

Traumatic Brain Injury – Hormonal Dysfunction Syndrome; “The Stealth Syndrome”

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INTRODUCTION AND OVER-VIEW

Until recently we have accepted the progressive and often premature loss of hormones as being a genetically predisposing process that we will all experience. It has also been considered as that natural sequence of events triggering the aging process. But there is nothing natural about a process that can be precipitated prematurely by external forces which can take from us our youth and ability to endure the challenges inherent in maintaining a long, productive, quality of life.

Traumatic Brain Injury (TBI) can be a condition that causes premature aging. It can result from a number of insults to both the exterior and interior aspects of the brain's encasement - the skull. Exteriorly, blunt force trauma caused by an object, an explosive, a shock wave created by an IED, as well as by G-forces induced by an amusement park ride. Interiorly, anoxia, hemorrhagic bleeding, subarachnoid hemorrhage, x-rays, and toxins found in our air, water, and food as well as numerous medications that can drastically influence hormonal homeostasis.

Regardless of the causation, the affect can be the production of a group of chemicals called Caspases (the Messengers of Death). These chemicals lead to a progressive dysfunction between the Hypothalamus and Pituitary gland with subsequent loss of hormonal regulation and production through a process called Apoptosis. In effect, the wiring between these two areas is damaged or destroyed, interrupting hormonal communication.

It has been documented that the deficiencies of Growth Hormone, Testosterone, Estrogen, Progesterone, Thyroid, and Cortisol (singularly and in combination) are responsible for the majority of psychological, physiological, and physical symptoms that are characteristic of post-

concussion syndrome (PCS), post-traumatic stress syndrome(PTSS), and post traumatic brain injury(PTBI).

Symptoms frequently precede the detection of the underlying hormone deficiencies, that is, if they are even looked at. In one clinical study, 56% of the group had one or more hormonal deficiencies within 3 months of the neurotrauma. In a meta-analysis of hormonal deficiencies arising out of TBI, the outcome was between 48% and 80%.

Radiologic assessment of the intracranial impact of TBI has become a science unto itself with the newer technologies helping to better define damaged areas of the brain. A number of contemporary radiologic studies have statistically documented common areas of the brain that fall first victim to TBI. It was not surprising to see that the Hippocampus was a commonly damaged area knowing that many patients with TBI suffer from memory related deficits.

Early laboratory assessment of the patient with TBI can monitor and document the sometime sudden if not progressive decrease in hormones. Then the logical challenge becomes treatment based upon replacement or supplementation of the insufficient or deficient hormone(s).

Traditionally, treatment has been with psychotropic drugs (anti-depressants, anti-anxiety, anti-psychotic, anti-epileptic, and anti-life) and psychotherapy with poor quality of life outcome. This has been nothing more than treating the superficial symptoms and not the underlying cause and that is the “Stealth Syndrome”.

This paper will consider the incidence, clinical course, diagnosis, and treatment of post TBI hormonal dysfunction syndrome – **pTBI-HDS**.

A CHANGE IN CONCEPTS BASED UPON SCIENCE

In the beginning of the anti-aging revolution, physicians (*Interventional Endocrinologists*) accepted the on-set and progression of hormone deficiencies as being a part of the natural aging process. This was loosely taken to be around the 4th decade of life when males start to lose testosterone and females begin the downward spiral leading to menopause based upon estrogen, progesterone, and testosterone deficiencies. During this progression there are

variable but significant adverse changes in one's psychological, physiological, and physical well-being that seems to correlate greater with pituitary hormone deficiencies than with one's age.

Although the relationship between neurotrauma and hormonal deficiencies has been in the medical literature for decades, its place in clinical medicine has been obscured until recently. Nonetheless, there is still academic resistance challenging the criteria that we use to define someone with a hormonal deficiency as well as the optimal treatment.

INCIDENCE

Post Traumatic Brain Injury-Hormone Dysfunctional Syndrome is typically associated with severe head traumas with a *Glasgow Coma Score* (lowest 3 and highest 15) of less than 7 or 8 with loss of consciousness and coma. Survivors of such head trauma often suffer from impairment of cognition, language, and mood, as well as physical functioning. However, more recent research by Kelly *et al* suggest that relatively mild head trauma can be enough to cause a TBI with development of hormone regulatory dysfunction.

Motor vehicle accidents and sports, such as boxing, martial arts, wrestling, football, are common causes of TBI. As are slip and falls, blunt trauma, and shaken trauma. Even seemingly innocuous rides at amusement parks can be violent enough to cause jarring of the stock of the pituitary that can predispose us to TBI.

An estimated 1.9 million Americans sustain a TBI each year with approximately 52,000 of those people dying from their injuries on the spot. Anywhere from 300,000 to 380,000 end up in an emergency room or are hospitalized for observation. The remaining individuals “shake it off” and go home unaware of the smoldering process that continues as they sleep. Of those that survive, many will go on to develop progressive hormonal deficiencies (accelerated by subsequent TBI), which leads to pTBI-HDS. This “Stealth Syndrome” is frequently subtle, frequently unaddressed, and frequently under-diagnosed.

The leading causes of TBI are:

- Falls (28%);
- Motor vehicle-traffic crashes (20%);

- Struck by/against events (19%); and
- Assaults (11%).

VETERANS AND TRAUMATIC BRAIN INJURY

Neurologists affiliated with the U. S. military now estimate that up to 30% of troops who have been on active duty for 4 months or longer (in both Iraq and Afghanistan) are at risk of some form of disabling neurological damage. This is partly based on the knowledge that closed head injuries far outnumber the penetrative head injuries on which official statistics are based. So, while official figures put the number of U. S. troop casualties in Iraq and Afghanistan at 22,600 (as of November 2006), there may be up to 150,000 already suffering from TBI.

These same neurologists are among those who have highlighted the Bush administration's neglect of its injured troops. They emphasize the need for prompt diagnosis and evaluation of troops who have sustained TBI, as well as improved methods for screening returning troops for brain damage and better monitoring of injured troops' progress during treatment and rehabilitation. The Veterans Affairs and Armed Services Committee set aside \$3.75 million for the creation of a computer-based system for the measurement of cognitive functions in troops before and after deployment to war zones. The Pre-deployment Testing was started this past year at Fort Collins, Kentucky. Congress recently authorized \$450 million from the Iraq spending bill for research into TBI.

SYMPTOMATOLOGY

Whether the trauma is mild, moderate, or severe it still can cause the brain's ability to regulate important life maintaining hormones to fail. The loss of these hormones increases the risk of heart attack, stroke, emotional instability, depression, anxiety, mood swings, memory loss, fatigue, confusion, amnesia, poor cognition, learning disabilities, decreased communication skills, poor healing, frequent infections, poor fracture healing, poor skin quality, increased body fat, decreased muscle strength and size, infertility, and loss of sex drive.

NEURORADIOLOGY AND TBI

Radiologic evidence for identification of specific neuroimaging findings indicative of TBI has been advanced with use of the 1.5- and 3.0-Tesla high-field MRI. In a 2009 study

presented by *Dr. Orrison, et al*, They assessed 100 unselected consecutive examinations of professional unarmed combatants to determine the extent of identifiable TBI findings. The percentage of positive findings and the localization of lesions were quantified using the checklist that included the MRI findings previously reported in the medical literature. Seventy-six percent of the unarmed combatants had at least one finding that may be associated with TBI: 59% hippocampal atrophy, 43% cavum septum pellucidum, 32% dilated perivascular spaces, 29% diffuse axonal injury, 24% cerebral atrophy, 19% increased lateral ventricular size, 14% pituitary gland atrophy, 5% arachnoid cysts, and 2% had contusions. The improved resolution and increased signal-to-noise ratio on 1.5- and 3.0-Tesla high-field MRI systems defines the range of pathological variations that may occur in professional unarmed combatants. Additionally, the use of a systematic checklist approach insures evaluation for all possible TBI-related abnormalities. This knowledge can be used to anticipate the regions of potential brain pathology for radiologists and emergency medicine physicians, and provides important information for evaluating unarmed combatants relative to their safety and long-term neurocognitive outcome.

CLINICAL COURSE

There are three phases to post TBI hormonal deficiency syndrome: acute, recovery, and the chronic phase.

Aimaretti et al found GH deficiency and secondary hypogonadism were the most common acquired pituitary defects induced by TBI in the transition phase (pediatric to adolescent). The results of this study suggest that it is extremely important to give all prepubescent children who have sustained a head injury a total hormone assessment, because that head injury may cause pTBI-HDS, which could cause a whole range of problems, including short stature, personality changes, functional disability, and problems with language skills and school skills. The most recent literature suggests that hormone levels should be determined immediately after the injury and then again a few weeks later.

Schneider et al studied the prevalence of anterior pituitary insufficiency at 3 and 12-months after TBI. Results showed that 56% of TBI patients had anterior pituitary insufficiency at 3 months and 36% at 12 months. *Leal-Cerro et al* conducted a similar study investigating the prevalence of TBI-mediated hypopituitarism in patients who had sustained a severe TBI within

the last five years. Results showed that 17% had gonadotrophin deficiency, 6.4% had adrenocorticotrophic (ACTH) deficiency, 5.8% were with thyroid stimulating hormone (TSH) deficiency, and 1.7% developed diabetes insipidus. Overall, 24.7% of participants developed some type of pituitary hormone deficiency.

Kelly *et al* found that chronic GH deficiency developed in 18% of patients with complicated mild, moderate, or severe TBI, and was associated with depression and diminished quality of life. Whilst Powner *et al* found chronic hormonal deficiencies occurs in 30-40% of patients after TBI, with 10-15% of patients having more than one deficiency. Like Kelly, Powner documented 15-20% of TBI patients go on to develop GH deficiency. Results of the study by Powner *et al* showed that 15% of TBI patients develop gonadal hormone deficiencies and 10-30% developed hypothyroidism. The researchers found that chronic adrenal failure is widespread amongst TBI patients and that nearly a third have elevated prolactin levels.

Koponen *et al* conducted a 30-year follow-up study on patients who had suffered TBI to determine the occurrence of psychiatric disorders. Their results showed that 48.3% of study participants had had an axis I disorder that began after TBI. The most common disorders after TBI were: major depression (26.7%), alcohol abuse or dependence (11.7%), panic disorder (8.3%), specific phobia (8.3%), and psychotic disorders. Nearly a quarter (23.3%) developed at least one personality disorder. These findings led the researchers to conclude: “The results suggest that traumatic brain injury may cause decades-lasting vulnerability to psychiatric illness in some individuals. Traumatic brain injury seems to make patients particularly susceptible to depressive episodes, delusional disorder, and personality disturbances. The high rate of psychiatric disorders found in this study emphasizes the importance of psychiatric follow-up after traumatic brain injury.”

THE MILLENNIUM’S APPROACH TO NEUROTRAUMA RELATED HORMONAL DYSFUNCTION

In order to optimally treat pTBI-HDS those hormones that are insufficient or deficient need to be identified. Important points to remember when you suspect that a patient may have sustained a potential neurotrauma;

- It is vital not to use the intensity of the trauma to predict the onset of post TBI hormonal dysfunction syndrome – even the most subtle of injuries can precipitate TBI.
- It is vital that you perform comprehensive hormonal testing immediately after the precipitating event to establish a baseline (IGF-1, TSH, LH, FSH, PR, Cortisol, etc).
- Do not use age as a predictor. Even in a 45-year-old patient it is vital to inquire about any historical head trauma – even head trauma that occurred in their childhood.
- Although GH cannot be used at present for the treatment of TBI, it can still be used to treat Adult GH Deficiency Syndrome (AGHDS). However, being aware of the etiology of such a deficiency is extremely important because you may need to adopt a totally different approach to a patient's treatment.
- Consider early hormonal supplementation to minimize the psychological, physiological, and physical sequelae.
- Hormonal assessments can be done at three-month intervals from the date of injury, or more frequently based upon treatment.
- A comprehensive cognitive, laboratory, radiological, and confrontational examination of the TBI patient is being developed by the Millennium and will be available at www.tbimedlegal.com

CONCLUSION

There are already 4.7 million people walking around with the residual affects of Traumatic Brain Injury. On top of this number there are an additional 300,000 – 380,000 more individuals who have sustained a significant TBI. At the present time, treatment has been based upon therapies that only mask the underlying condition of hormonal deficiencies and do nothing to correct them.

Addressing the 300,000 plus returning veterans with TBI, the government has set up a center at Fort Collins Kentucky under Dr. Twillie, who puts the soldiers through a battery of tests to measure different cognitive functions. Visual tests show how fast and accurately a soldier can recognize letters, a driving simulator gives soldiers the feeling of driving under different environmental conditions and a Nintendo Wii game system, with its motion-sensitive controller, helps with coordination skills. Once a soldier's individual deficiencies are identified, therapy can be designed to help retrain the brain to overcome those problems, Twillie said.

In a review of the available government protocols, there was no document found that discussed the association of TBI with hormonal deficiencies in light of the overwhelming medical literature that addresses the underlying and stealth condition of TBI-HDS.

For that reason, the Millennium Health Centers, Inc. through its new division of “**TBI-MEDLEGAL**” has set up a free to veterans program of hormonal assessment. Once they have been documented as being deficient they can return to their physician for treatment. If you are interested in participating with this patriotic program, go to www.tbimedlegal.com and sign in under “physicians sign-in”.

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Originally residency trained and board certified in Family Medicine (1984), Dr. Mark L. Gordon continued his medical education in Clinical Orthopedics (1990), Cosmetic Dermatology (1993), and Sports Medicine(1995) prior to culminating in Interventional Endocrinology(1997) a term which he coined in 2003. Dr. Gordon has been a strong advocate of the American Academy of Anti Aging Medicine and the promotion of preventive medicine thought the correction of underlying hormonal deficiencies. He was instrumental in opening up the recognition of Traumatic Brain Injury as a cause of hormonal deficiency in the hallmarked presentation on ESPN's Outside the Lines (2007). His book, *The Clinical Application of Interventional Medicine* (2008), is recognized by his peers as a dissertation on the standards of care and assessment for anti aging medicine. His academic standards and medical knowledge have been recognized by UCLA and USC where he holds the position as Clinical Professor (1998). As Medical Director of CBS Studios (2001), he has been used for projects at HBO, CBS, ESPN, CNN, FOX, and a number of international programs. Dr. Gordon is owner and Medical Director of Millennium Health Centers -- Medicine for the 21st century, in Encino California. Most recently (5/2009), Dr. Gordon is the expert on the first litigated case of Traumatic Brain Injury causing a subsequent myocardial infarction.