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Riders Safety Summit

Moderator:
Richard Valeriani, Journalist/Media Consultant

Speakers:
Dr. Dalton Dietrich, Scientific Director, The Miami Project to Cure Paralysis Kinetic Concepts, Leonard M. Miller School of Medicine, Lois Pope Life Center
Dr. Edward D. Hall, Director, Spinal Cord & Brain Injury Research Center (SCoBIRC)
Brad Kimbrell, Executive Vice President, InCompass
Ed Martin, President, The Association of Racing Commissioners International
Dr. Oswald Steward, Director, Reeve-Irvine Research Center, University of California at Irvine School of Medicine
Mike Ziegler, Executive Director, NTRA Safety & Integrity Alliance

Ms. Wendy Davis: Well, welcome to the Symposium on Racing and Gaming. I can't tell you how pleased we are to have the Jockeys' Guild with us again today and again this year. Thank you for bringing your organization here to Tucson. This afternoon's panel session, thank you so much to ARCI also for coming together. I think this is going to just be a fantastic session this afternoon. Also, don't forget that there is some session's tomorrow afternoon and they are listed in your Symposium on Racing and Gaming programs and you are invited to attend those also.

There is certainly a huge amount of information to go over this afternoon. It's really important, really important information and I know you're all going to get a lot out of it. What I would like to do again is just welcome you on behalf of the Race Track Industry Program, the Symposium on Racing and Gaming, the Jockeys' Guild and the Association of Racing Commissioners International. Now I'm going to turn the podium over to our moderator for this afternoon and it's Richard Valeriani. He was an NBC correspondent for over 20 years and a White House correspondent so he certainly has been around this game a long, long time and I know you guys are in really good hands this afternoon. Richard, thank you very much for being with us today and he will also be with us tomorrow afternoon.

Mr. Richard Valeriani: Thank you. Thank you. I just want to point out that the audio is prepared by guys from CBS. You're wondering what a White House correspondent is doing here. I just want to point out that I've been a horse player most of my life. While at the White House as a correspondent I went to the Kentucky Derby with Richard Nixon. I went

to Dover with Henry Kissinger. I've done features whenever I could on horse racing. John Henry. Snow Chief. I've been a contributor at the windows. None of that is important compared to the very excellent credentials of our distinguished panelists here for this rider's safety summit. I think we could probably dedicate this session to some names you are familiar with this year who last year suffered tragedies like Rene Douglas and Michael Straight and just recently Michael Martinez and Tad Leggett.

Leadoff hitter this afternoon will be Ed Martin who is the executive director of The Association of Racing Commissioners International. Take it away Ed.

Mr. Ed Martin: Thank you Richard. This session kind of got together – Terry Meyocks and I were on the phone and we said we've been working together on a number of different issues over the past couple of years trying to get uniform safety standards for helmets and vests; trying to deal with the changes in the riding crop to be more humane to our horses; issue of safety reins. Over the past few years we've gotten a real good dialog going. I don't know why Terry made all the jocks sit over here this afternoon. Is this like the version of the jocks room for the symposium?

The concept between regulation and those being regulated we all really want the same thing. We want the fair game but most importantly we want our riders and we want our horses to be safe. It's a dangerous job our jocks do. You're going to hear some information this afternoon. We initially were talking about kind of a round table between the guild and RCI and then we got the University of Arizona involved and said this information is really great and we'd like everybody to have the opportunity to hear it and we'd like to record it and make it available and so forth. That's kind of how we kind of blossomed into here.

One of the great challenges that we face — and then I'm going to shut up and let you listen to these fine gentlemen who have knowledge far in excess of mine on some of the specifics of the issues that we collectively must deal with. One of the great challenges we have is to try to get to some degree of uniformity. Uniformity of the rules — uniformity of safety standards. The game has evolved over the years. It used to be — you used to go to the local track to watch the local horses run. There wasn't anything such as simulcasting. Now there is the television and technology has evolved. Most of the action you know is off-track. The regulatory structure has not evolved the way the industry has so what the regulators have proposed through RCI and working in collaboration with a number of industry organizations who have been at our table and helping us craft this proposal.

We got a legislative proposal to create an interstate racing regulatory compact. You can call it whatever you want. You can call it a national racing commission. You can call it a compact. You can call it whatever. It is a mechanism for states to act collectively and uniformly and consistently to deal with the issues we all face. If you've not had a chance to really look at it we have a website that we launched today, racingcompact.com. It probably has a little more information than you want to digest but you go there and check it out and you can digest some of the specifics of it. I would urge you to consider this so if you can be supportive of it — it has to be enacted by the individual state legislatures. It can't be enacted by the racing commissions. It's an act of the legislature and governor. It would authorize the commission to join this compact and then act collectively through this entity and the promulgation and implementation of rules.

With that being said I want to thank you all for the opportunity to be here. The regulators are most interested in hearing and understanding the science and the facts. At the end of the day we want to do the right thing because we are accountable. We are accountable to

the participants in this sport, the general public who are fans in this sport and we want to make sure that this sport can thrive and grow honestly and safely for our riders as well as our horses. Thank you.

Mr. Richard Valeriani: Thank you Ed. Now you're all going to have a chance to ask questions after everybody has spoken but just to give you a sense of participation in the mean time, does anybody have any questions for Ed now? There are microphones stationed in both aisles if you have a question. None? Okay. Next up Doctor as in PhD, Dr. Dalton Dietrich. Listen to this. Scientific director, the Miami Project to Cure Paralysis Kinetic Concepts; distinguished chair in neurology and cell biology and anatomy at University of Miami; Leonard M. Miller School of Medicine; Lois Polk Life Center. It's a pleasure. Dr. Hall, he is not here. Dr. Dietrich is coming later.

This is Dr. Edward Hall. Doctor as in PhD. Director of Spinal Cord and Brain Injury Research Center; Professor Anatomy Neurobiology; Neurosurgery; Neurology and Physical Medicine and Rehabilitation; University of Kentucky Medical Center, direct from Lexington.

Dr. Edward Hall: Thank you Mr. Valeriani. Sir, could we have my — great. You're on top of things. Thank you. It's a pleasure for me to be here today. This is a different sort of meeting than I typically go to. I'm used to talking to mostly scientists so I've been told by Mr. Meyocks, who invited to me today to try and keep it in English and I will do the best I can. I was asked by Mr. Meyocks to put together a panel of speakers like myself to talk to you about the problems of spinal cord and brain injury because it is an important issue related to the safety of jockeys and horse riders in general. I'll show some statistics supporting that.

The second speaker will be Dr. Steward, from the University of California at Irvine. Then the third speaker Dr. Dietrich when he gets here from the University of Miami, where he is Scientific Director of the Miami Project to Cure Paralysis.

Without further ado, I'm from the University of Kentucky. I've been there eight years. I'm Director of the Spinal Cord and Brain Injury Research Center. As I said I'll be followed by Dr. Steward and I don't know if that's showing up but I tried Os to capture your school colors up there and everything. He'll be talking about things going on at the Reeve Irvine Research Center. Dr. Dietrich then, these are the University of Miami colors although I think they got kind of changed with the projector but anyway he's from the University of Miami as I indicated and he'll be here shortly, hopefully.

There are about 11,000 cases of spinal cord injury that occur every year in the United States. Depending on where you get the statistics it ranges from 7,000 to 11,000. The 11,000 is a recurrent number that seems to be fairly stable despite the advent of seat belts and other protective devices. The incidence of spinal cord injury in the US population has stayed steady. It's not a major population, compared to many other neurological disorders, but if you're one of those 11,000 that sustains a spinal cord injury it's an extremely devastating thing to happen to your life. The changes that not only affect the individual but his or her family and society are often devastating. Spinal cord injury is a major unmet medical problem and it's something that is of great concern to anybody who knows the field like we do.

I was able to come up with some statistics through Mr. Meyocks of over the last year since I've known him and I have also been able to collect some information. This is a paper that was published in 2008 that looked at a series of official races at US official racing facilities, 114 of them, between January of 1993 and December of 1996, a three-year period. This

involved a licensed jockey population of 2,700. There were 6,545 injury events, 606 per every 1,000 jockey years was the way they put it in this paper. The important thing I want you to know is about almost 20 percent of those injuries to jockeys involved the head and the neck. Those injuries to the head and the neck producing spinal injury or brain injury respectively are — as I said a moment ago — very, very devastating things to have happen.

I think either Mr. Meyocks or perhaps you Mr. Martin sent me these statistics recently. I can't remember who sent them to me but it was a listing of the injuries that have occurred, jockeys who have sustained fractured vertebrae at different US tracks during the last year. There are 24 listed here. It's not clear from this list which of these resulted in an actual spinal cord injury or the severity. For instance, it is possible that you could just break the vertebral bones and not necessarily get a spinal cord injury within the bony spinal column. Nevertheless you can see that in a years' time there is a rather lengthy list of jockeys who have sustained serious injury to their spinal column.

Just to orient you, this shows the anatomy of the spinal cord. It's divided into the cervical region, which is up in the neck; then the thoracic region and the lumbar and the sacral. Basically the spinal cord is a cable that carries information from the brain down to the periphery, to the muscles and other organs of the body. Also, the spinal cord carries sensory information from the body back up to the brain and integrates that information and that affects motor activity coming the other direction as a result.

If you have a spinal cord injury and about 50 percent of spinal cord injuries occur in the neck region, you're going to end up being a quadriplegic. That means all four of your limbs are going to be affected by the paralysis. If it's a high injury in the upper cervical vertebrae closer to the brain we call that person a high quad and if it's lower down in the neck region we refer to the patient as being a low quad. The lower the injury then the more residual arm function the patient can expect to have. Paraplegia involves loss of function at the first thoracic vertebrae or below and that only affects the legs as well as the chest and lower half of the body but it spares the arms. Somebody who is a paraplegic has much more independence and motor function than someone who is a quadriplegic.

There is also the issue that many injuries are complete. That simply means that at the time of the injury the individual can not feel any sensation or elicit any movement below the level of the lesion. On the other hand some injuries are incomplete when the individual may have some residual sensory of motor function and there are gradations of that.

This shows the statistics across the population of people who sustain spinal cord injuries. Quickly, about half are either incomplete or complete quadriplegics. About 50 percent of injuries are in the neck region in other words. If you're a high quad the only option for you is to spend your life most likely in a wheelchair. That's not very desirable of course. Incomplete and complete paraplegia represents approximately the other half of the patient population. If you look at the overall spinal injury population without any kind of treatment, the chance of making a complete recovery back to where you were before the injury is probably only one percent to a few percent. These statistics are a little bit old. However the chance of recovering completely after a spinal injury remains pretty low.

The other thing about spinal cord injuries is that they are mostly survivable these days as far as early survival but it does take a toll on ones life. These are some recent statistics looking at if you're 20 years old when you have your spinal cord injury, if you didn't have a spinal cord injury and you were 20 years old you could expect on average to live another 57 years. If you are a high quad, a very compromised paralyzed person, you can only expect on average to live another 32 years to the age of 52 or 53. If you're a low quad it's a little

bit better. If it's a paraplegic it's still a little bit better but life expectancy is a lot less than somebody who never sustained a spinal cord injury. This is not only something that robs people of their mobility and function. It's also robs them of years of their longevity.

It's also a very expensive thing to happen to you. These statistics are a little bit old. They're from 2004 but they make the point that if you have a high quadriplegic injury or tetraplegia as they call it in the United Kingdom, the first year expenses for your care are astronomical and the expenses to keep you going every year thereafter are also substantial. As you have more and more residual motor function the costs are less but it is clear even if you are in pretty good shape and you're a paraplegic it costs you more to live because of the things you need and the extra medical care than an able-bodied person.

The good thing, or good news about spinal cord injuries if I could put it that way, is that most, spinal cord injuries do not involve actual transection or cutting of the spinal cord. Obviously if you cut this cable then you've got serious problems and the only thing you can do is make a new cable, which we haven't yet figured out how to do.

Most of the spinal cord injuries involve a breakage of the vertebral bone. This is looking at the spinal column and the spinal cord from the side. Here for instance is somebody who dove into a shallow swimming pool, hit their head, broke their neck in the process and those bony fragments put pressure on the spinal cord which then robs the spinal cord of blood flow. One wants to do something about that. However, the good thing is that the cable is still in tact. If you can operate quickly to remove the bony fragments and then do something to protect the tissue of the injured spinal cord then you might be able to promote recovery of function.

Mostly spinal cord injuries occur in the young between the teens and the mid-30s. There is also an increasing population of older people that for instance fall in the bathroom, slip on the bathroom floor and hit their chin on the tub and sustain sort of a hyperextension injury of the neck. Here again, even though this looks very devastating the cable (or the many wires in the cable) are still left in-tact.

If we look at this in the animal model, this is actually a section from the cat's spinal cord showing the tissue of the spinal cord, the surrounding tissue here is what we call the white matter even though it's not exactly white and inside here this sort of butterfly shape thing is what we call the gray matter even though it's not really gray in this picture. Here is what a normal spinal cord looks like. If we injure that cord by putting a weight onto the exposed spinal cord for five minutes and take it back off, in a matter of five minutes you see a small hemorrhage that develop within the gray matter showing injury in the cord. As time goes by over the next several minutes there's a coalescence of this hemorrhagic injury and much of this central area called the gray matter is consumed by this hemorrhage and a lot of damage to nerve cells in that area occurs.

Between that point and several weeks thereafter there is progressive destruction of the spinal cord tissue, which we call secondary injury. The chance of you having an outcome of recovering function is dependent upon how much of this rim of tissue survives. If you look at this more carefully, what's particularly important is not only how much of this rim survives, this rim containing wires or what we call axons that carry information up and down the spinal cord; sensory information up and motor information down. Each of these wires have to be insulated just like a cable in the individual wires in a multi wire cable has to have insulation around each wire. Otherwise they will short circuit. Similarly in the injured spinal cord if you lose your insulation, which occurs around these fibers and which we call myelin, then they're not going to conduct impulses. This blue staining represents those nerve fibers

that still have their insulation. You can see that there is relatively little blue staining compared to the amount of tissue here.

Now to look at this in a higher power; this is what we call an electron microscopic picture. Here is a normal spinal cord cut across and here you see these wires. The wires are cut across. The black rim around each wire is this insulation or myelin that they have to have to conduct impulses.

After a spinal cord injury you've got a lot of wires that survive but the insulation is either gone or it's severely reduced in terms of its thickness. As a result you've got fewer fibers to carry information up and down the spinal cord and because of that they don't have their normal insulation and therefore, the surviving fibers don't work. The whole point of treating spinal cord injury is to try to preserve the wires and/or the insulation around the wires.

The primary injury that we speak about is mechanical damage to the spinal cord where you have shearing of nerve fibers and blood vessels. The only way we're going to do something about that is through what we call neuro-restorative approaches to bring about regeneration of the injured nerve fibers; to re-insulate the surviving wires with new myelin. Dr. Steward will be talking about that approach. In addition, there is a need to form new blood vessels to bring oxygen back to the tissue which might help to restore function.

A good part of the injury that occurs is this secondary process that many laboratories, including my own, have been focused on for many years. This is a secondary cascade, we often call it, of events that make the primary injury worse just as I described in those progressive pictures. We now know that there are many factors that contribute to that process and many of these factors offer several targets that we might be able to go after with a drug to try to interrupt that secondary injury, stop the damage and promote recovery.

This is just one of my diagrams. We draw lots of diagrams. The only purpose of flashing this up with a lot of words you don't understand is that this is a very complex, multi-faceted process with lots of feedback loops. We're working to determine which aspects of this secondary injury are most effective to interfere with.

We also know that following this early secondary injury, which the first slide really kind of represented the first 24 to 72 hours, is critical if we are going to effectively intervene. However, thereafter there are also inflammatory processes that take place. Some of those inflammatory processes are involved in making the secondary injury worse and some of them are involved in repair mechanisms. We're actively trying to figure out now what inflammatory processes we want to promote and which ones we need to stop in order to reduce the secondary injury from progressing.

The other thing about spinal cord injury is it doesn't just rob you of your ability to have motor function and sensation. Dr. Kim Anderson, who is a quadriplegic and formerly a scientist in Dr. Steward's group at UC Irvine, conducted a survey of a large number of quadriplegics and paraplegics concerning the primary limitations they faced that they would hope to first have addressed by spinal cord injury research efforts. Interestingly, the people who were quadriplegics said my top priority is not necessarily to walk again but if I could just use my arms I would have a much better quality of life. When they asked the paraplegics they were concerned about having sexual function returned. If you think in terms of curing spinal cord injuries as we typically talk about, we also need to focus on limitations in bowel and bladder function that are important to try to address; pain and spasticity which occurs in many spinal cord injured patients; the loss of motor function,

which is the primary thing; the loss of sensory function rather obvious but also your control of blood pressure is a problem. You could have a potential for pressure sores to occur because you can't move and you're sitting in a wheelchair all the time. Sexual function is not impossible but it's difficult and requires some heroic efforts often times. It's a very complicated disorder.

Right now the only treatment that is available to try to deal with this is a drug called methylprednisolone, which is an old drug that's been used for 40 or 50 years or more for a variety of inflammatory diseases. My colleagues and I several years ago discovered that if you gave high doses of this drug during the first hours after spinal injury in animal models that you could improve functional recovery.

What this drug does we think is interfere with the role of what we call free radicals, which play a major role in the secondary injury process. Based upon our work there was a clinical trial that was done 20 years ago that showed that the drug if started within the first eight hours after injury could promote recovery of motor function.

Here you just see some of the statistics in patients treated with methylprednisolone within eight hours versus patients who only got the placebo (the water-based vehicle in which methylprednisolone was given) that there was a significant increase in motor recovery over the course of a year.

That is the only treatment that we have and as Dr. Steward well knows this is a fairly inadequate treatment. And we've been trying for the last 20 years to come up with something better and we believe that we can in the years to come.

The other things that are going to come on the scene I think in the near term is that neurosurgeons and orthopedic surgeons who treat spinal cord injuries are increasingly realizing what they should have realized a long time ago which is that they need to go in and do early surgery to decompress the spinal cord, stabilize this broken spinal column so that there isn't further pressure put on the spinal cord. There is currently a clinical trial that is about to end from which the preliminary results are showing that if spinal cord-injured patients are operated on within the first 24 hours they make a better recovery.

Dr. Dietrich is very interested in the role of hypothermia, cooling of the injured spinal cord. He'll speak about that later. Then of course there is a possibility of combining hypothermia with methylprednisolone and early surgery.

Just turning quickly to traumatic brain injury — these are the statistics. Traumatic brain injury is a much bigger deal in terms of the numbers of at least 1.5 to 1.7 million traumatic brain injuries every day. Only about 1.2 million of those seek medical care of some type. In patients who are admitted to the hospital because their injuries are severe — we divide them into severe, moderate or mild and the numbers are fairly high. The numbers in Europe are roughly similar. That's the epidemiology of traumatic brain injury.

Traumatic brain injury is complex in a different way. The brain is much more complicated than the spinal cord. The spinal cord is basically a cable whereas the brain is much more complex than that. Likewise the injury is complex. The EDH represents an epidural hematoma. You can have contusions in the brain. These are all CT scans by the way that display other manifestations of the injury that require individualized treatments to deal with.

Fundamentally a major aspect of the injury process after brain injury, like it is in spinal cord injury is the interruption of the wires and loss of function because of disconnection of

different parts of the brain from one another. This is illustrated here in this picture showing the fibers running through an area of the brain. These little balls are where the wires have been cut and retracted forming little balloon type structures. The more of this that you get as a function of the injury force, the worse the damage and the worse the neurological dysfunction will be.

In closing, I just want to say a few words about our center. The University of Kentucky Spinal Cord and Brain Injury Research Center was founded in 1999 to try to stimulate research aimed at doing something about the problem of spinal cord and brain injury. Our center over the last eleven years — we just celebrated our tenth anniversary a year ago has been working hard to figure the secondary injury process and what it would take to regenerate the injured nerve fibers after they're damaged. Very importantly we're interested in trying to take treatments into clinical trials as soon as possible.

I'll put these up very quickly. Our faculty, we have eight different laboratories working on different aspects of injury process. Some of our jockey friends over here have visited our center along with Mr. Meyocks and have met some of these people.

One final thing, in relation to head injury we're working with a drug that's been on the market for a long time for the treatment of transplant rejection known as cyclosporine. If you have a kidney transplant or a heart transplant or a lung transplant, any of those things you will take cyclosporine chronically to prevent rejection of the transplanted organ. However, we've shown that cyclosporine is able to protect the injured brain and it does this by protecting a particular part of the nerve cells called the mitochondria, which is important for energy production and cellular function.

We are also looking at a drug, an analog of that called NIM811, which we're exploring in TBI, traumatic brain injury and spinal cord injury models. This newer drug differs from cyclosporine in that it doesn't have the immunosuppressive properties which are useful for preventing graft rejection but are also the potential for side effects in the treatment of brain and spinal cord injury.

We've done some studies in our animal models, rat models, in traumatic brain injury and what this slide shows is that if you look at the sparing of an area of the brain called the cerebral cortex that NIM811 treatment improves the preservation of injured nervous tissue compared to untreated animals, and that even if we delay cyclosporine treatment out to eight hours we still get some significant improvement in tissue sparing. We have done an early clinical trial to look at the safety of cyclosporine in patients with traumatic brain injury and we've shown that at the highest dose we've tested seems to produce a significant improvement in outcome in those patients that got cyclosporine beginning within eight hours after injury.

Let me just close. This is a picture of many of my colleagues at our center and my contact information. Thank you very much for your attention.

[Applause]

Mr. Richard Valeriani: Thank you Dr. Hall. Do you have any questions for him now before the end of the program? Sure.

Audience Member: In your opinion, should race tracks have an emergency medical technician or a paramedic on site to deal with possible spinal cord or brain injuries

Dr. Edward Hall: I would say it probably should be a paramedic. The paramedics are the ones that can potentially initiate early treatments such as methylprednisolone. As Dr. Steward knows and I know all too well that the use of high dose methylprednisolone that I talked about is highly controversial and maybe only half of the centers in the US routinely use it in spinal cord injuries.

For those of us who believe in the treatment and those sites that use it, it would be better to have that started with the initial dose on the way to the hospital if at all possible. For that it takes a paramedic.

Also, cervical spinal cord injuries, sometimes if they're high cervical injuries respiration is acutely interfered with so you need somebody who is reasonably well trained and able to get an airway established and airway support fairly quickly.

Mr. Richard Valeriani: All right. Next up is Dr. Oswald Steward who is the director of the Reeve Irvine Research Center at the University of California at Irvine School of Medicine, named obviously for Christopher Reeve, our Superman.

Dr. Oswald Steward: So I will say something about that last question also in my talk. Let me just start by saying who I am. I am the director of the Reeve Irvine Research Center. I'm also a member of what's called the Independent Citizens Oversight Committee, which is the governing board for the California Institute for Regenerative Medicine. This is the board that's giving out roughly $3 billion for researching stem cells in California. I'll tell you a little bit about both of those roles.

A disclaimer, I will talk about stem cells. My disclaimer is that my lab is not allowed to receive funds from CIRM. That is one of the penalties from serving on the governing board. I'm prohibited from holding any stock in any stem cell company. I'm not quite sure what the benefits of being on that board are other than helping to move science forward for others.

Reeve Irvine Research Center was established in Chris' name. It was actually established by a gift from Joan Irvine Smith, who is a horsewoman in southern California, the family for which the city of Irvine is named. She gave a founding gift to start our center because she really highly respected Chris and the way he handled his devastating injury.

Truthfully the thing that she most respected was the fact that he did not blame his horse and that's absolutely true and I've heard it's both sides. That's the reason she decided to give a million dollars to establish the center there.

That's how it started and our mission is shown there. It's to find new treatments for spinal cord injury. We try to do that by collaborations throughout the world. We actually have ongoing collaborations at Ed's center at Kentucky off and on and at the Miami Project as well — really, with centers all over the world.

That's just a view of our folks. I put that up there because it emphasizes what really these research centers are all about. What you have here are people ranging from scientists like me to surgeons like this fellow over here that is an orthopedic surgeon, and studies injury to people who are the nuts and bolts of the team. Students, people who are in wheelchairs themselves. Some of them are doctors.

Doctor Suzy Kim here is a physiatrist, somebody who specializes in spinal cord injury.

Doctor Kim Anderson you already heard about. She suffered a spinal cord injury in an automobile accident when she was 16 years old and is a quadriplegic as a result. This is what it takes to move things forward in research. There are several centers around the country. The one that Dr. Hall has, of course, and the Miami Project and mine but several others as well.

I'm going to come back to that because these centers are important. Not only for moving research forward. They're actually important in terms of treatment as well and I'll come back to that.

Our specialty at the Reeve Irvine Research Center is I'd say regenerative medicine. That term really came to be defined over the last decade. It means therapies that promote repair and regeneration following injury and disease. It's not just injury and disease but it certainly has I think some of the highest visibility there brought largely by people like Christopher and Dana Reeve, who really brought forward the image of research and what it could do; especially stem cells.

There are things beyond stem cells in generative medicine. Lots of things — most of the rest of the things don't have the same political undertones of stem cell research but there are many others. I'll tell you about one because really regeneration is as Dr. Hall mentioned, the single most important thing we could accomplish to repair the injured spinal cord but we're not there yet.

This doesn't show very well. It shows beautifully on my computer I'm afraid. Just to give you a sense of what this all means, Dr. Hall mentioned the connections, the wire between the brain and the spinal cord.

This is just an MRI of a person who suffered a spinal cord injury. Here it's a very common level of the injury C4 to C5. With this kind of an injury this person will be paralyzed in their arms and their legs. They will be totally dependent on others for most of their functions including feeding themselves.

The reason that they are paralyzed is that these connections; that maybe you can barely see in the red, are coming down from the brain, the wires, are cut. They don't regenerate. Not without interventions. What we're trying to do and of course many others is to make them regenerate. Maybe you can see this.

We've actually just published a paper last September that for the first time showed an ability to regenerate connections in the injured spinal cord of a mouse. If this could be translated to people, what could it mean? It could actually mean in this case even a limited regrowth, regeneration after a cervical injury could make it possible for a person who wasn't able to use their hands again to feed themselves, brush their teeth and do the things of daily living that mean so much.

We haven't been able to actually get that translated yet but those are the kinds of things that we're working on and many others are working on.

I do think that there are strategies that are going to be coming forward in the next few years.

Obviously the most visible of these human embryonic stem cells and these are really coming forward now and I'll talk really for the rest of the time about human embryonic stem cells.

If you've heard about human embryonic stem cells for spinal cord injury, you probably heard about this gentleman here. He is actually one of the professors from our shop, Dr. Hans Keirstead. He was featured on 60 Minutes a few years ago. This is Ed Bradley before his death. Hans was the person who developed the first treatment that really came online for using human embryonic stem cells as a treatment for spinal cord injury. I want to tell you a little bit about this because this is really now just coming to people.

The trial was approved earlier this year and the first patient actually — the first patient received stem cells just about a month and a half ago. What is this? I'm sure most of you know about stem cells but for those of you who haven't thought about them recently let me just say a little bit about what they are. Where do they come from? First of all stem cells don't come from babies. They don't come from anything that even looks like a baby.

They come from something called a blastocyst. It is made up from about 100 cells. Human embryonic stem cells are derived from these blastocysts that are discards from in vitro fertilization clinics.

People who are not able to have children on their own go to these clinics, have some sperm from the man, eggs from the woman and they are brought together in a dish and these fertilized eggs grow for about five days and develop into a little ball of cells called a blastocyst.

Inside that ball of cells are stem cells. To harvest those stem cells this blastocyst, which you can think of as a tennis ball basically is just broken open and the stem cells are taken out and then they are put into a Petri dish, or a vat these days.

We are at a point now where we can literally grow these things up in many, many gallon quantities. They're grown for various periods of time. They're treated with factors that cause them to differentiate into particular cell types like the nerve cells that we need for transplanting into the nervous system. Then they can be used for therapeutic purposes.

At this point the therapeutic application that's furthest along is the one that Hans Keirstead developed. I'll show you a cartoon that we had made for the 60 Minutes. Maybe some of you have seen it. The idea here is to take these stem cells and actually turn them into a useful cell type.

Dr. Hall told you about the wires and that the wires need insulation. The insulation is formed by a cell type called an oligodendrocyte. When there is a spinal cord injury these cells die and the wires are stripped of their insulation. As a consequence of that there is a failure of transmission between the brain and the spinal cord.

What Dr. Keirstead did was figure out how to make human embryonic stem cells growing in a dish, or in this case a vat, in the Duron Corporation labs; how to take those and turn them into oligodendrocyte precursors that are called OPC.

What he was actually able to show in experimental animals was that these things actually had some benefit. Here's the situation.

In a rat for example the transmission between the brain and spinal cord with a spinal cord injury that transmission actually is blocked. The reason as I told you is that these nerve cells here, the wires extending down depend for their ability to transmit on this insulation. With a spinal cord injury the cells that make the insulation die and transmission stops. The message coming from the brain is actually blocked right here.

The idea is to actually inject in these human embryonic stem cells. They will grow and differentiate and reform the myelin sheath and as a consequence of that transmission between the brain and the spinal cord is restored.

This actually has benefit to the animals. Keirstead's great discovery here was to show that not only did these cells reform the myelin sheath but that there was actually some repair of the animal's ability to walk. These animals would have walked anyway but they walk better with stem cells.

This is not a cure that is going to take you from a wheelchair to doing the cha-cha but it will, we believe, improve function to some extent if the injury is partial and if there is some spared connection there that can benefit from this restoration of the insulation.

Where are we now? The clinical trial involving human embryonic stem cells just began. This October Geron Corporation launched what's called the phase I safety trial and that's based on the work of Hans Keirstead.

In this trial, many of you may have heard about it, people with complete injuries — that is they're totally paralyzed — at the thoracic level, which means the middle of the back will have stem cells implanted into their spinal cord within 14 days of the time the injury occurs. If it's later than 14 days you are not qualified. You won't be accepted into the trial. If your injury is not complete you wont' be accepted into the trial. If your injury is not at the thoracic level you won't be accepted into the trial.

There are a lot of constraints here. Only a few patients are going to receive these transplants, about eight to ten. I'll tell you more about that in a second.

The other trial that isn't going yet but this October, this is how really recent all this stuff is, the Geron trial started in October. One patient so far has received the stem cells. This October, Stem Cells, Inc.; which is a company up in Menlo Park area in California, filed an application to carry out a phase I trial and this is actually based on the work of Eileen Anderson and Brian Cummings from our shop.

They are even a step ahead of Keirstead because what they have been able to do is now show some functional benefit in animals, again, with chronic injuries. They have been able to go up to 30 days after an injury, which they believe translates into roughly a year for people.

Making that translation is hard. Lots of people might argue that a month is really equal to a year but the point is that it's a lot longer than anything that has been seen before. Stem Cells Inc. has applied for permission to undertake this trial. This is a trial that, if occurs, will be going on in Switzerland, not the United States. I will be able to say more about that tomorrow.

This will be the first ever stem cell trial for chronic spinal cord injury. Keirstead, the one that is based on Keirstead's work — he is not running the trial. It's Geron Corporation that's running the trial. That will be the first ever stem cell trial for acute spinal cord injury.

What can we expect? Is this going to be a cure that you're going to see coming out of the pipeline here? For those of you who are sitting in the audience, if you're getting stem cells two weeks after an injury obviously if you're going to get stem cells your injury has yet to happen. That's kind of a scary thing to think about. All of the people who would get these

cells have not had their injury yet. That's very important — even given that only a few patients will meet these very tightly defined criteria.

What can you expect in terms of speed? Things will be done very slowly and carefully. I believe — this is my own personal opinion; I have no inside information — I believe it's likely that one person will receive stem cells. They will wait a while. This is a safety trial and the most important thing is safety. They will wait a while before doing a second patient.

At least in the Geron trial the plan is to do the first set of patients and that again is eight to ten within a two-year period. Roughly that is how long it will take to get all the patients enrolled but that doesn't mean we're going to know anything. We shouldn't know anything. We hopefully won't know anything and I'll tell you why.

The only reason that we will know anything is if something bad happens and they have to discontinue the trial. The information from the trial will have to be gathered, collected, analyzed and then presented. That will be a couple of years. After that we will move to the next trial.

Trials come in phases and this is a phase I trial. It's a safety trial. The important thing to recognize is that the trial is actually designed in such a way that it's probably going to minimize our chances of seeing anything beneficial. I told you in a sense a reason why but maybe it wasn't clear.

These are going to be limited to people with complete injuries. That is the highest bar you can set. A person with a complete injury I think Ed said has a one-percent chance of showing any kind of recovery at all.

The likelihood that these things are going to actually show significant benefit is low unless it's just a super home run. None of us expect a home run. We expect small, incremental improvements in function. That means we really won't be expecting to see any evidence of efficacy until the next trials.

The ones that are actually designed to test efficacy and the ones that are designed for patients whose injuries are less severe than the ones we are seeing right now.

If we see results, I've already said that — small and incremental. If we see results, what do we make of them? What if somebody gets stem cells and shows substantial recovery? We can't make too much of that. There are cases where people with a severe spinal cord injury and still severe at 14 days still exhibit substantial recovery so we may get one of those in the trial. If we do we can't over interpret those results.

At the same time the trial tends to be biased for people with more severe injuries for whom we don't see results so we shouldn't be disappointed if we don't see really positive results in this first trial either.

In a sense we're going to have to sit back, wait and see what happens for both of these trials as they go forward; the one ongoing and the one for which an application has been filed. Actually, I've already said that. Again, these trials are based on patients who have complete paralysis.

How long will these generally be available? New treatments have to go through three stages of clinical trials. Phase I. Phase II. Phase III. That's before it's approved for general use.

Completing a clinical trial for something simple like a drug is estimated to take about seven years. We don't know how long these spinal cord injury trials for stem cells are going to take but it could take longer than seven years before there is going to be a treatment that is available for use.

That doesn't mean that they won't be available for clinical trials but it does mean that there is not going to be something you would go to your local hospital and have prescribed. Only one trial has started so far. Only one patient has received stem cells. That gives you some idea of the timing — again, two to three years probably.

A general question — I talk to a lot of people who say gee this is going so slowly, the people who have suffered a chronic injury, the people who are recently injured and desperate — is the FDA, the Federal Drug Administration holding things back? The answer is absolutely not.

These trials are designed to prove that a drug is safe, or stem cells are safe and actually has some sort of therapeutic benefit. Any treatment that hasn't gone through this process as a clinical trial as we define the clinical trial process in the United States and other Western developed nations, those treatments have not been shown to be either safe or effective and that's really important.

What about these stem cell treatments that you hear about being offered in other countries? This is just my personal opinion and I'll stand by it. There are no stem cell therapies in other countries that have been shown to be safe and effective.

That is true even though you hear reports, even though you hear testimonials from people who have received stem cells. They may have gotten better but there is no scientific proof that they have gotten better because of the stem cells.

Sometimes the surgery just makes people better afterwards and I can talk about why that can be.

First of all, people do improve over time without any treatment at all. Beware of testimonials. These are commercials. That's all they are. If the improvement comes after treatment that doesn't mean it's because of that treatment. That's very important.

Most importantly if the treatment costs money, beware. If you are going to be checking out the web sites in other countries and you see that you can go to India, and you can, and get stem cells for somewhere between $25,000.00 and $50,000.00 beware.

These are honestly, these are situations where someone is making money on it and they're doing so in a way that has not gone through the safety and efficacy testing that we require in our country.

When there is a clinical trial, when there is a treatment being tested in a way that we in the Western world believe is the appropriate way that treatment will be free because it is a clinical trial. It is an experiment. It's covered by whoever is running the clinical trial.

Once a therapy is approved then it's probably going to be covered by your health insurance. It should be covered by your health insurance. Those are just some really easy guidelines. If it's going to cost you a bunch of money then beware.

What about this one? I'm desperate. I'm willing to try anything. If it doesn't work then at least I tried. I've talked to a lot of people who say that. People who have been injured usually for a shorter period of time but as Dr. Hall said, a spinal cord injury is devastating. You lose the ability to control everything. Control your bladder, your bowels, your sex, everything.

It's not — just not being able to walk or use your hands. For a lot of people that really is almost a death sentence. Many people are willing to say okay, I'm just going to go out and try it. It's worse than if it doesn't work, at least I tried.

The problem is not just that the therapy didn't work. Therapies that are not properly tested for safety can cause serious injury or they can kill you.

Over the past year I know of at least three people who have died of a consequence of stem cell transplants in other countries. You read about them more and more in the news. It isn't something that's just oh well it didn't work. I'm just back to where I was before.

There's real danger out there about therapies that you can buy out of the United States, for whatever spinal cord injury or anything else.

Where are we now? What is the best hope for the immediate future in terms of treatment and cause? Let me just say research has made a difference. Research has made a difference in terms of lots of things. There is a matter of weighing risk. Probably some of you can't see what this is.

Somebody asked me on the way here, do you have any opinion on surfaces? When the question was asked I thought of this slide. For those of you who can't see it, this is a very rocky slope at Mammoth and this is one of my students on a mountain bike and he is just starting down that rocky slope. My thought when that question was asked was whatever the surface is it's got to be better than that for sure.

The point is that we have come a long way through research in identifying ways to prevent injury for all the different ways that you can have an injury. Of course there are more things that are more dangerous than others.

This particular activity, he's in a race but he doesn't actually get any money if he wins. I think what it does is motivate him to study spinal cord injury, which is good. He spends more time in my lab. All this came from research. That research is going on at centers all over the world. That's important. Gear is important. I don't know anything about gear but I know in terms of mountain biking gear has made a huge difference.

What about EMTs versus paramedics? I believe and again this is a personal opinion, I have an expert on hand and the more experienced person the better. Let me just give you a statistic.

If you talk to any neurosurgeon who has been around for a while who is in his 70s for example, and who has been seeing people with spinal cord injury for many, many years, what they will tell you is that the incidence for severe injury has gone down dramatically over the years. It used to be that pretty much everybody who came into the emergency

room with a spinal cord injury was completely paralyzed. Now, that is not true. Probably about half of the people that come into emergency room with a documented spinal cord injury have some residual function.

It is because we have learned how to handle people. The team that is responsible for that is the team that — this is one of them shown here. This happens to be my son. He is a paramedic in Albuquerque. These guys are trained. They know what they're doing. They can administer protocols.

It really does matter when you start. Have an expert on hand. Every second counts. A spinal cord injury is not unlike a heart attack or a stroke. It is important to intervene early. It is important to manage properly. I believe it actually even goes a step forward.

If I were setting up something to reduce the likelihood of serious injury — you're going to have injuries but just to make things a little bit better I would have not only paramedics there but I would actually have a trauma expert.

A paramedic can carry out a protocol that is supervised by a doctor but a trauma expert on site can actually act much more proactively.

For example the hypothermia treatment that Dr. Dalton has developed and will talk to you about in just a minute — that is something that can be administered on the site.

We all know about some of the stories about this — Kevin Everett for example, the football player who was injured on the field. The treatment began as he was being taken off the field. Was that the cause of his miraculous recovery, I don't know.

You hear a lot of this in professional sports. People who have apparently incredibly serious injuries and recover — I personally believe that it's because of guys like this and real experts who are sitting on the sidelines and get to the people immediately while they are still on the field, handle them properly and initiate the protocols that are necessary.

Again, all of that is based on research. To get the best and the promising you don't do it in the routine way.

A couple of other things that I think are important for you guys. Know your area hospitals. Not all hospitals are equal — I will — again, personal opinion. If one of my family had a spinal cord injury in southern California I would insist that the paramedics bypass the nearest hospital and go to the best hospital.

Once you are in the good hands of the paramedic then you are better off getting to the place where there is going to be a spinal cord injury protocol.

If you go to a community hospital there may be no one there who has seen a spinal cord injury ever. They will have standard protocols. They will not have anything that is particularly recent. They won't have a group of experts there.

The best that you could do is to look for a center with an established program of spinal cord injury management and ideally ongoing research programs.

The good thing about professional sports and I would say the good thing about the racing industry in this case is that in a sense you choose where to have your risk. If you're a

person who suffers a spinal cord injury in an automobile accident in the middle of the desert you don't have a choice.

If you're in a major population center at a racetrack you do have a choice. I would just say that that's one of the ways that you could really improve the situation for ultimate recovery for people who suffer spinal cord injury in the racing industry.

Best hospital. Level I trauma center — ideally one that has spinal cord injury research programs. You can go on the web site and find out.

If you are in Miami you are going to go to the Miami Project.

If you are in Kentucky you are going to go to SCoBIRC.

That is the kind of thing that you can do really in any city. Be informed. If someone close to you suffers a spinal cord injury seek out all sources of information. Be proactive. Be your own advocate.

Again, this is something I think your industry could do and it would have a huge difference. Post-injury rehabilitation, retraining is critical.

If you go in with a spinal cord injury today, if you're lucky and have pretty good insurance you're going to be in a rehab center for about a month. That is not enough. You're barely out of the period of an acute injury by then. What you need is continuous aggressive retraining. That can tap into the brain's native mechanisms of plasticity.

The things that we all do every day to do things better — things that professional athletes practice every day. A person with a spinal cord injury can use those very same techniques to improve whatever function they have. It makes a huge difference.

Frankly, I think if every industry has a situation where spinal cord injury is perhaps more likely I would encourage you to sponsor what's called a retraining center, restoration center or something like that for your athletes to optimize whatever function is possible.

With that I'll just go back to our group and say it's a wonderful thing to work in a situation with a group like that. We are all out there trying to do things for the future. Just to say cures for tomorrow come from research today. In a latent commercial message, think of your local research center and thank you very much.

[Applause]

Mr. Richard Valeriani: You can sign up for the donations right after the end of the session up here. Thank you very much. Any questions? Down here? Yeah. Go ahead.

Audience Member: Thank you. You brought up Kevin Everett. My daughter happened to be at that home game three years and three months ago when Kevin Everett ran down the field and made that heads down tackle that left him paralyzed on the field.

Their football team must have thought ahead of time that this could happen because somebody on the paramedic team was able to inject into his spinal cord, icy cold saline solution. As you said, we don't know if that made the difference. However, since icy cold saline solution would likely prevent inflammation we have to consider that it's very likely that that made the difference.

I wonder in the intervening years have we thought about should we teach these protocols to the paramedics in the ambulances that follow our jockeys around the racetrack and the nearby hospitals. The ones that are the first responders for our injured.

Dr. Oswald Steward: Let me say that — that treatment, hypothermia was developed by Dr. Dietrich who will be the next speaker so certainly he is the one that should answer that question in detail.

I would say that there are protocols that are state-of-the-art protocols that are different than you would get with your routine EMT. Absolutely your paramedics — and if you choose so — the other experts that you would employ at the racetrack to be there sure. You bet.

There are going to be things that are changing. That really is the key. This is a rapidly moving field. There are going to be things that are experimental that can be tried in people like hypothermia. The people that are the first ones there should be the ones that should be able to administer whatever treatments that are available that are time critical. I believe that there are many treatments that are time critical.

Mr. Richard Valeriani: I have a question. You mentioned funding. You can't accept money from certain sources. Do you feel that you are getting sufficient funding for what you want to do? You never feel that way.

Dr. Oswald Steward: Me personally?

Mr. Richard Valeriani: As an institution.

Dr. Oswald Steward: I think we are incredibly lucky in California because stem cells research is being funded by just an unbelievably forward looking venture that the state undertook six years ago, Prop 71.

Stem cell funding in California is pretty good. Funding in the rest of the nation and for research other than stem cells research is dismal right now.

We all talk about the impending cliff. We're literally coming up on a period where funding in NIH is going to fall off the cliff.

All of the things that all of us in the field have been working on all these years are potentially going to get harder and harder to bring to fulfillment.

Private funding is going to become more and more important over the next few years even than it has been in the past.

Mr. Richard Valeriani: Dr. Hall? What about you in terms of funding?

Dr. Edward Hall: I would agree with Dr. Dietrich. I'm getting a little bit concerned about the time so we might want to go a little bit.

Mr. Richard Valeriani: Okay. I've already introduced Dr. Dietrich in that sense.

[Applause]

Dr. Dalton Dietrich: I greatly appreciate the invitation to speak to you today. I think I spoke to this group maybe three years ago and at that time we were just talking about the excitement in terms of early cooling and what difference we could make in brain injured patients as well as spinal cord injured patients.

Dr. Hall suggested that I give you a brief update of what we're doing at the Miami Project. It's kind of like a scientific update and hopefully you'll get some ideas of what's going on in Miami and how we think we're changing the way we treat people with severe injury. There you go.

The Miami Project to Cure Paralysis was started in 1986 when a young man, Mark Buoniconti, had a high cervical injury and everybody started asking what do you do for these people and there was very little research going on in 1986, the dark ages of spinal cord research.

Today we have about 250 scientists, clinicians and staff working on brain and spinal cord injury, CNS injury and repair.

We have a lot of basic scientists, molecular biologists, neurosurgeons, neurologists, rehab medicine people all working in the same building to target these very complicated problems. As you can see we work with researchers all over the world because this is a really complicated problem.

It's a holistic approach if you will. Many laboratories will target regeneration. Many laboratories may target regenerative medicine and rehabilitation. We try to use this holistic approach because as Dr. Steward just said there is so much that has to be done at each stage of the injury if you will.

We try to develop new therapies to stop the injury cascade after damage to target these re-profusion injuries, these secondary injury mechanism that we think may guide the best possibility of return to function.

Transplantation regeneration, what types of cell therapies, what type of growth factors, what type of regeneration inhibitory molecules can we target to enhance plasticity and repair? Rehabilitation? Even if we are at the point where we can get axons to grow, are they functional? Do they make functional synapses? Do you have a good neurological effect from that regeneration?

Many times you get abnormal sprouting in the brain and spinal cord and that can produce plasticity or neuropathic pain or seizures. Quality of life? Yes it would be great to get people out of chairs, to walk but how about bowel/bladder function and all these things that are very important in terms of getting out of bed each day and going to work and making a living.

Clinical trials? Can we move our exciting rat data to people, which is a very difficult phase of the overall science? Finally, education/training? Can we train the next generation of scientists to continue this study?

We think about the very early molecular biology of cell death and cell survival. We think about regeneration, transplantation strategies, bridging strategies to get axons to grow across a gap in a spinal cord, rehabilitation and training.

There are maybe some ways that you can prevent injuries, and I think many times in terms of the training the jockeys may use these vests that may inflate to actually protect them and of course using helmets as well. There are obvious ways that we can prevent the injury but what do we do after the injury has occurred?

The Miami Project is the classic "bench to bedside" and, "bedside to bench" research project. We try to move things to clinic but at the same time we're talking to the clinicians, what do you think the key problems are that we should take back to the lab? Obviously we still do a lot of discovery research. We do a lot of animal studies with rodents, pigs and non-human primates, clinical investigations and ultimately move our studies to clinical trials.

First we'll just talk about traumatic brain injury. It's a major problem in the United States and elsewhere throughout the world. One point five million Americans sustain TBI. More and more in terms of the funding question, we are getting more funding from the Department of Defense because of the blast injury problem that we're having.

I'll go up to the Pentagon in two weeks and we'll be talking about mild head injury and hyperthermia. We think that is a key element that needs to be looked at in our military personnel. For a variety of reasons there is a lack of treatment for TBI. I think we know that. It's a very complicated problem.

I just want to talk briefly about therapeutic hypothermia. It is the first treatment that has demonstrated efficacy in terms of protecting neurons from dying that has been successfully translated to the clinic. We made a couple of home runs here.

Cardiac arrest. If you have a cardiac arrest, if you are fortunate they will cool you as you come in the hospital. That is the only therapy that limits the neurological damage that occurs and these patients are living and the studies are coming out in terms of cognitive function years after injury. We started working on this particular study back in the middle 80s. It took this long to actually move to the clinic.

We're also now cooling babies, term babies that have some sort of a hypoxic insult. We used to warm them and now we cool them. That's now been shown in multi-center trials to be effective. Finally you're going to see the big stroke research coming out in the next couple months where we're cooling patients before we give the thrombolytics to open up the blood clots in the brain. That extends the therapeutic window for TPA treatment from three hours to six hours. A lot of combination approaches and temperature seems to play a part.

What about hypothermia in traumatic brain injury? This is the model that we use in the lab. We can produce a contusion and we can look at the size of the contusion in the brain and then we can count neurons in the penumbral region, the area surrounding the contusion. This is the first paper in '94 that showed if you traumatized a rat, you waited an hour, you brought the brain temperature down to 33 degrees you could actually look at the brain and several days later it actually had a smaller contusion and it saved neurons. That was kind of exciting.

Why does hypothermia work and why do other drugs not work? We think there is a lot of injury cascades that we have to consider when we're trying to develop new drugs to stop the secondary injury mechanisms.

It appears that mild cooling affects all these injury cascades. Free radicals, excited toxicity, Apoptosis, Inflammation, all the things that we're trying to develop drugs for. It's kind of like a cocktail approach actually targeting brain injury.

We can improve the way the brain looks. Can we improve the way it functions after traumatic brain injury? You know there is a really complicated spectrum of neurological problems associated with mild, moderate and severe so what we use in the laboratory is the Morris water maze.

We can train the mice and the rats to look on the wall and see these symbols and we can look at retention acquisition memory and sure enough this has worked for Dr. Helen Bramlett that showed for the first time compared to normal thermic animals who could not find these submerged platforms, post traumatic hypothermia animals did it beautifully. Actually they protected their ability to learn new things and remember new things. That's been now shown in clinical studies.

Where are we with traumatic brain injury and hypothermia? I think there is about 18 clinical studies that have been done and all of these studies are positive.

Hypothermic treatment seems to decrease ICP elevations after severe TBI and increase survival. Then we came along and said to really change the way we treat people and make everybody convinced we have to do a multi-center trial.

Guy Clifton and colleagues first got money from NIH and did a multi-center trial with mild hypothermia in severe TBI patients and it was negative. We've spent the last five years trying to figure out why it was negative. One of the things was maybe we just didn't cool fast enough. We talked about this already today.

We actually got NIH funding to do another trial with ultra early cooling so we cooled within three hours after injury. The results were also negative. We didn't even get through the whole trial. They stopped us and found out the effects were detrimental rather than beneficial.

We're not smart enough yet to know why hypothermia doesn't work in this very heterogeneous population of TBI patients and, as a neuroscientist, these are the kind of questions I think about in the laboratory — these factors regarding how to use hypothermia and how not to use hypothermia.

What's exciting is this last slide. Is there a sub group of severe TBI patients that benefit from early cooling?

Guy Clifton called me up a couple months ago very excited. He's the PI of the multi-center trials that failed. He pulled out a sub group of patients and it appears that patients that have a contusion that undergo decompression surgery — in other words the surgeon goes in and does a craniotomy and takes the blood out — if the patient is cooled prior to removing the blood it's an amazing effect. We're going back and hopefully starting a new clinical trial looking at that sub-population in severe TBI. Hopefully we'll figure it out in the future.

Progesterone clinical trials, I don't know if that's already been mentioned today. It's very exciting. Progesterone is a dirty drug and it was found that it seems to protect in a sub-population of patients in terms of severe TBI mortality rates lower as you could see. This is a second trial that's seen efficacy too. That's going into a larger multi-center trial.

In the future maybe progesterone plus methylpredinisolone maybe plus mild cooling might be the answer. That's where the future is. We're pretty excited that we're making some progress.

Let me now turn to spinal cord injury. Dr. Steward and Dr. Hall already summarized the problem. It's a severe problem — very high number of young people having severe spinal cord injury. We've done a really good job of keeping these people alive. They are living 50 years now. What do we do in terms of these long-term deficits?

Are there things that we can do to prevent a complete paralysis and make it more incomplete and that gives us the ability maybe through rehabilitation and other strategies to promote recovery.

There are a lot of promising treatments and I'm sure you've been introduced to a lot of those already. In my program we're working on Rolipram, which is a phosphor diastrease inhibitor. It's pretty cool. It elevates your cyclic AMP levels which makes neurons survive and regrow.

We're working on a multi-center trial on Riluzole, which is a sodium channel blocker. After injury, Dr. Steward made mention of this, a lot of the axons the processes of the brain become demyelineated, uninsulated and they don't work very well. At the Geron Corporation, which you have already heard about has got stem cells to remyelinate those axons and we are using the patients own Schwann cells which normally myelinate peripheral nerve fibers, to remyelinate demyelinated axons in the injured spinal cord.

You already know that one patient has been injected with the Geron drug, with the Geron trial in terms of the embryonic stem cells targeting oligodendrocyte remyelination.

What I'm hearing about this one patient is that due to the drug induced immunosuppression that they require since they are not getting their own cells, they are not tolerating the immunosuppressive treatment very well at all. That's going to be a major, major problem when you think about what cells to inject. This problem could be avoided if the patient could receive transplants of their own cells rather than cells from a donor source.

Let me go back to moderate hypothermia really quickly. Is it protective in spinal cord injury? This is the first study in 2000 where we spinal injured a rat. We waited about 30 minutes. We brought the spinal cord temperature down to 33 degrees, which we could do in people these days.

What was exciting is that we got this very impressive improvement in walking. That's been replicated in different laboratories using different variety of cooling and injury models. We really do believe it works. We also have shown it after cervical spinal cord injury to improve hand function in rats. Wow, that's exciting.

Prior to the adoption of hypothermia as treatment modality for patients with spinal cord injury, controlled multi-center trials have to be done. We started doing hypothermia in people when Andy Cappuccino, Andy was at one of these meetings I'm talking about today. It was at the Cervical Spine meeting. I think it was in Palm Beach. It was about 600 people. I talked about the Miami Project and about five minutes of it I talked about hypothermia but he came away from that lecture saying I don't have anything that I can really give the patient right now to protect. I'm going to carry cold saline around in my emergency room. He did that on his own. Kevin Everett went down. He injected the cold saline, a very early methylprednisolone and then calls us up and goes, what do I do next?

We took him through the next 48 hours and 72 hours and thank heavens Kevin did all right. Was it hypothermia? Was it early methylprednisolone? I believe it was a combination of everything we learned over these 20 years.

Really good emergency care, stabilization, decompression surgery, and everything else that we know about. That really kicked us in the pants. If you say that hypothermia is good and you have people actually trying it in people so what are we going to do? We started cooling patients in Miami.

This paper came out in 2009, our first 14 patients. The exciting thing was that we didn't seem to do any harm because when you cool a patient you can actually produce increased inflammation and immune responses and things like that. We're convinced it was safe. This is some of the controlled temperature values. We have some of these endovascular catheters that you just put in the patient in the femoral vein and run it up to the inferior venal cava and you type in what temperature you want that patient to be and it's there.

For 72 hours you can keep that temperature down to 33 degrees and then it can really control this warming phase, which we found in rats is critical and maybe why the hypothermia didn't work so well in the past.

We're just targeting the Asia As. They're the complete worst case scenarios. Statistically that's the group where they're not really going to do really well. If we can make a difference, maybe move them to an Asia B that's pretty exciting. This is the data that just came out this year in neurosurgery. Allen Levy is a neurosurgeon MD, PhD and what's exciting about this data is that we have a 73 percent conversion to Asia As to Bs and Cs. This knocks the socks off of any treatments that we have right now.

We've gone to NIH and we're asking them for $20 million to do a clinical trial. Seventeen centers to this ARCTIC, acute rapid cooling therapy for injury and spinal cord injury. We've got a pretty good score but of course NIH is NIH right? We have to resubmit in March and hopefully we have all of our Ts crossed and Is dotted.

Finally, leaving hypothermia; what is the Miami Project doing in rehabilitation? You now know from the lectures this morning you have different types of cells and I don't think we're smart enough to know what cell is best. We are going forward with the Schwann cell because we think it can induce some axon sprouting and we think it can save neurons from dying if you give it early enough and we think it can remyelineate demyelinated fibers. Mary Bunge and Richard Bunge came to the University of Miami many years ago with the vision of using Schwann cells to promoting regeneration.

Why am I excited about Schwann cells? Well, you can take a biopsy from me today and in three weeks I can give you 250 million of my cells to inject back. You can give the patients own product. In both rodent and non-human primates we've seen a good success of recovery of function. We're using combination approaches. This is rolipram and Schwann cells that Damien Pierce and Mary Bunge published a couple years ago. Inducing really nice axonal regeneration across the gap in the spinal cord and pretty impressive walking.

Dr. Steward is currently trying to replicate those findings so we have this really cool NIH program, where if you publish something really exciting your colleague calls you up and says this is really exciting. I have money to try to see if I can make the rats walk as well as you published. He's in the process of publishing that. It's a really good program. It's really making sure that what we're getting out there is clinically relevant.

This is that proposed clinical trial. We're going to do a phase I clinical trial in a severe spinal cord injury patient. The project was initiated in 2007. I have to make a decision where the Miami Project was going in stem therapy. It could have been stem cells. It could be transduced cells. It could be adult's stem cells. Based on what we were seeing in the lab we decided on Schwann for the reason I told you about.

We had a pre-PIMD talk with the FDA. We have a pre-IND in July. We hope the IND will be submitted first quarter next year if all goes well and maybe we'll get permission to put these cells in man, which will be pretty exciting I think. That will be the first brick in the wall as we start adding on other therapies.

Finally as we're thinking about spinal cord injury as a holistic approach we're looking at a lot of conditioning. If you come into our building you'll see at least 25 people in wheelchairs working out like you and I did to improve the cardiovascular function and target their muscular structure skeletal structure because if you have someone ten years outside of a spinal cord injury and you're lucky enough to grow axons across the gap and you think that person is going to get out of that chair and walk you're wrong. They're probably going to stand up and have a cardiac arrest on you. We really have to look at this aging effect on spinal cord injury.

We're doing a lot of robotics. I think this is a movie but we're not going to do it today. Robotics in terms of cardiovascular work and walking. We can actually put them on robotic walking machines and stimulate their intrinsic mechanisms of walking. We're looking at rehabilitation of hand function. We got this from the TBI and stroke literature.

In conclusion, it's pretty exciting times in spinal cord and traumatic brain injury research because of some of these guys that are up front today. We think combination approach, someone comes in, think neuro protection the first phase and then start thinking about rehabilitation early and cellular transplantation, more rehabilitation and hopefully in the future we're going to have this really complicated system down where we can actually provide the best hope for these people with very severe injuries.

I'm very fortunate. I got to go to places sometimes. Sometimes it takes me a little while to get here but I get here. Great group of faculty, we have about 27. We just recruited two great guys that I think are going to be the world experts in intrinsic and extrinsic molecular mechanisms of axonal regeneration so we keep doing some really fun things. If you're ever in Miami, look us up. Thank you very much.

[Applause]

Mr. Richard Valeriani: Thank you. We're glad you got here. Okay. Next up is Mike Ziegler, executive director of the NTRA Safety and Integrity Alliance.

Mr. Mike Ziegler: Thank you. It's pretty amazing stuff out there. I really appreciate the hard work that these guys and their schools are doing. We all benefit from it. I'm going to speak about the NTRA Safety and Integrity Alliance.

First of all I want to thank the Guild for asking me to present today about the Alliance. Many of you know what the Alliance does. Basically, in the fall of 2008 we were established as an accrediting body to make sure that racetracks meet minimum safety and integrity standards.

Fall of 2008, 55 racetracks and nearly every major thoroughbred horseman's association pledged to the Alliance that the health and safety to our human and equine athletes and the integrity of our sport are thoroughbred racing's top priorities. The fact that our human athletes are first was deliberate. It was consensus that really at the end of the day the safety of our riders, our exercise riders is integral.

Basically we accredit tracks based on a code of standards and this code of standards is in place right now. Many of the standards deliberately ask tracks to take into consideration human safety. There are five basic areas that I'm going to through and really briefly touch upon the areas that are important to the human safety element.

Participation in the Jockey Club equine injury database, basically it's an indirect correlation to human injury as if there is a horse injury. Pre-race veterinarian examinations — we don't want riders to get on horses that aren't racing sound.

Post-racing, post-mortem veterinarian examinations — we want to make sure that horses coming out of races continue to be safe to ride the next time. Vets lists we want people to only ride horses that are not currently on a vets list so sharing among jurisdictions is an important part of the vets list. Safer racing environment — we want front traction devices to be less than four millimeters. There is a direct correlation between horse injury and toe grabs.

We want safety helmets and safety vests on riders, on trainers, on anybody who is on horseback and assistant starters who are handling horses. We want a padded starting gate. A significant amount of injuries to riders takes place in the starting gate. We want tracks to have catastrophic injury planning and procedures in place.

A big element in this would be early warning system in the morning in case there is a loose horse or a rider is down. We want horse handler training. We want people to go through programs like Groom Elite so that they have a better understanding of how to indentify injuries ahead of time.

Medication and testing. Not a direct correlation but a lot of times horses running on medication could be masking potential injuries. We want to see a ban on TCO2. We want out of competition and frozen sample testing and a big element now is we want a controlled shock wave therapy to make sure that horses aren't racing with an analgesic effect. Research and training is important. We want racetrack surface studies conducted at all the tracks that we go to accredit on dirt turf and synthetic surfaces.

There is a big section about jockey safety and welfare. We want jockey weights to be uniform. We don't want riders weighing out with their safety equipment because we don't want that to be a propensity to take out necessary padding. Jockey health information. We want jockeys to participate in a Jockey Club program where their medical records beat them to the hospital. The most important thing I think today which we're going to talk about more is the human ambulance support and it's really the most important standard.

I'll read to you right now what the model rule says. "An association shall provide a properly equipped to transport ambulance, staffed with at least one certified paramedic during training and two certified paramedics during racing hours. If the ambulance is being used to transport an individual, the association may not conduct a race, or allow horses with riders on the racetrack, until the ambulance is replaced." That's the minimum standard that we expect at tracks. We're finding that one size doesn't really fit all.

Some tracks, you guys knowing better than I do, adhering to the model rule could provide inferior care to some who don't actually follow the rule to the letter.

We need to really look at each track on an individual basis. As an example, two paramedics in the afternoon who don't know what the eighth pole means could be driving around the racetrack for ten minutes looking for you if you're down on the racetrack. Preferred course knowledge and maybe an EMT knows better with a doctor in the room whose trained to take better care of you. One size obviously doesn't fit all.

We are finding some really good standards out there though. The Keeneland medical facility I think is nicer than many hospitals in other jurisdictions. A good example at Monmouth Park. If a rider goes down on the racetrack, Dr. Chinnici over there uploads a video of the spill to the hospital trauma center before the rider even gets there. The trauma doc can look at the video and have an idea of what caused the injury, which really helps him in knowledge and treatment.

Here is what I'm really here to talk to you about the most. This past October NTRA hosted a professional education seminar. It was really a gathering of different areas of the racetrack with different expertise. One of the most valuable areas that we talked to there were the track medical directors. We had about a dozen people get together as a course of action to share best practices and to determine minimum standards for the industry. There was representation of the track, of the guild and we had a trainer who also gets on horses in the morning there to give the perspective of someone who actually gets on horses.

Here is what came out of that meeting. The group provided recommendations and the long-term is to get the industry together and adopt these recommendations. It might take some time and we might have to take some steps but this is really important. The first thing they recommended was tracks have a medical director; preferably an MD; preferably a board certified physician and minimally family practice, internal medicine, emergency medicine, orthopedic, neurosurgery or the best case scenario would be trauma. Get together and perform the program at every racetrack.

We want from the on-site emergency medical staff, we'd love to see a registered nurse, paramedics during the races and EMTs to supplement. We want on-site first aid facilities to be OSHA and HIPAA compliant. Private rooms with adequate space for treatment. Facilities to stabilize injured riders. Transportation of riders to nearest the trauma level I facility as was stated before. Pass the nearest hospital and get to the best hospital. We want these ambulances to follow the race no more than a quarter mile behind, which would enable timely response. The use of trauma one level facilities was touched on earlier. Tracks will be strongly encouraged to develop a working relationship with the closest facility. Proximity and rider personal preference should also come into play.

There were some other areas of interest that were identified. Participation in the jockey health information system, which I think Brad will be touching on shortly. Should we mandate participation in that from the riders? Communication during an incident and afterwards to the public, to the media what should we be looking at there? Advanced life support versus basic life support, which is do we want paramedics or do we want EMTs? Do we want a medical director who is an MD with trauma? What really is the decision we need to talk about? Finally, we talked about relationships with other sports, which is one of the reasons that this group is here today. Share best practices with other sports so that for instance our track medical directors would know the proper procedures in place.

What are we going to do now? We have these recommendations in hand and our organization has an advisory committee, which is represented by Terry Meyocks. We'll go to that group right after the first of the year with this list of minimum standards that we think tracks should adopt and we will discuss them. How we gradually adopt them through the code of standards is going to be determined right after the first of the year and we'll come back and report on it. Tracks that were accredited in 2009 will be coming back for re-accreditation in 2011. Upwards of 30 tracks could be completely accredited by the end of 2011, which means that we can have these standards in place at a pretty good number of jurisdictions. Somewhere around 70 percent of pari-mutuel handle will be through an accredited track by the end of 2011.

We can then work on model rule amendments and take that standard where it is right now and move it up to include more specific requirements and then ultimately commission adoption so that the model rule isn't only the minimum standard. We can move it up to commission adoption of all these standards that we talked about today.

Thank you for having me here today. I'm frequently on stages like this and I feel significantly dumb compared to the rest of the stage but thank you for having me. I appreciate it.

[Applause]

Mr. Richard Valeriani: Thank you Mike. Our clean up hitter is Brad Kimbrell, the executive vice president of InCompass, which provides computers to the racing industry, I think.

Mr. Brad Kimbrell: That's correct. Thank you. I'm Brad Kimbrell and Terry Meyocks asked me to review with you today some of the things that the Jockey Club has done and InCompass Solutions have done in the gathering of information for guys like these to use down the road. We're a technology company and most of you in this room, many riders in this room know us from the horseman's bookkeeper or paymaster function that we do at racetracks. We cut the payments each week in jockey payroll. We create the statements and print those checks each week with our software. The racetrack operators do that for you. We also have a system where you can go online and look up balances so the horseman can see what's in their account at any time from the Internet.

We participate in the industry financially as well as producing products and services for the industry, which is a point of pride with us and the Jockey Club. It's a nice place to be able to work where you don't have to make a dollar on everything that you do but you can give back some of this. What we've done with the pre-race veterinarian exam in the last two years and led up to the equine injury database and the jockey health information system and now we're looking at a rider accident database much like the equine injury database.

In early 2008 Nick Nicholson, the president and chief executive officer of Keeneland and Dr. Barry Schumer approached us with an idea to capture jockey health information, medical record type information in a system so when a guy was hurt they could look in this system if he could not communicate with them. They could look in this system and send a report along with that fellow to the hospital or treat him and know what allergies he had or what previous ailments he had. We launched that at Keeneland and Keeneland has since made that a requirement now. If you're going to ride at Keeneland you have to register in the jockey health information system.

Anybody that's here that is not in the system should call us, call the Guild, talk to the medical director at the racetrack you're riding and get a log in and password and set yourself up in that system. Once you do it one time it's available to all authorized medical personnel at all participating racetracks.

We collect six different pieces of summary data. We take your personal information, your emergency contact information but then we also get into the medications, any surgeries that you've had or broken bones, any treatments, allergies and things like that to protect you so that when you're being treated they can send that report. In fact, at Keeneland the week that we first launched the system — and I'm going to say it was John Velasquez but don't quote me on that. I believe that is correct. He went down and was unconscious at Keeneland. They were able to go in the system and print out a report on his information and send that to the hospital before he got there and obviously that improves your chances for better treatment.

The system is also available in Spanish. We have a Spanish screen. The information is fed back to the caregivers in English but we do have Spanish prompts on the screen for guys that are more comfortable with Spanish.

In August 2008, we were called upon to develop this equine injury database. The purpose of that was to try to identify several correlating factors that led up to horse injuries. Take that database, once we had enough information in that database, give that to an epidemiologist to study to try to draw those correlations to see what led up to an injury and what common events or circumstances were involved in that injury.

Based on the good work that was accomplished with equine athletes, the Thoroughbred Safety Committee called for the development of a rider accident database. Reading from their official recommendation the primary objectives of the rider accident database would be to identify the frequency, types and outcome of rider injuries using a standardized format and generate standardized statistics so those can be handed over much like they have with the equine injury database.

The second point was to identify circumstances of increased risk of rider injury and the third was to serve as a data source for research directed improving safety and preventing injuries to riders. The Thoroughbred Safety Committee has called in this resolution for the standing commitment by all racetracks, state racing authorities, horseman, exercise riders, riders and the Jockeys' Guild to participate in this rider accident database.

Since this recommendation was made at the round table conference in August, the Jockey Club industry initiative staff have met with various industry participants to identify the essential data elements that needs to be captured and to determine what data is currently being captured. During those meetings it was suggested that certain insurance carriers provide coverage to these racetracks. I think there are about six that provide the coverage around the country and we might be able to work with those guys and look at what data they've captured to date and take that information and consolidate it. We're following up on that suggestion. We've met with some of these carriers and there's obviously with humans there is more of the HIPAA, Health Insurance Portability and Accountability Act. If you've been to the doctor lately you know how that works.

It's for your protection but it's also limiting in what we can get from these carriers and what they can release to us. We're doing our legal due diligence at this point. We're going to continue talking to the carriers. The converse of working with the carriers would be to go to each racetrack like we did with the equine injury database. I can tell you that was a

herculean effort carried about by the Jockey Club going back and forth with racetracks and agreements. It would be much easier to do this with six carriers than with 140 racetracks but we'll keep having these meetings. We'll keep discussing this and we'll come back to you and give you an update on where we stand and what the best track will be. Thank you.

[Applause]

Mr. Richard Valeriani: Thank you very much. I'd like to learn more about that paymaster function at the racetrack. I don't seem to be too familiar with that. Okay. Are there any questions? All right. I have one question I'd like to ask because Mike referred to approved helmets and vests and I'd like to ask about possibly improving. Is there any research going on that you know about to improve safety features for jockeys?

Mr. Mike Ziegler: There is currently and the Jockey's Guild is taking the lead on it running — I guess the Jockey's Guild has joined ASTM, which is really the organization nationally that writes the standards and the Jockey's Guild has recently participated in their meeting to work on improving helmets and vests and to make sure that the best possible is out there.

Mr. Richard Valeriani: Okay. Speaking of working on there's a workshop tomorrow. You're all invited 2:00 to 4:00. I'd like for you to give a final round of applause to this outstanding panel.

[Applause]

Mr. Richard Valeriani: To all of you, thank you very much for coming.