5.1mIU/ml
Prolactin	13	14 ng/ml*
Zinc	68	95mcg/dL
Insulin	19	<30mIU/L
Vitamin D3	99	>60 ng/dl*
ACTH	42	35 pg/ml *
Cortisol	22	< 15 ug/dl

Joel P.

Testosterone Free	2.8	12-14 pg/ml*
Testosterone Total	262	690 ng/ml*

TSH	0.99	<2.5 mcu/ml*
T3, Free	3.1	> 2.5 pg/ml
T4, Free	1.8	> 1.5 ng/ml
rT3	32.6	80-250 pg/ml
T3/rT3 Ratio	0.95	>1.06
TPO	199	<35

Fixing Joel P.

Diagnosis

1. Hypogonadism/Excess Estrogen
2. Adrenal Excess
3. Hashimoto's Thyroiditis
4. Hyperinsulinemia (Mild)

Treatment

1. Testosterone 60 mg IM weekly or 1000 mg Pellets
2. Zinc Citrate 30 mg bid
3. DHEA/Pregnenolone 50mg/50 mg
4. Adaptogenic Herbs or Cortef 5 mg/d
5. Plant Sterolins/LDN (TPO)
6. Cinnamon/Chromium/Berberine
7. 4 Point Cortisol Saliva Test

3 Year Study-Millennium WAF Project

200 Vets and Active Military

- **History of TBI**
- **PTSD**
- **Blast Trauma,**
- **Treatment Resistant Depression**

3 Year Study-Millennium WAF Project

- Laboratory Evaluation as Noted Above
- Treatment
 - Supplements
 - N-Acetylcysteine
 - Tocopherols
 - EPA/DHA
 - Alpha Lipoic Acid
 - PQQ
 - Quercetin

3 Year Study-Millennium WAF Project

- **Hormone Restoration**
 - Clomid
 - Thyroid
 - Testosterone Cypionate/Propionate
 - Estrogen/Progesterone (when indicated)

3 Year Study-Millennium WAF Project

No. #	Mean Age	Program Time	History of Suicide	Medication Status (%off)	Median Improvement
57m/1f	39.8	415 Days	2 attempts	90%	73%
Ranges	23-77 YRS	125-1069 Days	1- 6x	4-16 meds	10% - 100%

No.	Clomid (CPC)	Testosterone (TPC)	Combination (CPC+TPC)
57/1	47	11	3

91% had a 50% improvement in 90 days.

58 military individuals, 57 males and 1 female, a variety of traumas(TBI), with and without PTS, all on multiple medications, multiple suicide attempts, and disrupted socialization. Average of treatment time 415 days (13.5mos), 90% off medication with a 73% improvement in overall condition.

Data: % Improvement & Ages

91% with a 50% or greater response.

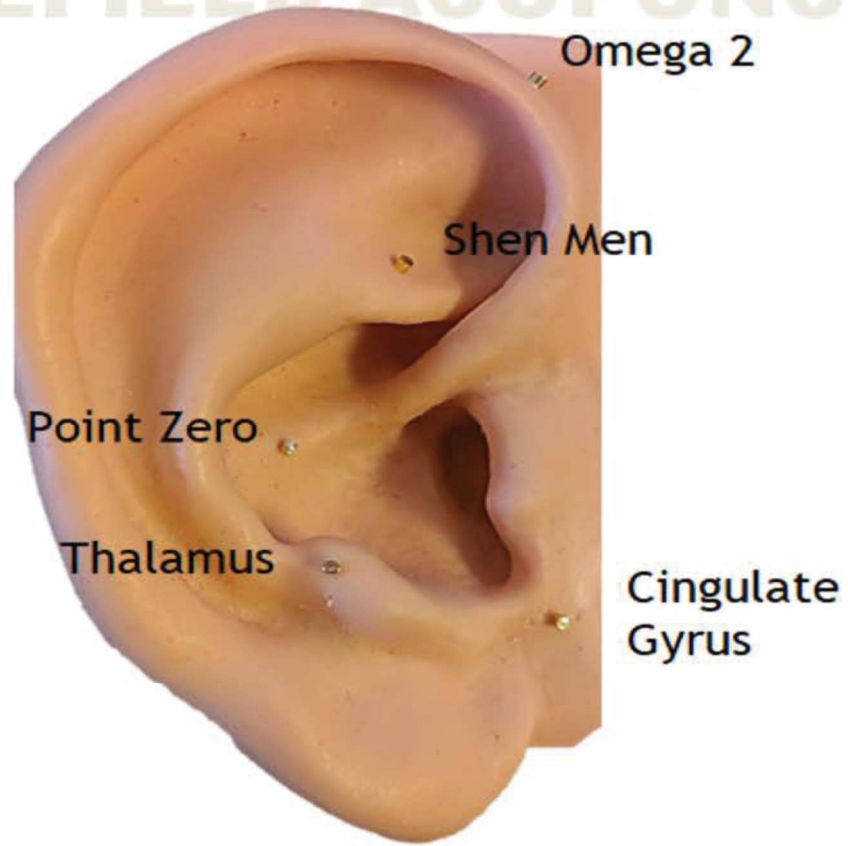
Population by Age					
20s	30s	40s	50s	60s	70s
6	29	13	5	3	2

Distribution - Percent Improvement									
10%	20	30	40	50	60	70	80	90	100%
4	1	0	0	6	7	13	8	9	9

Age Group to Percent Improvement						
Age	20-29	30-39	40-49	50-59	60-69	70-79
%	77.5	73.8	69.2	67.0	80.0	57.5



BATTLEFIELD ACUPUNCTURE (BFA)





Conclusion

- **80% of TBI Injuries are mild without LOC**
- **Acute hormone deficiencies occur in 56% of Head Injuries**
- **36% continue on to Chronic Hormone Deficiency**
- **Psychotropic Meds Mask Symptoms**
 - **Psychotropic meds do not address underlying cause**
- **Plan: Replace Deficient Hormones to Physiologic Levels**