A Paradigm Shift in the Diagnosis and Treatment of Traumatic Brain Injury

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Medical Director: Masters Men’s Clinic, Burlington Ontario
Medical Director: The Centre for Women’s Health, Burlington Ontario
Medical Director: Brant Medical Research Burlington Ontario
Traumatic Brain Injury
AIMS OF THIS PRESENTATION

Research shows that a large percentage of brain injuries result in hormonal disruption. However, hormonal assessment is not a routine part of brain injury assessment or management.

After more than 4 decades of hormonal restoration, I have used this experience to improve the lives of brain injured patients.

In this practical presentation I will discuss the new research looking at inflammation as a major factor in TBI, and also review hormone diagnosis and treatment as well as outline the often faulty misgivings regarding hormonal therapies. This will include case examples of such treatments and discuss why they were successful.
My Background

Exercise Physiology
MD
Ob/Gyn
Hormones (12,000 menopausal patients)
Masters Men’s Clinic (5,000 men)
Sports Medicine: Team Canada x 3
Toronto Rock Pro Lacrosse
Husband to Joan (Be Menopositive)
Father to Scott and Kim
There are a lot of questions to be answered regarding TBI.
Life is like a prism. What you see depends on how you turn the glass.

Jonathan Kellerman
Is it really true that:
“There is no treatment for a concussion but rest.”
Why do patients “hit a wall” in their recovery?
Are people depressed because of their slow recovery or is there another reason for mood changes?
Why is there so much time, money and talk about getting better imaging to show damage in the brain and so little discussed about treatment?
Why is there so much talk about CTE and gathering brains for study and media attention when an athlete is diagnosed with it....... and almost nothing said about preventing it?
Is a major component of illness and injury being missed in assessment and treatment?
A Key Question

Does lack of restoration of hormones, neurotransmitters and supplements increase the morbidity and mortality over that of the original injury?
TBI AND HORMONES

A 2006 study showed that hormone deficiencies associated with traumatic brain injury were prevalent in 56% of the cases within 3 months of injury and that by 12 months the number of persistent cases reduced to 36%. One additional observation in this study was that the only anterior pituitary hormone to continue to decrease was Growth Hormone.

<table>
<thead>
<tr>
<th>TIMING</th>
<th>3 MO</th>
<th>12 MO</th>
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<tbody>
<tr>
<td>Over-all</td>
<td>56%</td>
<td>36%</td>
</tr>
<tr>
<td>Gonadotropic</td>
<td>32%</td>
<td>21%</td>
</tr>
<tr>
<td>Corticotropic</td>
<td>19%</td>
<td>9%</td>
</tr>
<tr>
<td>Somatotropic</td>
<td>9%</td>
<td>10%↑</td>
</tr>
<tr>
<td>Thyrotropic</td>
<td>8%</td>
<td>3%</td>
</tr>
</tbody>
</table>
The finding of panhypopituitarism associated with traumatic brain injury is now a point in fact. How this translates into functional impairment was the basis of a 30-year study looking at patients who had suffered traumatic brain injury and the occurrence of psychiatric disorders.\textsuperscript{13}

Psychiatric Disorder associated with TBI:

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Major Depression</td>
<td>26.7%</td>
</tr>
<tr>
<td>Alcohol Abuse</td>
<td>11.7%</td>
</tr>
<tr>
<td>Panic Disorder</td>
<td>8.3%</td>
</tr>
<tr>
<td>Phobias</td>
<td>8.3%</td>
</tr>
<tr>
<td>Paranoia</td>
<td>8.3%</td>
</tr>
<tr>
<td>Axis I Over-all</td>
<td>48.3%</td>
</tr>
</tbody>
</table>
Symptoms

- Loss of memory
- Poor Mood
- Poor Concentration
- Fatigue
- Irritability
- Depression
- Joint Pain and muscle ache
- Sleep disturbance
- Headache
- Brain fog
- Loss of executive function
- Withdrawing socially
- Exercise intolerance
- Decreased enjoyment of life
- Headache
- Neck pain
- Brain fog
- Loss of executive function
- Withdrawing socially
- Decreased competitiveness
- Weight gain
- Inability to perform usual daily activities or tasks
- Decreased sex drive
- Erectile dysfunction
- Dry vagina
- Bladder dysfunction
- Nausea
- Hot flashes
- Aggression
- Palpitations
- Decreased enjoyment of life
Treatment: Menopause

- Restoration of the missing hormones
- Improvement in Symptoms
- Decrease in serious long term chronic illness
- Death rates for Stroke and heart attack decreases from 54% to 34%
- Diabetes decreases by 20%
- Significant reduction in Alzheimer's Disease, Bowel Cancer, Osteoporosis, Depression and Arthritis
- 29% reduction in all cause mortality
- 10% reduction in breast cancer
Treatment: Andropause or Low T

Treat with testosterone

Significant improvement of symptoms

Significant reduction in:

• Stroke and heart attack (40-50%)
• Depression and irritability
• Arthritis
• Metabolic Syndrome and Diabetes
• Arthritis
• Dementia
• **No increase in prostate cancer**
I feel inappropriately tired or lack energy during my normal day.

**THE MASI© VISUAL ANALOGUE SCALE WITH VERBAL RATING SCALE**

- 50 Questions/statements
  - 6 emotional/psychological
  - 7 energy
  - 5 mental/cognitive
  - 8 sexual
  - 3 social
  - 21 somatic

Scored out of 250

Pre-treatment, 12-26, 52 weeks

900+ patients
BASELINE vs 24 WEEKS TREATMENT

- I have a nap before or after dinner.
- I feel inappropriately tired or lack energy during my normal day.
- I would rank this fatigue as:
- I feel that I need my batteries recharged.
- I find it difficult to get to sleep.
- I wake up during the night.
- I wake up in the morning well rested.
- I am losing muscle size or strength.
- I am losing flexibility or range of motion.
- I have joint and muscle stiffness or arth.
From memory loss to depression, ‘it does add up’

According to Dr. Lily Hazrati, who sliced the brain into thin tranches, Montador’s CTE was not sweeping, but it was widespread. Tau clusters were found in the hippocampus, the temporal and parietal lobes, and especially in the frontal lobe, strangling neurons. And it was affecting him.

“The most obvious to everyone was his memory issues,” says lawyer William Gibbs of the Chicago-based firm Corboy & Demetrio, which is representing the Montador family in a lawsuit against the NHL, and which is also working on the suit on behalf of the late Derek Boogaard.

He was having a real, real hard time with his memory, and his father tells stories of stuff he’s lost over and over and over.

“And then the stuff that was a bit more subtle was certain decision-making deficits, kind of an inability to keep it all together. He was rather candid, really throughout his life, about that depression, which is unfortunately a part of post-concussion syndrome, and often a part of the CTE profile.”

“Monty went through some really trying times — he suffered a concussion and the team put him on waivers, and he didn’t take it very well,” Sharks winger Daniel Carcillo said in a video about Montador and depression for The Players’ Tribune.

“I think he was really worried about the future. Over the years I saw that deterioration of his mind, and he must have felt that as well.

“He was trying to reverse the symptoms and feel normal, and he just couldn’t.”

CTE is trauma-based, and Montador had 69 recorded NHL fights. Of the two other brains Dr. Hazrati examined, both belonging to ex-football players in their 70s, one anonymous ex- CFL and NFL player had CTE overlapping with dementia. The other, belonging to ex-Stampereder John Forzani, was clean. It doesn’t happen to everyone. But it happens, and hockey is not immune.

“Yes, I think you can draw a line between what we know of his behaviour,” says Dr. Tator. “We’re conducting a more thorough investigation of other sources, including his medical records … but it does explain what people recognized when they observed him — that he was depressed, that his memory for recent events was declining, that his behaviour was inconsistent.

“In our view, these are all manifestations of CTE. And the fact that his frontal lobes were affected, where the emotions and the executive functions reside, and the fact that his temporal lobes were affected, where memory resides — so in our view, it does add up.”

The NHL expressed condolences in a statement, but added, “We do not agree that the reports and allegations made today establish any link between Steve’s death and his NHL career.” They didn’t mention the mental deterioration, though.

The Montador lawsuit is still being assembled, and could still be blended in with one of the class-action suits that have been launched against the NHL. It could become a prominent case, in a landscape that is still taking shape. We don’t know what killed Montador, but his father Paul was a board member of ThinkFirst Canada, and of Parachute Canada, both organizations that try to bring awareness to and limit concussions. It’s how he knew Dr. Tator, and how Dr. Tator happened to be outside that locker room, on that night.

Paul, and the Montador family, are said to be determined. Whatever the shape of their lawsuit, the NHL’s handling and prevention of concussions could stand to be greatly improved.

“I think the suit was important to Steve, and to the extent that it’s important to the family to honour his legacy, I think that’s certainly a factor,” said Gibbs.

There is another ex-NHL player’s brain in the Toronto lab. It had dots of CTE, and its young owner was losing his mind, too. Meanwhile, the playoffs are roaring, the quiet room is a memory, and some players are deciding it’s worth playing with a rattled brain to stay on the ice. Maybe one day, that might change.
Hormones and Depression

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Google Scholar</th>
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<tbody>
<tr>
<td>Testosterone and depression</td>
<td>70,400</td>
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<tr>
<td>Estrogen and depression</td>
<td>99,300</td>
</tr>
<tr>
<td>Progesterone and depression</td>
<td>53,600</td>
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<td>Thyroid and depression</td>
<td>235,000</td>
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<tr>
<td>DHEA and depression</td>
<td>15,700</td>
</tr>
<tr>
<td>Growth Hormone and depression</td>
<td>432,000</td>
</tr>
</tbody>
</table>

References

20. Dysfunction of hypothalamic-hypophyseal axis after traumatic brain injury in adults. Journal of Neurosurgery September 2010 Volume 113, Number 3 David Kral, M.D., Jiri Zapletalova, M.D., Ph.D., Zdenek Pysak, M.D., and Miroslav Vavada, M.D.1 (Neurosurgical Clinic Faculty Hospital, 2 Department of Pneumatics, Faculty Hospital, and 3rd Internal Clinic Faculty Hospital, Olomouc, Czech Republic.)
How is this relevant to TBI?

• Head injuries affect hypothalamic and pituitary function.
• These areas are responsible for hormone production and regulation.
Outcome of a traumatic brain injury depends on a combination of structural and physiologic changes.
Mechanism of Injury

- Brain vs skull
- Shearing forces (axons)
- Post traumatic cystic cavitation (a spreading of the damage which enlarges the small area of direct trauma to a greatly enlarged secondary injury surround by a glial scar)
- Dead cells release toxic inflammatory molecules (cytokines, glutamate, prostaglandins, nitric oxide)
- This secondary phase of inflammatory-based progression of TBI has ben shown to be active for up to 17 years post-TBI Giunta et al, 2012
Every time you are tempted to react in the same old way, ask if you want to be a prisoner of the past or a pioneer of the future.

Deepak Chopra
Your Personal Health

3 major areas of concern with aging:

- Cardiovascular disease
- Cancer
- Neurodegeneration
An added approach to treatment of traumatic brain injury

*Regenerate a Neuro-Permissive Environment*

Evidence supports the hypothesis that CNS neurons fail to regenerate not due to their intrinsic inability to grow new axons but due to their growth state and the lack of a permissive growth environment.
Ewen: Stealth lacrosse goalie Tyler Richards retires over concussion worries


Vancouver Stealth goalie Tyler Richards is leaving the game after suffering a series of concussions due to hard shots to the mask.

Photograph by: Postmedia News files, Calgary Herald

Add Tyler Richards to the frightening concussion stories.

Richards, a goaltender with the Vancouver Stealth in the wintertime National Lacrosse League and the Burnaby Lakers in the summertime Western Lacrosse Association, announced his retirement from the sport on Friday, citing three concussions in the past five years.

They weren't from collisions around the net, as you might expect. They came from saves off his mask.

"The last one wasn't even a hard shot," Richards, 28, said, pointing to a stop he made against Jeremy Noble of the Colorado Mammoth on March 29 in Denver that led to Richards missing the next five Stealth games. "He hit me right in the chin, and it knocked my head forward. Right away, I could feel like I was zoning out. After the game, I didn't feel right. We flew home the next day and I felt awful."
How To Regenerate a Neuro-Permissive Environment

- Control Inflammation
- Enhance neuronal survival and neuroprotection
- Stimulate recovery
- Replenish hormones
If one believes that brain injury causes chronic inflammation, and that in turn causes chronic progressive degeneration, then theoretically it’s reasonable to assume intervention is possible.

Dr. Alan Faden
Director
University of Maryland,
Shock Trauma Research
April 2015
Many new articles on inflammation and the brain.
Inflammation Seems to Underlie Concussion Symptoms

By Traci Pedersen
~ 1 min read

Inflammation appears to be the underlying factor behind the symptoms of traumatic brain injuries, according to a new study by researchers at McMaster University in Canada.

The findings provide an explanation for why many people with very mild head injuries, or even injuries to other parts of their bodies, still suffer from debilitating post-concussion-like syndromes. These symptoms include headaches, dizziness, cognitive impairment, and other neuropsychiatric symptoms such as irritability, anxiety, and insomnia.

In fact, people who have a very subtle genetic change in a certain inflammatory protein tend to have poorer recovery after brain injury. The findings offer a new look at post-concussion syndrome and settle long-unanswered questions that have been plaguing experts in the field.

“It’s inflammation that they have in common,” said Michel Rathbone, M.D., Ph.D., a professor of medicine for McMaster’s Michael G. DeGroote School of Medicine and a lead author of the paper. “Rather than a concussion, we’d like to propose a unifying umbrella term of post-inflammatory brain syndromes or PIBS.”

He added that their new findings will encourage scientists to open up new lines of research into understanding the cause of post-concussion symptoms. So even in a situation where there is no obvious visible brain injury on conventional imaging scans, physicians may be able to still offer treatments that target inflammatory mediators.
Control Inflammation

• Hormones: DHEA, Growth hormone, pregnenolone and melatonin (may be the ultimate antioxidant)

• Supplements (Carnosine, vitamin C, vitamin B12, **Vitamin D**, N-Acetyl Cysteine, Quercetin, Coenzyme Q10, glutathione, nicotinamide, n-acetyl cysteine, phosphatidylcholine, **Omega 3**, Mucuna Pruriens), zinc

• Medications: Amantadine, Selegeline
Restore the hormones
(also many are neuroprotective)

- Estrogen
- Progesterone
- Testosterone
- DHEA
- Thyroid
- Growth Hormone (Healing Hormone)
- Cortisol
- Prolactin
- Pregnenolone
Why Replace Thyroid Hormone?

Symptoms:

• Fatigue
• Headache
• Depression
• Memory loss
• Cognitive dysfunction
• Anxiety
• Insomnia
• Arthralgia (muscle ache)
• Weight gain
Thyroid and the Brain

- Low T3 linked to neurodegenerative process and progressive cognitive impairment
- T3 can treat affective disorders
- Small changes in T3 and T4 in brain have major impacts
- Cognitive effects of thyroid dysfunction can mimic deficits observed after TBI
- Depression post TBI (as high as 50%) may be due to hypothyroidism
- Thyroid reduces Beta amyloid (Alzheimer’s D.)
What If Low Thyroid Is Not Treated?

• Increased death rate due to CVD due to increased CRP, homocysteine, vasospasm, arrhythmias and congestive heart failure

• Low T3 is the strongest independent predictor of death in cardiac patients
Controversies in Diagnosis

• TSH range 0.35 -5.0 Ideal 0.1 to 1.0
• T3 is the active hormone Need it in upper quartile i.e.. If range 2-6 pg/mL, T3 should be 5-6
• T4 in lower quartile
• Reverse T3 range 18-25 optimal lower quartile
• Factor that impairs T4 to T3 conversion: inflammation and low Vitamin D
Why Replenish Growth Hormone

- Low GH increases cardiovascular morbidity and mortality
- GH stimulates the immune system.
- Low GH increases the risk of infections and cancer
- Low GH associated with an increased risk of osteoporotic fractures and reduced healing
- Low GH leads to increased obesity
- GH stimulation reduces pain (fibromyalgia)
Why Replenish Growth Hormone?

-GH reversed atherosclerosis in a 5 year prospective controlled trial
-low IGF1 associated with short telomere length
-highest IGF1 associated with longest telomere length
(study of 2744 elderly men)
Why Replenish DHEA?

- Supplementing DHEA for 3 months resulted in a remarkable increase in physical and psychologic wellbeing in 67% of men and 84% of women.

- Low DHEA associated with a significant increase in ischemic heart disease in middle aged men.
Why Replenish Pregnenolone?

- Low pregnenolone associated with **social phobia**
- Low pregnenolone is associated with **generalized anxiety disorder** in men
- Pregnenolone has a strong effect on **learning and memory** by regulating neurotransmitters in the hippocampus
Hormones relegated to the “Reproductive and Sex hormone” genre offer much more.

THESE NEUROSTEROIDS AND NEUROACTIVE STEROIDS HAVE MAJOR EFFECTS ON THE BRAIN AND MANY OTHER NON-REPRODUCTIVE ORGANS
# Detailed Hormone Analysis

<table>
<thead>
<tr>
<th>Hormone Testing</th>
<th>Results</th>
<th>Range</th>
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</thead>
<tbody>
<tr>
<td>Growth Hormone*</td>
<td>&lt;0.03</td>
<td>5ng/ml*</td>
</tr>
<tr>
<td>Somatomedin C (IGF-1)*</td>
<td>188</td>
<td>&gt;200 ng/ml*</td>
</tr>
<tr>
<td>IGF BP-3</td>
<td>4600</td>
<td>4000 ng/ml*</td>
</tr>
<tr>
<td>DHEA-S*</td>
<td>140</td>
<td>~255 ug/dl*</td>
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<tr>
<td>Testosterone Free*</td>
<td>3.92</td>
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<tr>
<td>Testosterone Total*</td>
<td>176</td>
<td>690 ng/ml*</td>
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<tr>
<td>Dihydrotestosterone (DHT)</td>
<td>28.6</td>
<td>&lt;55 ng/dl*</td>
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<tr>
<td>Sex Hormone Binding Gb</td>
<td>22</td>
<td>&lt;45 pg/ml*</td>
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<td>Estrone (E1)</td>
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<td>Progesterone*</td>
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<td>Pregnenolone*</td>
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<tr>
<td>FSH</td>
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<td>LH</td>
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<tr>
<td>Prolactin</td>
<td>7.1</td>
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<tr>
<td>Zinc</td>
<td>114</td>
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<tr>
<td>Vitamin D3</td>
<td>45</td>
<td>&gt;60 ng/dl*</td>
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<tr>
<td>TSH</td>
<td>1.05</td>
<td>&lt;2.5 mIU/ml*</td>
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<tr>
<td>T3, Free</td>
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<tr>
<td>T4, Free</td>
<td>1.35</td>
<td>&gt;1.5 ng/ml</td>
</tr>
<tr>
<td>rT3</td>
<td>113</td>
<td>80-250 pg/ml</td>
</tr>
<tr>
<td>T3/rT3 Ratio</td>
<td>2.8</td>
<td>&gt;1.06</td>
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<tr>
<td>TPO</td>
<td>-</td>
<td>&lt;35</td>
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<tr>
<td>ACTH</td>
<td>59.55</td>
<td>&lt;35 pg/ml*</td>
</tr>
<tr>
<td>Cortisol</td>
<td>14</td>
<td>&lt;15 ug/dl</td>
</tr>
</tbody>
</table>

* The IDEAL RANGE is at the 50th percentile of optimal. Treatment is geared to 50th – 75th percentile.

I cannot find a Canadian lab that does pregnenolone levels.

Our testing is 2 generations out of date.

I see a 100% variation in values between certain labs.

I can wait 6 weeks for an IGF1 level.

Testing in the USA is available within 24 hours and can be accurate within a decimal point!
Hormone Interpretation

- Ranges are way to wide
- Total testosterone 8-38
- Need to establish optimal ranges of our own (Precise Medicine)
TESTOSTERONE LEVELS CHANGE BY THE HOUR
(IN HEALTHY MEN)

Older men
M = age 68

Young men
M = age 25

ng/ml

24 hours

0800 1200 1600 2000 2400 0400 0800
Lawrence Komer MD FRCSC
Medical Director: Masters Men’s Clinic
Gordon Tonnelly  B Sc. CCCP
Director: Masters Men’s Clinic

**TESTOSTERONE LEVELS**

<table>
<thead>
<tr>
<th>Testosterone Level</th>
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<th>Noon</th>
<th>Evening</th>
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<tbody>
<tr>
<td>Significant Low</td>
<td>8.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sub Optimal Levels</td>
<td>28.0</td>
<td></td>
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<tr>
<td>Optimal Levels</td>
<td>38.0</td>
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</table>

**25 YEAR OLD MALE**

Test between 8:00 – 9:00 AM
Safety of Hormones

- Bioidentical hormones are safe!
- Need to restore in a physiologic way with optimal physiologic levels
- Earlier notion that GH supplementation increases cancer risks has been disproven (25 year study 1985-2009)
The Importance of Route of Administration in Estrogen Therapy

There are significant differences between oral and percutaneous hormone therapies. The different ways in which the hormone is delivered into the circulation have clinically meaningful implications for the selection of therapy, particularly for women who are at risk for cardiovascular events. For most women, it is wise to recommend a percutaneous therapy over an oral formulation.

By Lawrence D. Komer, MD, FRCSC

With the recent controversy surrounding the publication of the Women’s Health Initiative (WHI) results,1,2 hormone therapy for peri- and post-menopausal symptoms has been under greater scrutiny than ever before.

While the WHI has provided a wealth of excellent data for the population, the agents and the dose that it studied, the applicability of these data to other populations of women and to other types of therapy is limited.

One of the biggest problems with extrapolating the data from the WHI to clinical practice is the fact that the WHI (and most other hormone therapy studies, for that matter) have studied only patients taking oral therapies. Therefore, these studies do not provide insight into percutaneous treatment modalities (i.e., patches and gels).

The way the body absorbs estrogen from oral therapies is different than the way it absorbs estrogen from percutaneous delivery methods, which can translate into significant clinical differences.

This review examines the biochemical distinctions between oral and percutaneous delivery methods and reviews some of the clinical trial literature that has compared the two modalities.
Testosterone replacement does not increase the risk of prostate cancer.
What if you don’t restore hormones?

- Will not get optimal improvement in TBI
- Potential liability as there is a large increase in chronic and potentially fatal illness (stroke, heart attack, diabetes, bowel cancer, osteoporosis, depression, arthritis, Alzheimer's Disease, dementia, ?CTE, Parkinson's Disease, etc.)
The Mountain of Illness
Case Studies
So what do you do now?

• Think about getting a hormonal evaluation for everyone with a TBI
• It may not be easy but you must persist if you want the best for them
• Be open to new ideas but do not be afraid to challenge them as well. “Don’t wait for a light to appear at the end of the tunnel, stride down there and light the bloody thing yourself.” - Sara Henderson
THE CALL TO ACTION

The injured party/patient often has greater injuries than traditionally assessed. Finding hormonal abnormalities opens up a whole new category of injury assessment and of treatment options for recovery and optimized short and long term health.
People who say it cannot be done should not interrupt those who are doing it.  George Bernard Shaw
Thanks to Mylan EPD
International Educational Travel Grant
doc@drkomer.com