My objectives are really to review the history of CTE, the pathophysiology, discuss common risk factors and also introduce some potential alternative forms of therapy. Does football cause brain damage? Any trauma to the head if it’s excessive certainly can lead to brain damage but we want to define how much, how soon, how little, how much forces does it take, and also to make note of the fact that as this article from our colleagues in Australia emphasizes does available evidence suggest that it is as prevalent as the news media seems to impute?

So what is CTE? In – correct in 2005 Ben Omalu, a Neuropathologist here in the Department of Pathology at the University of Pittsburgh and also in the lab, the forensic lab here in Allegheny County was able to acquire the brain of Mike Webster, an all pro legend here for the Pittsburgh Steelers who died in a – with profound depression, dementia, poverty and market memory impairment and he described in his brain neurofibrillary tangles, the deposition of tau and a few amyloid plaques and really suggested could this be due to football? Well we knew that Mike Webster really had no recognized concussions during his play during his tenure here in Pittsburgh but it was calculated that he had over 10,000 hits to his head as an offensive center. Every time he centered the ball he got hit and the speculation was perhaps these sub-concussive blows led to progressive dementia.

Ann McKee and her associates in Boston subsequently reviewed the literature on athletes dying from brain damage and made the observation that tauopathy, degeneration of tau which is a protein making up the microtubules of the axons and subsequent degeneration of (inaudible) might be associated with sub-concussive blows to the head. And there were several proposed characteristics.
Number one may be from sub-concussive blows there is a prolonged latent period in these individuals, the mean survival is up to 18 years, early behavioral personality changes and progressive dementia. These were the characteristics that were elicited from a review, but what we don’t know is how to diagnose it premorbidly. It’s now a postmortem diagnosis. Is there a treatment? How to prevent it? What is the actual prevalence? Millions of people play football and relatively very few cases have been reported, and what are the risk factors and the severity of the trauma, the type of trauma, the genetic characteristics? There has been a proposed classification 1 through 4 depending on headaches progressing to dementia. But what happens to the brain? As Bill may have talked about, what happens, what is the pathophysiology?

If you, any of you get a splinter under your finger what happens to your finger? It gets red, hot, tender and swollen. Why? Because over 300 million years our innate immune system has been developing in our body to protect us from foreign trauma and foreign objects. There are cells that release various agents, cytokines, chemokines, proteases, various molecular agents that are drawn to the splinter, cause the inflammatory response and after it’s controlled a reparative mechanism sets in to repair the damage that occurs.

Now recently Dr. Russell Blalock and I, another neurosurgical colleague, put together a paper entitled Immunoexcitotoxicity as a Central Mechanism in CTE as well as perhaps concussion and PTSD. And we proposed a unified hypothesis. We know there are several mechanisms involved with head trauma. There is a metabolic component that Bill described, there is a biomechanical component that Kevin has described, there is an immunological component that is much less
emphasized and there is an excitatory component that has been proselytized for quite a few years. These are the 4 mechanisms that lead to brain damage.

Now what happens in the brain? Well in the brain there are microglial cells that constitute 15% of the cells in our brain that are the brain’s resident microphages, an infection, a intoxication with lead, a trauma results in a neuro inflammatory response with the same release of cytokines, chemokines and proteases are the same as the innate immunological response as the splinter in our brain that leads to an inflammatory response and if you get hit before that reparative mode goes into effect again it doesn’t turn off the immunological neuro inflammatory response continues. It’s like a burning bush in a dry forest, a forest fire can develop. So we speculate that what may happen in chronic repetitive head injuries that enough time is not allowed for repair as those microglial priming and the subsequent release of many immunologic as well as excitotoxic agents that lead to degeneration of the tau which are the structural mechanisms holding together the axons and subsequent neurodegeneration. So that in a nutshell is what we believe at this time happens in CTE.

Now the spectrum of neuroinflammation we also believe that in the post-concussion syndrome in PTSD, PTSD what happens, even if you don’t get hit in the head and there is a – and you are in a foxhole and an arm gets blown off or a head gets blown off next to you there is a huge shock to your brain-mind connection, brain-body connection. We know from doing CFS assays in PTSD patients that there is also a release of these same cytokines in those soldiers in war zones. So we have really good evidence for a neuro inflammatory response of the brain that unless it’s turned off and controlled by our immunologic system leads to problems, big problems.
Now having said that, if we look at CTE and we talk about confusion, depression and suicide as hallmarks let’s look at it another way and say well are there other things, might there be other reasons for this? Well we know if we take individuals 60 years and older who have not played football 10 to 15% of these individuals will have memory impairment as they age, never played football. We know that 1 in 10 patients age 65 will develop Alzheimer’s. We know that 1 out of 2 over 85 is going to get progressive dementia and Alzheimer’s. We know that depression is very common in the elderly, we also know that suicide, 40,000 people a year kill themselves and 5 times as many try to kill themselves. So these aren’t unique problems to the NFL or to athletes who have had sub-concussive blows. ADHD, depression and suicide are common.

Daniel Amen who has treated quite a few NFL athletes in California did psychological profiles and found that ADHD is really very common in retired NFL players and we know that actually entering the NFL it’s not an uncommon finding. We also know that depression is higher in NFL players. I mentioned earlier Kevin demonstrated in 2007 when he surveyed retired NFL players that depression was significantly higher in that cohort than in the ordinary population. In the ordinary population it’s still 10 to 15%, but many of these athletes also have chronic disabilities, knees, shoulder, neck problems that also can lead to depression.

So the conclusions, we know that dementia findings can occur in people ordinarily as they age that alcohol abuse, steroid abuse are all very common in these situations. African-Americans who form a predominant number of athletes in the NFL in particular have a higher incidence of hypertension,
diabetes and also small vessel disease. And the – we recently did a survey of the individuals that I mentioned earlier, reviewed all of the literature on CTE and we came up with 27 papers and this is on the exhibit, and we discovered that there are 151 reported cases of CTE.

Now many of the people in this room have played sports, how many have had concussions themselves? We are talking about almost half the audience have had concussions. Do you have to worry about CTE? The answer is no. We have 151 reported cases in the world’s literature to date, of these 68 have been reported in boxing and yet I have to say when I watch mixed marshall arts and I read the articles about this it is inconceivable to me how we continue to allow this to occur in a sport, in quotes a sport, a blood sport and it’s acknowledged as a blood sport when the ultimate goal is to create brain damage to win, to give an concussion to an individual, to injure the brain and you are the victor. I don’t get it. And then we are talking about all the ways to reduce trauma in sports, in practice and everything else, it just I find that very hard to believe.

But in our results we found that the cohort neurodegenerative conditions in these patients that were reported with CTE are very high. We also found that the genotype in those that were surveyed is the same as the normal population and that the most common positions we mentioned are offensive linemen and defensive linebackers.

So in summary we know that dementia occurs from many different causes, from lack of social connections, lack of exercise, a high fat diet, obesity and then the prior head trauma in CTE in my mind certainly there is evidence suggesting that that does occur but there is a major, major question
mark in terms of its true incidence. But the emphasis is good in that it helps us emphasize what we can do to reduce the problem.

As Kevin said we have 87 billion neurons in our brain and when I was taught in medical school we lose so many of these each day and each year until our brains dry up and become a prune and we shrink and die. Not true. We know that neurogenesis, neuroplasticity and new synapses can occur in our brain by doing the appropriate things. And this – these are two slides that I could talk for the next 2 hours on, but I’ll be thrown off the stage if I do. I would emphasize the new science of epigenetics, it’s those factors above the genes. Our genes are like blueprints in a – for a house. The factors that tell the blueprint what to do are nutrition, exercise, environmental factors and stress control. If we eat the right diet, exercise. What’s the main thing we can do to increase our brain cells in our hippocampus, what’s the one main thing we can do? Aerobic activity, exercise. You increase new neurons in your hippocampus by physical aerobic activity and controlling stress. If we do the wrong thing our bodies release inflammatory cytokines just like the splinter in our finger and leads to the release of agents that create inflammation in our brain, our joints, our heart and throughout our body.

So are there things we can do? Yes, we can control our diet, our exercise, environmental factors and our stress, and this is a paper that we put together showing that various natural plant products can indeed reduce immunoexcitotoxicity in our brain and in our bodies. And this is a paper again from Daniel Amen who had used these agents that you can see on your right, fish oil, omega 3 fatty acids, resveratrol found in red wine, N-acetyl cysteine which helps glutathione reproduction,
vinpocetine, all of these agents there are a plethora of reports that indicate how these help reduce neuroinflammation and also can be used for the post-concussion syndrome.

This is a paper Jeff Bost and I and others have put together and published in the Physician and Sports Medicine last month that summarizes a nonpharmacological approach so that the treatment for a better brain which is what we are looking at are all the things – it’s not complicated. Chuck Noll used to say football is not complicated, it’s about blocking and tackling. Helping our brains develop and last longer and healthier isn’t complicated, it’s doing the right thing that all of you in this room know and as you see here.

My current treatment protocol for the post-concussion syndrome is to use high dose fish oil, vitamin D-3, we recently did a study on the Steelers, 58% of the Pittsburgh Steelers were deficient in vitamin D-3 because blacks, African-Americans in particular have reduced vitamin D-3. I would urge all of you to know what your own vitamin D-3 is and to measure this in your athletes. Magnesium is frequently deficient, Curcumin is one of the best natural antiinflammatories, green tea and we are looking at hyperbaric oxygen as Jason Mihalek and Kevin is in North Carolina.

So in summary these are the risk factors, you know what you can do about these, particularly the people in this room. And finally in closing we are talking about – I was very pleased to hear Kevin say that his boys are playing football because Douglas McArthur said it I think the very best, on the portals of the gymnasium at West Point he had this inscription embossed in marble as it overlooks the playing fields at West Point. Upon the fields of friendly strife are sown the seeds of other fields
and on other days will bear the fruits of victory, the leadership, the team building, the tenacity, the perseverance that’s learned on the fields of friendly strife I think in a controlled environment are some of the best lessons we can ever learn. Thank you very much.