April 2013 DVBIC Webinar Audio

Welcome and thank you for standing by. During today's conference all lines will be in a listen-only mode. Today's conference is being recorded. If you have any objections you may disconnect at this time. I would now like to turn the meeting over to Katherine Helmick. You may begin.

Thank you. Live closed captioning is now available through Federal Relay Conference Captioning. Please see the pod beneath the presentation slide. Good afternoon, thank you for joining us today for the April DVBIC Webinar. My name is Kathy Helmick, and I serve as the deputy director of the Defense and Veterans Brain Injury Center. I will be your moderator for today's webinar. Before we begin, let's review some webinar details.

As many of you know, continuing education units and continuing medical education credits are available from St. Louis University. This webinar is approved for the following CE credits: 1.5 AMA PRA Category 1 Credits; 1.5 credits for Psychology; 1.5 Nursing contact hours; 1.75 CE contact hours for physical and occupational therapists and assistants; 1.5 CE hours for social work.

Please note that DVBIC's awarding of continuing education credit is limited in scope to health-care providers who actively provide psychological health and traumatic brain injury care to U.S. active duty service members, reservists, National Guardsmen, military veterans, and/or their families. To receive CE credit you were required to register for this webinar prior to 11:59 p.m. on April 15th, 2013. For full accreditation information, visit www DVBIC.org and click on medical providers to access the webinar series.

We encourage you to submit your questions throughout the presentation via the question-and-answer box located on your screen. There will be a question/answer session at the conclusion of Dr. Marion's presentation. I will provide details on how to complete the online CE eval and download your certificates following the presentation. We encourage all participants to complete the interactive customer evaluation at the conclusion of today's webinar.

The slides from today's presentation are now available at the link on your screen. Recorded audio from the presentation will be available at that link beginning May 1st, 2013. Please note that there may be a delay as we advance the slides during the webinar. Please be patient as the connection catches up with the speaker's comments.

Throughout the webinar you are welcome to submit questions via the Adobe Connect or Defense Connect Online question box located on the screen. The presenter will respond to as many questions as time permits at the end of the presentation.

To begin today's webinar, I would like to provide an overview of our topic. Severe traumatic brain injury occurs much less frequently than concussion, otherwise known as "mild traumatic brain injury," but typically results in long-term disability. Severe TBI is the most common cause of death and disability in those between the ages of 1 and 40 years. Among the estimated 1.5 million people diagnosed with TBI each year, approximately 50,000 have severe injuries. The quote I just gave you of 1.7 million is from the CDC, representing the years 2002 through 2006. Recent data in an article published by the CDC into the year 2013 represents 3.5 million as their epidemiology statistics showed from the year 2009, so a one-year cohort, we were looking at 3.5 million total. Dr. Marion will be discussing this further.

In this overview the speaker will define severe traumatic brain injury and identify its causes and incidence in civilian and military population. He will review the most commonly associated intercranial lesions and examine the focus of acute treatment of severe TBI. Finally, he will explore possible reasons for the limited success of current clinical trials and discuss recommendations for future trials.

Our presenter today is Dr. Don Marion, an academic neurosurgeon who has focused on the clinical pathophysiology and treatment of traumatic brain injury for more than 25 years. He was among the charter authors of the Brain Trauma Foundation's "Guidelines for the Management of Severe Traumatic Brain Injury" and published the first clinical report to show the benefits of therapeutic moderate hypothermia for TBI in the "New England Journal of Medicine 1997." Dr. Marion is the editor of a book

entitled, “Traumatic Brain Injury,” and he has authored or coauthored more than 200 journal articles and book chapter, mostly related to traumatic brain injury.

Dr. Marion’s previous positions have included professor and chair of the Department of Neurosurgery, the Boston University School of Medicine, professor and vice-chair, Department of Neurosurgery, the University of Pittsburg School of Medicine, and director of the Brain Trauma Research Center at the University of Pittsburg. Please join me in welcoming Dr. Don Marion.

Thank you, Kathy. It is indeed an honor to be presenting today to this very large group. I see almost 172 people are dialed in, and I appreciate it, and I hope can provide something to help you better understand the nature and incidence of severe traumatic brain injury and things that we can do.

I want to just start out by saying that, you know, when I started in my lessons in training just a few years ago, I didn’t think originally that I would be interested in severe traumatic brain injury because the teaching at that time was often that, you know, the damage was done at the time the baseball bat hit the head or the head hit the windshield and there wasn’t much more you could do. As I went through my residency I began to realize that that probably is not true, that there is something called “secondary brain injury,” and as a result, that there is probably a lot of things we can do if we treat these people appropriately. Next slide, please.

Oh, and I do need to start out with this disclaimer, that the views I am going to express to you today in this presentation are those of my own and certainly do not reflect the official policy of the Department of Defense, the Department of Veterans Affairs, or the U.S. Government, and I am a contractor working for the Henry M. Jackson Foundation, so I’m not a government service person. Next slide.

So let’s start out by asking the question, have current acute care practices actually improved outcomes for patients with severe traumatic brain injury? Next slide. And I’d like to point out that back in 1977, and as an institution near and dear to both myself, and especially to Miss Helmick at the Medical College of Virginia, 160 adults who were looked at in their database with severe closed head injuries, and the rate of good recovery was 36%, almost 40%; moderate disability, 24%; and the mortality rate was actually only 30%. And I’d like you to keep those numbers in mind as we go through this presentation. And I’ll give you a hint up front that numbers may not appear to have changed much but the demographic of the people being injured has changed dramatically since 1977. Next slide.

So what is the epidemiology and the incidences? As Miss Helmick pointed out below, in 2009 there were an estimated 3.5 million people who sustained a traumatic brain injury, and I would remind you that those are the people we know about. And certainly a lot of people who have had a concussion, particularly s sports-related concussion, don’t appear in these figures, so the figure is probably even much higher if you include people with concussions.

TBI is a contributing factor to a third of all injury-related deaths in the United States. As Miss Helmick pointed out, it’s the most common cause of death and disability of those between the ages of 1 and 40. It’s estimated to cost at least $50 billion a year, and 75% of injuries are concussions. Next slide.

And so this is kind of a famous pyramid published by the CDC that shows that, at least from the period of 2002 to 2006, there were approximately 52,000 deaths a year, 275,000 hospitalizations, and 1.365 million emergency department visits per year. Next slide. During that timeframe at least, the incidence seem to be increasing. So in 2002 we have 1.248 million Emergency Department visits. In 2006, there were 1.4 million Emergency Department visits, and the same increase reflected in hospitalizations and in deaths. So about a 13% increase for Emergency Department visits, and 16% increase in hospitalizations over that time. And I, frankly, don’t have a clear explanation for that. Next slide.

In terms of annual TBI-related deaths, it is clearly related to age, and this is a very important point I want to make; that as I’ll show in the next few slides, there has been a shift in the cause of TBI, which has been reflected in the change in the age group that’s primarily affected. So please note on this slide that the older you are the higher the likelihood of dying from a brain injury. Next slide.

This is, I think, a very dramatic slide, at least in my view. When I started training in neurosurgery, again, back just a few years ago, the most common cause, by far, was motor vehicle crashes and, in fact, that, in 1975, accounted for about 56% of all TBIs that we saw in the United States, motor vehicle crashes. Now, remember, that was during a time when we didn't have the passive restraints like the air bags, and seat-belt laws were inactive and people just, frankly, weren't using them.

Now, in 2002/2006, falls are the most common cause. Next slide. Next slide, please. And so what you see is is that there's also been a shift in the age group that's affected, and so it's the older people who are falling who are sustaining the TBIs rather than the young people, between 16 and 25 or 30, involved in motor vehicle crashes. Next slide.

In the Department of Defense, the incidence had been increasing up through, I guess 2011, and then, since 2012, seems to be decreasing somewhat. But, again, the most common cause is mild TBI or concussion, clearly illustrated in this slide, and in the next slide, if you look at just severe and penetrating brain injuries, they really represent a very small proportion of those injured in the military, so the total number from 2000 to 2012, for example, is about 266,000, out of which only 1% or 2,709 had severe injuries, and even fewer, actually, in just the year of 2012, only about .6% or 174 cases, which is, frankly, kind of good news, because I'll tell you it's unusual for someone with a true severe brain injury to make a complete recovery, where those with concussions or mild brain injuries, the assumption is they will make a complete recovery.

On this slide I'd just like to point out -- we're going to shift gears here a little bit, and we'll talk about the causes or pathophysiology of brain injury, the kind of lesions we see. And so what I've done for you here is just taken sort of a montage of CT images from my library to demonstrate some of the common lesions. These are axial CT scans obtained kind of with axial slices through the center part of the brain, and for those of you who might not be familiar with CT images -- I hope you all are, but if you're not, imagine a loaf of bread, a sliced loaf of bread and you just take and turn back each of those slices, and that's essentially what you're looking back here, if the brain is the loaf of bread standing on end.

In the upper left-hand corner is the most common lesion that we see with severe traumatic brain injuries that might require surgery, and that's an acute subdural hematoma. I have these blue arrows there so you can kind of see what we're talking about. You see a white rim that's slightly less white than the bone, which is the bright white cranium around the edge. So that's a subdermal hematoma, and, again, that is the most common. About 24/25% of people who are comatose and end up needing to have surgery will have a subdural hematoma.

Also relatively common are contusions. That's the CT image to the right of that on top, the sort of dark area is a simple very large contusion, and then a lot of times contusions will have hemorrhage into them, and, therefore, be called "hemorrhagic contusions," which is the CT image to the right of that.

In the lower left-hand corner is the classic epidural hematoma, classic because of that lens shape and that very smooth inner margin, which is a tearing away of the dura mater, normally tightly adherent to the skull. And the dark spots in the middle of that subdural hematoma, by the way, are areas of active bleeding, so active hemorrhage on a CT scan looks dark. In the middle on the lower row is an example of diffuse axonal injury. You see those white spots throughout the brain -- the arrow is pointing to one of them -- that's kind of what that looks like.

And then on the right-hand side is actually the most common type of hemorrhage in the brain, though it's never surgical, and that's subarachnoid hemorrhage, and you're looking at the Sylvian fissure there where the arrow is pointing, and that white area is subarachnoid blood. But that doesn't [inaudible]. Next slide.

One of the injuries that we've been very concerned about in the military has been blast injury with the improvised explosive devices. And for quite a while now we've divided blastings into four categories, what we call primary, secondary, tertiary, quaternary. And basically, primary blastings reflects the blast

over pressure waves that can cause -- actually one of the most common things it can cause is eardrum rupture, but also significant damage to any air fluid interface or tissue interface, or fluid tissue interface, and the brain, of course, has that with those [inaudible] filled with cerebrospinal fluid and the brain tissue surrounding that. Lungs take a lot of injuries in that, as do hollow abdominal organs. Secondary injury is material striking the person, tertiary injury is the body thrown and hitting a solid object, ground or a wall, and quaternary injury is things like burns and toxic inhalation. Next slide.

This slide is a slide I created in 1991, and it was a slide that I created to remind me of why I'm in this business, and this can be summed up by the phrase "secondary brain injury." Were it not for secondary brain injury, I wouldn't be very interested in this area, because, again, going back to what I said initially is there wouldn't be much we could do. Secondary brain injury though, I believe, does occur, and my own personal view on this is that at the time of impact there probably is a period of cardiac arrest or respiratory failure. It may last only a few seconds, but sometimes I think lasts as much as 30 seconds to a minute or more, causing ischemia and breakdown of the blood/brain barrier, disruption of autoregulatory mechanisms.

And then this goes on to lead, in the next day or two or three, to a release of these high levels of extracellular toxins if you will. In many cases they're normally occurring neurotransmitters like glutamate, but in high levels that can be toxic; excitatory amino acids, one of which is glutamate; cytokines; free radicals; and then the cellular inflammatory response; regional hyperthermia; and, ultimately, cytotoxic edema, vasogenic edema, and hyperemia or brain swelling. And the brain swelling then goes on, and if unchecked or uncontrollable leads to brain death because the pressure inside the cells becomes greater than the blood pressure, and blood can't get into the cell and feed the brain.

So the challenge for us in neurosurgery, in treatment of these patients, has been how do we intervene? We have time here. The point of the slide is there's time. There's hours, there are days, where we theoretically could intervene somehow to stop this cascade and prevent brain swelling. And that's been a challenge, I think, of all neuro trauma researchers managing patients with severe traumatic brain injury. Next slide.

So basic assumptions, ischemia is common early after injury. There is some significant regional heterogeneity of this posttraumatic, physiologic, and metabolic abnormalities; in other words, a blood flow metabolic mismatch, and secondary brain injury occurs for several days. Next slide. Next slide, please.

So a good friend of mine, David Hovda at UCLA, has published a relatively classic slide in which he has demonstrated in both a rat model, as well as in humans, using test studies and Xenon CT cerebral blood flow studies that there is, in fact, a mismatch of blood flow and metabolism that you have, early after injury, a reduction of blood flow by about 50%. Normally cerebral blood flow is 50 to 55 CCs per hundred grams of brain tissue per minute. But if you measure blood flow within an hour or two after a severe traumatic brain injury in a comatose person you'll find levels as low as 20 to 25 CCs per hundred grams of brain tissue per minute. At the same time, there's this hyperglycolysis or hyperglycolytic period of time and hypermetabolic period, so a mismatch. This can go on for several days. And, you know, to a much lesser extent, I think we're thinking that this may, in fact, be something going on with people with concussion and the reason why you don't want to send someone back who is still having a headache or is still traumatic. But I digress. Next slide.

So goals for acute care: We want to provide an optimal environment for recovery of damaged tissue; we want to enhance or preserve profusions of ischemic tissue; and we want to avoid therapy that has the potential to limit regional cerebral profusions. As an aside or an anecdote, I might mention that years ago I remember sitting in a bar with Randy Chesnut and Jan Dijara and some of our other colleagues, and we were talking about what it would take to -- this was actually in Vancouver. We were talking about what it would take to improve outcomes for people with severe traumatic brain injuries, and we were lamenting the fact that the PEG-SOD study, superoxide dismutase study had just failed, and yet it was another of these clinical trials that had failed.

And we all kind of came to the same realization that, you know, if we could just treat people the same way consistently and based on the best levels of evidence in every ICU in this country that would make the greatest difference of all, and if we could treat them in spite of the presumed early ischemia and enhancing cerebral perfusion, that this was likely to be much better than any single novel drug that was out there. Next slide.

So that's kind of been the goal in the last several decades. And how that translates, in the civilian sector at least, is in pre-hospital setting we recommend rapid resuscitation of blood pressure and oxygenation, organized trauma centers with neurosurgery input, early intubation of comatose patients, and transferred to a facility with immediate neurosurgical availability. Next slide.

One of the members of that group, Randy Chesnut, published this paper back in 1996, I think, where he went back and looked at 699 patients entered in the Traumatic Coma Data Bank, a study that was done in the late 1980s, and Randy found a dramatic effect of hypotension, pre-hospital hypotension on outcomes. So it's those who were hypotensive prior to arriving at the trauma center had about a 65% or 64% mortality rate, whereas those who were not hypotensive had a much lower mortality rate, 55 or 52% I guess with recovery with moderate disability rate. So hypotension was known early on to make a big difference. Next slide.

So in the emergency department, assuming that you've had adequate resuscitation or the beginnings of resuscitation of blood pressure and respirations in pre-hospital setting, in the Emergency Departments advanced life support practices are recommended, a trauma team led by a fellowship-trained trauma surgeon. Ellen MacKenzie up the road at Johns Hopkins did a study back in 2002, which showed a huge difference in outcomes for TBI patients treated at Level I trauma centers led by fellowship-trained trauma surgeons, as compared to those who were not. So this has been shown in good quality clinical studies. Immediate availability of an OR, and surgical priorities are certainly laparotomy, thoracotomy, prior head CT, that's been shown to be important. Next slide.

Another question I think we ask is about early fixation of long-bone fractures, and I'll talk about that in a minute. Indications for craniotomy are large-mass lesions with associated neurologic compromise, treatment of uncal herniation, and intractable intracranial pressure, and that's a little bit controversial. Next slide.

Monitoring techniques that currently are recommended: I've placed this slide, and you can kind of look this over at your leisure, but the things that I consider that are critical are intracranial pressure monitoring for any patient who's comatose and suspected of having a severe TBI; blood pressure monitoring and central venous pressure monitoring to make sure that you maintain normovolemia or slight hypervolemia. The rest of these monitoring techniques, I think, are somewhat arbitrary, and I don't think they're always necessary. I think they can help in centers that are capable of not only doing the monitoring but interpreting the results correctly. Next slide.

So what are the indications for ICP monitoring? Anyone who is comatose, a GCS of eight or less, mass lesions or contusions on CT scan, and prolonged hypoxia or hypotension. Sometimes if someone is brought to the emergency department and appears to be comatose, but is thought to be intoxicated, for example, the physicians may not choose to do ICP monitoring. You can quickly tell on a CT scan, however, whether or not the brain is in control or whether or not there's more than just the alcohol that's a result of the coma. Next slide.

And there are a number of different ideas about how we manage elevated intracranial pressure, the stepwise therapy versus directed therapy. Is paralysis and sedation a reasonable first step, for example? For a number of years, my preference has been intermittent CSF drainage as a pretty benign way of initial management of elevated intracranial pressure. Mannitol is the classic drug used for this, and decompressive craniectomy. Not so much barbiturates anymore. Next slide.

A medical student and I wrote up this paper a number of years ago, Matt Schreckinger, first off in the paper, and we just kind of looked at mean ICP changes for various therapies. We did kind of a large

meta-analysis of all the studies that provided this data. And it's interesting that we found that decompressive craniectomy was the single most effective treatment for reducing elevated intracranial pressure, followed by CSF drainage, hypertonic saline, and then hypothermia. And these classic treatments like mannitol and hyperventilation were actually the least effective of the common therapies for reducing the elevated intracranial pressure. But as you'll see later on in the talk, we've learned from this exercise and a number of other papers that one has to be careful about using a successful reduction of intracranial pressure as the surrogate for efficacy of a treatment, because, again, as you'll see, decompressive craniectomy and hypothermia, for example, have not clearly been shown to be effective therapies for severe TBI. Next slide.

Hyperventilation, this has kind of been a big change, I think, in my professional lifetime. When I started training in neurosurgery, hyperventilation was sort of a cornerstone of treatment. And in part because of efforts of mine and some of my colleagues, we have managed to change that and recommend, again, that that's the type of ventilation that's a routine therapy. And at the present time, I think we would only recommend aggressive hyperventilation in someone who is deteriorating in front of you, and then only for brief periods of time, because, again, going back to what I said at the start of this talk, ischemia is an important concern, and hyperventilation has a further reduction in cerebral blood flow by causing vasoconstriction, which is probably not the thing you want to be doing. Next slide.

And this is a study that I did back in 1990/91 that was, obviously using Xenon-CT cerebral blood flow studies to measure the blood flow of -- the typical blood flow of people that came into the Emergency Department comatose. But then I also did this study, looking at the effects of hyperventilation. So in this particular patient I obtained a Xenon-CT blood flow study on the left with a pCO2 at 36, which is roughly a normal pCO2, 36 to 40. The red indicates high blood flows. The purple and black indicates critically low blood flows. So I got the Xenon blood flow study of the brain on the left, and then I hyperventilated the patient to a pCO2 of 25 and repeated the Xenon blood flow study 15 minutes later, after I started hyperventilation.

And notice that on the left side, when you look at the slide, it would be on the right-hand side of that image -- it's actually the patient's left -- where that patient had a severe hemorrhagic contusion of their left temporal lobe. And what you can see there, by kind of squinting a little bit and looking bit and looking at where the black and blue areas are now, is on that side where the temporal lobe would be there now is critically-low blood flow in the ischemic areas around that hemorrhagic contusion, and then right in the center of that contusion where the vessels are probably paralyzed or maximally dilated, because the tissue is dead, you have high flows. So that wasn't doing that patient any good by hyperventilating them. And this is the kind of data that we developed our recommendations about hyperventilation on, they're based on. Next slide.

Speak up.

Speak up? Okay. So decompressive craniectomy, we'll kind of go through a few of the treatments, the common treatments that have been thought about for controlling uncontrolled intracranial pressure or brain swelling. Certainly, decompressive craniectomy has been around for a while, and recommended by a number of investigators, as you can see on this slide. But Cooper in the "New England Journal of Medicine," in 2011, came along and provided us with, really, the first prospective controlled randomized trial of this therapy. Next slide. I'm sorry, go back. Can you go back one slide? So in that study, he found that there was actually a twofold greater risk of unfavorable six-month outcomes in those who underwent decompressive craniectomy as compared to those who underwent standard therapy, and we'll talk about that a little bit further. Next slide.

ICP versus cerebral perfusion pressure: Claudia Robertson and her colleagues at Baylor, and a number of other people over the years, Mike Rosner, actually, originally from Medical College of Virginia, brought up this notion that, you know, we shouldn't just be thinking about intracranial pressure in isolation, but rather we should be thinking about an index, if you will, or intracranial pressure as compared to what the blood pressure is. And so he calculated this cerebral perfusion pressure number, which is the difference between ICP and the mean arterial pressure. And Mike suggested that we needed to have CPP of 70

millimeters of mercury or higher to optimally perfuse the injured brain. Since his writings back in the 1980s, others have come along and said, "Well, you know, it sort of depends on whether or not there's vascular autoregulation," that is to say it sort of depends on whether or not the blood vessels in the brain are able to constrict or dilate according to the blood pressure they see.

A common problem that we see following severe traumatic brain injury is that the blood vessels lose -- not a common problem, but it does occur -- the blood vessels lose this ability to control the kind of blood pressure that they're seeing and become pressure passive. So I think in 2013 the recommendation would be that you need to adjust the cerebral perfusion pressure according to the patient's seeing, and if you find that increasing blood pressure causes an associated increase in ICP, the suggestion is that cerebral autoregulation or vascular autoregulation is lost, and so you need to treat that person at a lower cerebral perfusion pressure. And a group from England has actually shown that this is probably the smartest way to treat them. Next slide.

What about things like nursing activities and so forth? My colleague at the University of Pittsburg Medical Center, Mary Kerr, and others, have shown the effects of suctioning, turning, and bathing. And the point of this slide, I think, is that, for the most part, intracranial pressure increases that go up with these activities come back down once the patient is settled again. So it shouldn't prevent routine nursing care of these patients. Next slide.

Family contact, likewise, has not been shown to significantly increase ICP enough and demonstrated -- or it has been demonstrated in some cases to actually result in the decreased ICP, particularly those who are more alert or awake. And, you know, I just find all of these things very interesting as a neurosurgeon because, again, when I was training, a lot of these things were said to cause terrible things to happen to your patient. We would often -- I remember one of my mentors would tell me, "No, don't let family members or the spouses come in to see the patients. That will cause them to be too excited and cause worsening of the brain swelling." Not true. Next slide.

And significance of hyperthermia, this is something we're very concerned about. I know that the group over at Walter Reed, in particular, Rocco Armonda has written quite a bit about hyperthermia and the importance of preventing this. Rocco has shown in some excellent studies the effects of hyperthermia on vasoconstriction and vasospasms in TBI patients. So hyperthermia should be prevented aggressively. It's been shown in laboratory studies to cause cell death, even at 24 hours after injury. Next slide.

And I would caution you that brain temperature is typically higher than rectal or bladder temperature. This is a study that Danny Brown and Mr. Henker and I did several years ago. And we actually simultaneously measured brain and rectal temperature in a number of individuals once a minute for five days, and this is what we found. So brain temperature is always between .1 and 2 degrees higher than rectal temperatures. Next slide.

So with blood pressure you want to assure normal intravascular volume and you want to measure that optimal fluids or saline or Lactated Ringers solutions, hypertonic saline, perhaps; colloid, no. Next slide. And so a number of studies have been looking now at hypertonic salines. We still are kind of in need of a prospective randomized clinical trial to show us whether or not 3% or even as high as 23% saline solutions are beneficial. But, clearly, there's good solid anecdotal evidence, and I know that the Joint Theater Trauma Systems Program likes to use hypertonic saline. Next slide.

Now just a few words about timing of extremity fractures, this is a controversial issue in some trauma centers in that the orthopedic surgeons and the nursing staff will tell you that, yeah, you know, we really want to internally fix those femur fractures or pelvic fractures as quickly as possible so we can mobilize that patient, and there's a lot to be said for that. On the other hand, in a person with a severely injured brain, early operations associated with hypotension can be a problem. Gary Gruen, who's an orthopedic surgeon that I worked closely with at Pitt, did a brief study while there and showed that for at least open fixation of the femur there was often between a two and four-unit blood loss and, typically, hypotension associated with that. So that needs to be carefully considered, and certainly the anesthesia team needs to be cautioned that hypotension has to be avoided. Next slide.

Here is just a study Pietropaoli did with intraoperative hypotension in severe TBI. There was an 82% mortality; no intraoperative hypotension, 25% mortality, so a big issue. Next slide.

And I just wanted to briefly run through the Joint Theater Trauma Systems recommendations for acute care of severe TBI because I think that they have kind of led the way, especially in the last decade, in terms of the innovative principles that they've used. And, you know, I listen with interest on the stuff we hear on TV right now about the Boston terrorist attack. All of you I'm sure have heard a number of times people talking about tourniquets. Well tourniquets didn't used to be such a commonplace practice in modern medicine and modern trauma care until it was shown in Joint Theater Trauma Systems and the conflicts in Iraq and Afghanistan that these were key to helping to save lives. And I think it's through that demonstration that they became so commonplace and are now just the standard of care at these horrible incidents like we saw in Boston. Next slide.

So these recommendations are reviewed every year. They're up for review on March 6th of this year – or in -- yeah, in March of this year, probably. Next slide. And so you can just kind of go through those, but they certainly are state-of-the-art care. And some things that are even new and not necessarily proven through prospective randomized clinical trials, but if you go to the major trauma centers throughout the United States you see things like this being done. For example, the use of recombinant factor VIIa for life-threatening intracranial bleeding is still awaiting large prospective randomized clinical trial, but most people, that I know at least, are using that. Next slide.

And, you know, again, management of hypotension or avoiding hypotension, avoiding hypoxemia, serial neurological examinations. Next slide. And, again, get these patients to Level III facilities as quickly as possible, especially if they're injured in theater, and trying to avoid long-lasting sedation or paralysis so that we can follow the neurologic assessment of these folks. Next slide. And, you know, again, I'm not going to go through each of these recommendations, but I have obviously gone through them very carefully and helped in advising on some of them. And I'm very proud of these recommendations. They're state-of-the-art and very foresighted, forward-thinking.

Notice also, by the way, the 3% saline is commonly used in the military, especially in folks who we think may have brain swelling. I was a little bit curious about that when I first saw this recommendation of 3% saline and a notable absence of mannitol. But, you know, it turns out that mannitol on the shelf will precipitate, whereas 3% saline doesn't so much. And so 3% saline is actually as effective, I think, as mannitol. Next slide. And, again, antiepileptic medications for seizure prophylaxis, my friend, Nancy Tempkin, was responsible for a study that showed that this is helpful, but probably only for the first week. Next slide.

Another program that the military should be very proud of, I think, is the Critical Care Air Transport Team, or the CCATT. It was piloted in May of 1994, at Wilford Hall, formally approved and adopted by the United States Air Force Aeromedical Evacuation System in '96. Now our 92-CCATT Team, 60 in active duty and 11 in different places, they transport more than 4,000 patients on ventilators. Next slide. And they are actually like ICU teams who are trained to function and do pretty much anything in large transport aircrafts. Next slide. There are some studies now coming out that I think are going to be used by the CCATT team to help improve the care they give. This particular study was done to show that hyperthermia is still a common problem in these transport aircrafts, and hypoxia occurring rarely, however, during CCATT flights. Next slide.

So the guideline management of outcome to a traumatic brain injury, this whole concept or notion that I was talking about before, when I was having a beer with my buddies in Vancouver, has now been looked at, and has been shown to have, I think, an important impact in outcomes. In this particular study by Palmer, there was about a nine times higher likelihood of good outcomes in those folks who were treated according to TBI guidelines. Next slide. In perhaps somewhat more carefully and scientifically done studies, there still was shown to be improved outcomes, at least at six months with an odds ratio of 3.84 for a favorable neurologic outcome as compared to those patients treated without a management protocol. Next slide.

So let's conclude the talk with some words about the clinical research that's going on, what's on the horizon. Next slide. Therapeutic moderate hypothermia, how did that get in there? All right, so I've been very interested in moderate hypothermia for quite a while, as Kathy knows, and I'll tell you why. I'm interested because for a long time I felt that there are multiple mechanisms responsible for secondary brain injury, multiple metabolic and cytotoxic mechanisms. And so I think that those mechanisms are occurring in parallels. So I think that if a therapy is to be effective in improving outcomes, or preventing as much secondary brain injury, it's going to have to effect multiple mechanisms. And hypothermia has, for a long time, struck me as a therapy that could do that. Next slide.

So by now there have been quite a few studies looking at therapeutic moderate hypothermia for severe traumatic brain injury. And, typically, the treatment is used either for a day or two or more days, sometimes for several weeks actually. The Japanese have done a phenomenal job in looking at this, as have the Chinese investigators. And interestingly what I'll tell you is that if you look at this dispassionately that all of those investigators who have looked at the therapy at single centers have found significant benefit of the treatment. Our study in 1997, we found at six months a rate of 56% good outcomes compared to only 33% in the normothermia group. However, in any of the studies, which are in the white at the bottom, those four studies, in any of those studies that have looked at multiple hospitals, you can see Shiozaki, 11 hospitals; Clifton, 11 hospitals; Hutchison, 17 hospitals; and so forth, a benefit could not be demonstrated. And, in fact, in Hutchison's study -- actually, it was a pediatric study, there was actually quite a bit higher incidence of mortality with hypothermia. So we have a ways to go before we can recommend therapy overall. Next slide.

I will say that every study I've looked at, including the multi-center trials, do show significant decrease in elevated intracranial pressure, or an improvement in brain swelling, as this slide shows. But, again, I mentioned at the beginning of the study that that doesn't necessarily translate into improved outcomes. In other words, you can reduce brain swelling, but you may not improve outcomes, which then would suggest that the cause of the brain swelling is the problem and not so much the brain swelling itself. Next slide.

However, having said all that, Fox and company came out with this meta-analysis in 2010. And their conclusion was the best available evidence supports the use of early prophylaxis mild or moderate hypothermia in patients with severe TBI to decrease mortality and improve rates of good neurologic recovery. So I think individual people, we do kind of look at this data and draw their own conclusions. Next slide.

Decompressive craniectomy, we talked about that earlier as a last resort to control uncontrollable intracranial pressure. And certainly individual investigators in small studies have shown beneficial results. Next slide. However, there was a very large prospective randomized trial done in Australia and New Zealand, published in the "New England Journal of Medicine" in 2011 that actually did not show any improvement in functional outcomes of six months in a group assigned to the decompressive craniectomy group. So it's hard to promote this as standard of care certainly. Next slide.

Progesterone is currently being looked at. Dr. Stein at Emory University for years has been testing progesterone in the lab, and his work and a number others' work has resulted in a multi-center trial, I believe 18 sites, one of which is actually a military site, looking at the use of progesterone for severe TBI. And, you know, this is just an example of a number of anecdotal studies or individual studies that have shown benefits, potential benefits. Next slide.

I, for quite a while, have been interested in supplemental oxygen. When I was back in Pittsburgh in particular, we were using tissue oxygen sensors that we placed in the brain to see if it would improve tissue PO2 by providing supplemental oxygen, and, in fact, you can, especially in a ventilated patient, if you increase the FiO2 significantly, like to 100%, you can see a change in tissue PO2. But recent clinical studies that the effect is controversial. Next slide.

So in this Brenner study, they looked at patients with high PaO2 levels of about 200mmHg or more compared to those who have lower levels. And patients who had low PaO2 levels had increased mortality and a lower GCS score as discharged than patients with a normal PaO2. Next.

This study by Asher, PaO2 between 250 and 486 during the first 72 hours after injury was associated with improved all-cause survival. So there it was suggested supplemental oxygen is important and beneficial. Next slide. So as a result of that study, there is an ongoing hyperbaric oxygen trial that the military is involved with. I'll just remind you that in a few of the Cochrane Reviews you can get kind of an idea. You know, Cochrane Reviews are a nice analysis or meta-analysis of all available data. And they have appeared recently for HBOT, for progesterone, and for barbiturates. For hyperbaric oxygen the Cochrane Reviews suggest that hyperbaric oxygen may reduce the risk of death and improve the final GCS. Progesterone, current clinical evidence from three RCTs suggests it may improve neurologic outcomes. For barbiturates, there's no evidence that barbiturates are worthwhile. Next slide.

Fish oil, a favorite of a former colleague of mine here at DVBIC, and what we know about that is that available trials so far don't show a benefit of Omega-3 polyunsaturated fatty acids and cognitive functioning, at least in otherwise cognitively healthy older individuals. Next slide.

Vagal nerve stimulation is another interesting therapy that has been looked at. And, you know, again, that's kind of in its infancy, I think something to look out for in the next several years. Next slide. Next slide, please.

All right, and so I'd like to just conclude with a couple of slides on biomarkers and effectiveness of care, and so forth. Next slide. So biomarkers have been talked a lot about. We'd like to have some serum marker that would tell us early on, maybe in the first day or so after injury, how that patient's going to do. You know, these patients come in, they're comatose, maybe they're younger, and you might ask yourself is it really worth aggressive therapy or is this person going to end up in a vegetative state, so a lot of people have been looking at this. At the forefront, I think it's probably Banyan Biomarkers in Florida. And what we know so far is that serum S-100B levels have the greatest predictive value for poor outcome at 72 hours, and CSF S100b profiles can reliably predict six-month GOS and DRS. Next slide.

Serum levels of ubiquitin carboxyl-terminal esterase L1, or UCH-L1, were found at least by the Banyan Group, to be the only independent predictor of death at discharge. But both UCH-L1 and glial fibrillary acidic protein, or GFAP, levels strongly predicted death at six months post-injury. So the point I guess I'm trying to make here is that I think, to date at least, these biomarkers are really only useful for telling you whether or not the person is going to live or die. But there's a whole big range of outcomes in between that. And so they're not very useful for telling us, so far at least, whether or not you're going to be functional in six months or be able to live independently. Next slide.

The other issue that has been talked a lot about is the influence of volume of cases on outcomes. And there's this great study by Dr. Tepas and Flint and others, where they show that after controlling for severity, demographics, and insurance status, the highest-volume centers treating severe TBI have about a 9% lower mortality risk and improved TBI patient survival, and probably improved quality of life. So I think the whole concept of designation of level I trauma centers does make a difference. Unfortunately, politics gets involved in some towns because hospitals feel like if they're not a designated trauma center their community will think less of them. But community leaders need to step up, and these kinds of data really should be looked at carefully. Next slide.

This is another study that suggests level I trauma centers have better outcomes. And, again, for my money, Ellen MacKenzie's study is one of the best. Next slide.

Mortality rates in the military have improved. And, you know, I won't go through each of these points, but it is kind of exciting to note that compared to Vietnam War the mortality rate is dramatically reduced, and perhaps a sevenfold decrease or more, and even reduced compared with a matched age and sex sample with the National Trauma Databank. And that's most exciting of all. Again, I'm very proud to be associated with the Defense and Veterans Brain Injury Center and in the leading edge or cutting edge

program because data like that, I think, demonstrates that we are doing very well with this compared to the civilian counterpart. Next slide.

One question that comes up a lot is the cost of care of severe TBI. And I would ask you to look at the Whitmore study fairly closely offline and think about that a lot. I guess I was kind of surprised by these results. But it does suggest that when all costs are considered, aggressive care is significantly less costly than routine or palliative care for individuals with severe TBI, and that remains true according to this study even up to the age of 80, so very interesting findings.

So, with that, I think I'm going to turn this over to Miss Helmick who is going to talk to you about the family caregiver guide, and then we'll take questions. Next slide.

Yes, building on Dr. Marion's presentation, I just wanted to discuss a resource for family caregivers. I do need to state – go back – that the views expressed by this moderator are those of the moderator and do not reflect official policy of the DOD, the DVA, or the U.S. government. I do not have a relevant financial relationship to disclose and do not intend to discuss an off-label/investigative use of a commercial product. Next slide.

So many of you are probably aware of this resource that came out about two years ago. It's a congressionally mandated Family Caregiver Guide. Congress asked DVBIC to develop a guide that would be supportive of caregivers who were going through the journey of moderate, severe, and penetrating brain injury. So this is not a guide for concussion. This is to be given to caregivers, by nature of the definition of a caregiver, those folks with moderate, severe, and penetrating brain injury. You can request the guide at the DVBIC website, www.DVBIC.org, or you can download the files at the TtraumaticbraininjuryAtoZ.org web address that you see up there on the screen.

This caregiver guide has four modules, and it allows for an approach to -- very interestingly has a whole module discussing the meaning of caregiving and may help to answer some of those questions that our family members face, which is "Why me" and "What does this mean in my life now." So I did want to make you aware of a significant resource that is available. Next slide.

Thank you for your presentation, Dr. Marion. Please submit your questions to Dr. Marion via the question-and-answer box on your screen. We are monitoring the Q/A box and we'll forward any questions onto our presenter for a response. And we will respond to as many as we can as time permits. We have received at least two questions. We'll go ahead and begin one that has to do with hyperbaric oxygen, Dr. Marion. And the question is that you mentioned the importance of enhancing and preserving perfusion to ischemic tissue, as that is the primary mechanism of hyperbaric oxygen therapy, what are your thoughts on using hyperbaric oxygen as a means of treating traumatic brain injury? I know you began to allude to that in one of your slides about research. So did you have what your thoughts are on hyperbaric in treating this questions says "traumatic brain injury?" I don't know if you want to break it up into severe and mild?

Well, let me just say a couple things about HBOT. HBOT has been used in a systematic fashion since at least 1990. Gaylan Rockswold was a neurosurgeon at Hennepin County General Hospital in St. Paul, Minnesota, started looking at that back then. And he's published extensively on this over the years. And so the actual clinical files of HBOT have been less than overwhelming. And I think a part of the problem, Kathy, is that there's so many variables. You know, there's how many atmospheres of pressure do you use, how long do you use it for, how many treatments do you give each day, for many days do you give those treatments, and no one has quite worked out all of those variables with hyperbaric oxygen. Moreover, I'm kind of concerned that most of the HBOT trials have not used normobaric hyperoxia as a control, or as one of the controls, because that would certainly make it a lot less expensive.

Now, yes, I did say that ischemia is a problem early after traumatic brain injury; however, you know, with enhancing blood flow, that's one thing. But if you're talking about enhancing actual oxygen delivery to the tissues or increased oxygen levels to the tissues, you have to remember that one of the toxic elements in this whole issue is oxygen-free radicals. And there is this possibility that by artificially enhancing oxygen

delivery to the tissues you might also be driving up higher levels of oxygen-free radicals, which could be toxic to the tissues. That's a mechanism where, despite the ischemia, it may not be (inaudible). Those are really my comments right now, and I kind of anxiously await the current ongoing trial.

Okay, thank you. Another question: "Are you aware of when the next update will be for the guidelines for the management of severe traumatic brain injury? I believe the last one was in 2005. And are there plans to update with current literature?"

I am not aware. I no longer have an affiliation with the Brain Trauma Foundation. And I would recommend if someone is interested in that, they can go to their website and contact them to find that out.

Okay. In your review of recent literature, do you believe that there's substantial inputs that could change the way that we're currently managing as evidence-based for severe traumatic brain injury?

I think there's a current exciting issue that's going on right now, and it's just kind of really starting up, is this whole common data element push sort of led by Geoff Manley at the University of California San Francisco. DVBIC is a part of that [inaudible]. And so studies are coming out now looking at outcomes with the implementation of the common data element. And for those of you on the line that aren't familiar, the NIH, the DOD, and a number of other organizations, put in a lot of effort in the last two or three years to come up with what are the best practices in terms of neuro-imaging, in terms of all aspects of care similar to the eye, and codifying those. And then four trauma centers and one rehab center have collaborated now to implement those common data elements and look at outcomes with them.

Okay. We have a couple questions that have been submitted on craniectomy. Let's take two right now for that. First question, "Is bilateral craniectomy better in outcomes than one-sided or unilateral craniectomy, any literature on that?"

You know, there are. There are a number of studies looking at both. And there's a study out of Charlottesville of bilateral or bifrontal craniectomy. And there's an Indian study on unilateral craniectomy. And it's hard to compare them. The Indian study on unilateral large craniectomy showed excellent outcome in severely injured patients, but they didn't really characterize the patients well enough so that you could compare apples and oranges. The Charlottesville study on bilateral/bifrontal craniectomy showed improved outcomes with the bifrontal craniectomy. And they claim that they showed good outcomes despite the DECRA study, because they cut the faults, and so they allowed upward movement of the brain. But I would go back, Kathy, to the second study and say to you that I really think that that is an important study to look closely at because it was prospective randomized and (inaudible).

And as we discussed that study last year when it was first published in our TBI quad service, we did have a lot of questions, as I recall, about the crossover, if you will, as somebody was in the control group and they're intracranial pressure rose, they were transferred over into the treatment group; and, therefore, there were some questions that we dialogued about at the DOD TDI community related to that crossover approach. Do you have any comments you want to discuss about the study and that particular caveat?

Sure. Any of you that are really interested in that and my feelings about that can look – I wrote a letter to the editor in The Lancet Neurology and described all of my thoughts on that issue, caveat. One of the things I felt in terms of that issue you raise is I would almost expect that the crossover group should have had worse outcomes because they sat around for two or three days before they qualified for a crossover with unmanaged [inaudible].

Okay, still talking about craniectomy here, a question about large decompressive craniectomy, "Are there studies that are looking at the use of this procedure in severely brain-injured service members in theater?"

No, there's no systematic study I'm aware of.

Okay. Let's switch over for progesterone and continue our discussion on research in severe traumatic brain injury, "What is the rationale or the physiology, if you will, for the reason for improved outcomes utilizing progesterone? What is the effect on the brain?"

Well, again, Donald Stein, who is kind of the principal investigator and proponent of progesterone over the years, at Emory, has suggested a decrease in inflammatory cascade of cellular inflammation in the brain as a result of progesterone. You know, if you look at the animal studies, it's a little bit hard to know exactly what's going on because the studies are not all consistent. The rat studies, the control protocol contusion injuries, it's pretty simple. Some of these studies in some people's labs showed estrogen rather than progesterone, and the levels of progesterone that are effective do not completely work out in my view. But it's an effect on the inflammatory cascade, cellular inflammatory cascade.

Okay, thank you. Let's shift to clinical care for a second. You showed us some slides on the effectiveness of hypertonic saline and then also some literature looking at the mannitol use and outcomes. What are your thoughts on why hypertonic saline is not used in the acute ICU setting for refractory increase in intracranial pressure? You did talk about it being used in the resuscitation phase, and according to the JTTS guidelines. But why do you think mannitol has such a strong footing, if you will, in the ICU setting, as opposed to hypertonic saline with all these studies that have come out showing efficacy?

Well not all studies have been consistent. Steve Shackford at the University of Vermont found that -- in a prospective randomized clinical trial Steve Shackford looked at hypertonic saline for the treatment of people with traumatic brain injuries, relatively small study, but still he did not find benefits in it, but he was widely published. It was published in the "Journal of Neurosurgery" and quoted by a number of people. So people who are purists and want to have that prospective randomized control study before they'll use something would look at that study and say it's not been proven to be effective. Now there were a number of questions about the study and some of the patients with other injuries that may have had an impact on the outcome, so other things are not so clear.

And remember what I said before too was that one of the reasons the military has embraced and the JTTS has embraced hypertonic saline is because of problems with precipitation of vials of mannitol in theater, and they don't have that problem with hypertonic saline. But I think that that's a treatment just waiting for a good quality, large prospective randomized trial for us to see benefit of it.

Are there any differences in electrolyte disturbances post-mannitol, post-hypertonic saline that would lend itself to one over the other?

No, I would say no. You can certainly have hypernatremia with mannitol. And, you know, obviously if you give hypertonic saline you're going to expect hypernatremia, but if your kidneys are functioning, and particularly the case in younger people, then that's usually not a problem. You don't give large volumes. You usually give, like, 50cc of 3% or 7%, or perhaps even less if you're using 23%.

Okay. Someone has asked to explain the difference between hypothermia and hyperbaric oxygen treatment? So what hypothermia –

So hyperbaric oxygen treatment, I think, is really a more straightforward treatment in terms of just trying to push more oxygen into the tissues, if you will, by increasing the ambient atmospheric pressure. And so I think there are fewer hyperbaric oxygen trials, clinical trials out there. And, as I mentioned before, there are a lot of variables with hyperbaric oxygen in terms of the optimal atmospheric pressure, optimal duration of treatment, and optimal number of treatments. Hypothermia is a little bit more nuanced, and, in general, the treatment is intended to limit progress of a number of metabolic cascades or pathways associated with secondary brain injury. Most people who use therapeutic hypothermia recommend 32 to 33 degrees Centigrade for at least two days. The Japanese prefer to use it for as long as necessary until the intracranial pressure subsides. But so hypothermia, I would say, its mechanism is to reduce inflammation and any cytotoxic cascade.

Could you convert those Celsius to Fahrenheit, or am I putting you on the spot there?

No. It's about 91 to 92 degrees Fahrenheit.

Thank you. What are your thoughts on using antiangiogenic agents following severe traumatic brain injury?

From what I've seen, they're still pre-clinical and more work needs to be done. You know, whenever you're looking at these specific types of therapies, chemical therapies or pharmaceutical therapies, we have to consider two things, not only the mechanism through which this might work, and whether or not that's a beneficial mechanisms, but what are the side effects, the downstream effects of that therapy. And those issues have to be clearly worked out in the lab before you consider a phase I clinical trial. I'm not aware that that's been done yet with any of the antiangiogenic agents proposed.

Okay. What's your opinion of a severe TBI patient's educational and lifestyle outcomes for recovery after hospitalization? Will they do better or decline?

I think all patients with severe TBI have the potential to do better. I do think that organized programs, particularly organized PMR programs, Physical Medicine Rehabilitation programs, can make a difference. And so, you know, it's sort of an active process. For example, if you took a person with severe TBI, one person, and sent them to a nursing home, and they were just left in a bed somewhere, and another person and sent them to a rehab hospital and a program of active outpatient rehab, outcomes would be dramatically different, given the same injury. So it's an active and interactive process, and it requires a lot of work in general.

I'm switching gears to the metabolic activity after severe TBI, and I want to ask you a question about microdialysis. You had that on one of your slides.

Sure.

How has microdialysis improved or advanced our knowledge of metabolic activity after severe TBI?
**
Microdialysis was key to Dave Hovda in that one slide, showing that there was a metabolic mismatch between blood flow and metabolism. Dave derived that slide and that conclusion, in part, based on data he obtained from microdialysis. So microdialysis can give you information about local glucose levels, local lactase levels, the lactate/pyruvate ratio, and a number of other molecules. Microdialysis, as you know, Kathy, is a process whereby you profuse fluids through a chamber that has a semipermeable membrane, and you can actually decide on how large the pores you want of those membrane pores in the dialysis membrane. But depending on how large the pores the more molecules you can collect that way.

But, anyway, getting back to your question, so in those who do it, it helps a lot in understanding the local metabolic activity and helps you understand such things as the effect of tight glucose control, which was popular for a while for patients with severe TBI. Vespa and his crew at UCLA showed us with microdialysis that tight glucose control actually caused ischemia, caused elevation of the lactate/pyruvate ratio in the brain, and so they stopped doing that. The one caveat or the one caution I would have though, is with microdialysis you have to remember you're only measuring what's going on in a small, small portion of the brain, like a centimeter in diameter or so. And TBI is a problem that affects the brain in very different ways in very different places.

Dr. Marion, if you don't mind, I'm going to take a question myself that somebody has asked. Do we have other recommendations for spouses or family members handling the aftermath of severe acute TBI beyond the resource guide you shared? And I think it's timely to discuss, since April is Military Children's Month, to discuss two books that have come out recently that are excellent resources for children whose parents have sustained a severe traumatic brain injury. Both of them have been written by Shannon

Maxwell and are available on any source on the web or hard copy through the DVBIC shopping cart. And these are excellent children's resources, of which you don't find many.

There's also some moderate and severe traumatic brain injury factsheets that are on the DVBIC website, so I would offer to go to the Defense and Veterans Brain Injury website. Two other very proliferative sites to include would be Brainline.org and Brainlinemilitary.org for specific spousal and family resources related to acute severe traumatic brain injury.

I think in the little time I just want to ask you one more philosophical and broad-based question, Dr. Marion. As much experience as you've shown us through your publications that you have in this area, what would be your vision, a realistic vision that is, of care in ten years from now of the acute severe traumatic injured patient? What bucket of areas do you think that we could make some significant advances that would really curtail complications and improve outcomes in this patient population?

I think two things, Kathy. I think the first is that we assure that in all trauma centers throughout the United States that we follow high-quality evidence-based care at designated Level I trauma centers so the acute care that you get in Alabama is going to be the same as the care you would get in North Dakota or the care you would get in New York City. That's number one, I think. And that gets you started off on a good path toward recovery and your best opportunities for limiting the early effects of traumatic brain injuries.

The second thing that I hope for ten years from now is a network of high-quality and well-organized rehabilitation programs, again, throughout the country, so that, you know, it's just a matter of fact that if you have a severe TBI, you will be enrolled in a good quality rehabilitation program and get the kind of rehab you need. Again, one of the most disconcerting things that I saw when I was practicing surgery was how the resources available to individual patients would have such a profound impact on their outcomes, and so that those young people who didn't have the resources would come back to my clinic or be brought back to my clinic often, still severely disabled, while those who did have the resources came back in much better shape. So those two things would be important.

Standardization of care and TBI rehabilitation.

Right.

Thank you.

And, you know, I think, frankly, the "Family Caregiver Guide" that you talked about is one example of how we can take an active role and really help families be involved in that.

Thank you, doctor. Continuing education credit is offered for attending this webinar if you met the eligibility requirements to receive CE credit and also registered on or before Sunday, April 14th. You must complete an online CE eval to obtain a CE certificate. Certificates of attendance are also available to all who registered on or before April 14th. Webinar pre-registration was required to receive CE credit. If you did not pre-register you will not be able to receive CE credit or a certificate of attendance for this event. Please visit the Swank Health Care website to complete the online evaluation and download your certificate. The Swank Health Care website will be open through Wednesday, April 24th, 2013 at 11:59 p.m., Eastern Standard Time.

In terms of saving the date, we want to thank you for joining today's presentation. We look forward to your participation in future DVBIC webinars. The topic of DVBIC's next webinar is "Advancing TBI Care for Veterans: Updates from the Polytrauma System of Care," and it is scheduled for June 19th, 2013, from 1300 to 1430 Eastern Time. Please visit the DVBIC website for registration and additional information.

This concludes our presentation. Thank you, again, to our presenter, Dr. Marion, for providing information and updates regarding acute care of severe traumatic brain injury. Please note that this webinar was conducted for awareness and informational purposes only. I would like to take this time to

point out where to find other TBI resources that you may find useful in your practice by DVBIC and the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury. Please visit the DVBIC website at www.DVBIC.org and click on the “Education Materials” tab to browse for materials for you, your patients, and their loved ones.

DVBIC is very interested in your feedback. Please complete the interactive customer evaluation found on the DVBIC website, as shown on your screen. If you are interested in downloading today’s presentation, the slides are available in the “Files,” link and the audio recording will be available online starting 1 May. Have a great day and thank you.