

# Using the magic of stem cells to treat equine injuries

*North American Trainer* published an article ["Tendon Treatments" by Kimberly French, Issue 11] that detailed how this therapy is used to treat tendon injuries, and another article that provided an overall look at stem cells based on an Italian study ["Stem Cells: are they the future in treating injuries in Racehorses?" by Niki Luciani, Issue 15], but because this is a rapidly growing area of research, we felt it is a subject worth covering again, with an emphasis this time on the adipose-derived stem cell treatment.

WORDS: DR. STACEY OKE

# W

hat if you had a magic elixir that could cure any bowed tendon or

stop a simple chip in the knee from developing into full-blown arthritis? What if you knew that this elixir could quickly and easily be extracted from the injured horse, then injected into the injury to facilitate the successful return of your horse to training and racing?

Musculoskeletal injuries, particularly the soft tissue injuries such as bows or suspensories, are common in athletic horses, yet many of these injuries remain challenging to treat. New, innovative, and effective treatment options for these injuries are needed.

With increased research efforts in the field of regenerative medicine, it appears that stem cell therapy may fit the bill. Stem cells are special cells in the body that have the unique ability to become virtually any type of cell possible such as tendon, cartilage, and ligament cells.

The goal of this article is to look at the types of injuries that these cells can treat, how these cells are collected then "regenerate" rather than simply "repair" damaged tissues.

## What injuries can be treated?

Stem cells are being used to treat racehorses with:

- Bowed tendons (superficial or deep digital flexor tendonitis);
- Suspensory ligament injuries; and
- Condylar fractures and chip fractures.

Trainer Eoin Harty, known for Well Armed's record-breaking 14-length win in the 2009 Dubai World Cup, has treated six horses with stem cells so far. He has used stem cells to treat suspensory ligament injuries, one filly with chronic bad spurs in her knee, and even a horse with white line disease.

Established New Yorker Tom Bush, trainer of Get Stormy, winner of the Grade 1 Maker's Mark Mile at Keeneland in April and the Grade 1 Woodford Reserve Turf Classic Stakes on Derby Day at Churchill Downs, has also used stem cells in several horses.

"I've used stem cells in one tendon with a minor lesion and a few suspensories. One suspensory was a classic branch lesion, and the other was a high suspensory," Bush recalls.

Although less widely recognised, stem cells are also being studied for bone regeneration to help with fracture repairs, laminitis, subchondral bone cysts, and even skin lesions.

## Collecting and Injecting Stem Cells

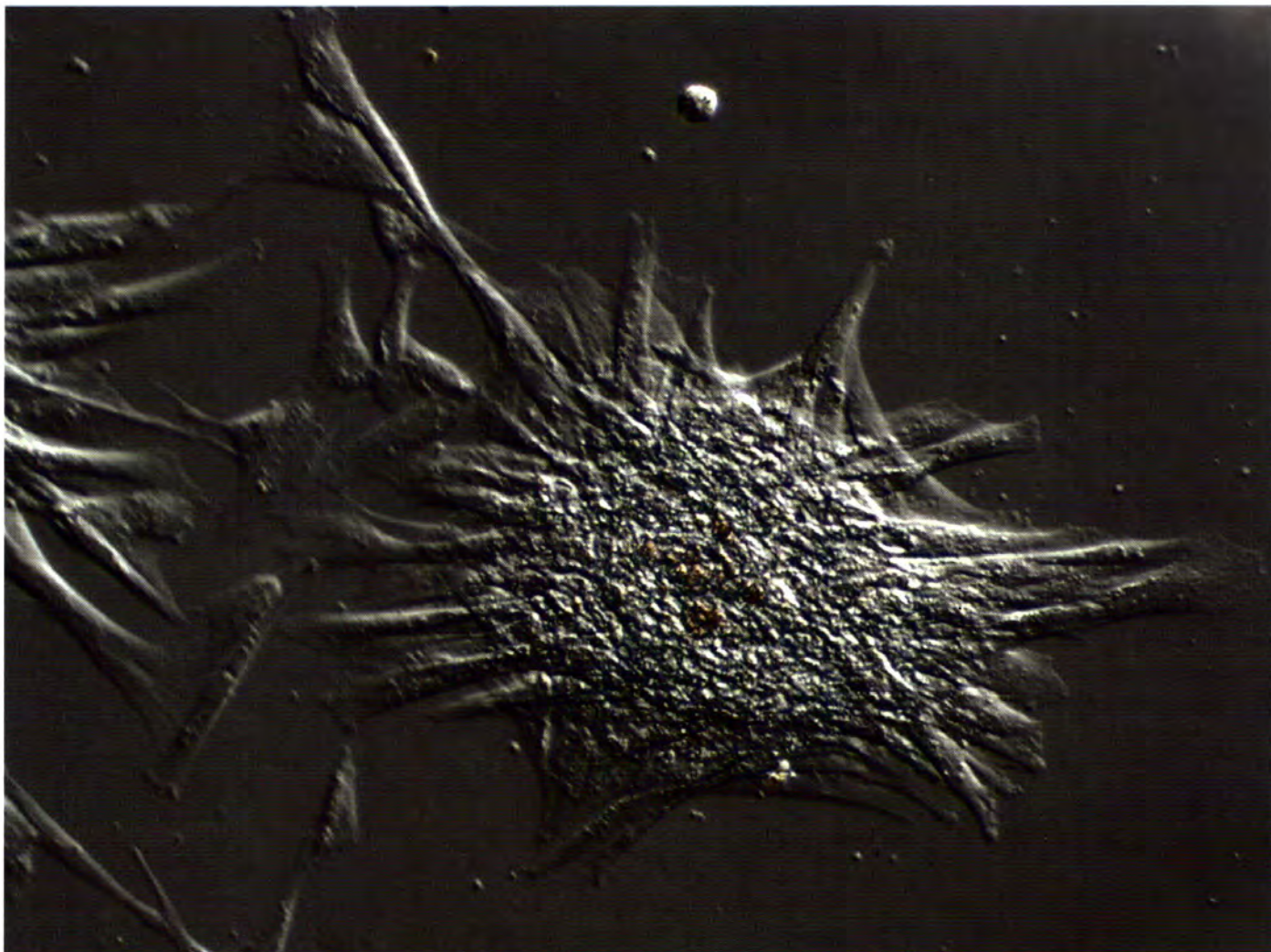
Adult stem cells are primarily found in bone

marrow and adipose (fat) tissue. Cells from both sources are currently being used to treat racehorses.

## Bone Marrow-Derived Stem Cells

According to Dr. Scott Hopper, a surgeon at Rood and Riddle Equine Hospital in Lexington, Kentucky, a bone marrow sample is collected relatively easily with the horse "standing under sedation, with a bone marrow needle." Once collected, the stem cells need to be cultured in a laboratory before they are injected back into the injured horse. It takes approximately two-to-three weeks to culture the cells. Rood and Riddle's Stem Cell Laboratory indicates that the process generates enough cells for multiple treatments and banking. Considering it can take six-to-twelve months for a horse to come back from a tendon or ligament injury, this delay may or may not be significant.

"I consult Dean Richardson [at the New Bolton Center in Pennsylvania] for my lameness and he uses bone marrow stem cells. It takes a couple of weeks, but we have enough that we can re-inject the cells 60 or 90 days later when we re-scan the horse," says Bush, who is not concerned with the delay between collecting the bone marrow and treating the horse.



### Adipose-Derived Stem Cells

In contrast to Bush, proponents of fat-derived stem cell therapy believe that time is of the essence when it comes to treating musculoskeletal disorders in horses.

"Once an owner or trainer decides to pursue stem cell therapy, they want it done yesterday. With adipose-derived stem cells, the horse can be treated within a few days of making the decision," says Dr. Faith Hughes, a surgeon at Peterson & Smith Equine Hospital in Ocala, Florida. "This is not the case with bone marrow-derived stem cells."

Adipose-derived stem cells can quickly be harvested from the fat pad located near the tail head. Depending on the company used to process the collected fat sample, either an incision can be made or a plug of fat can be obtained via "liposuction" using a small needle-like instrument.

According to Hughes, collecting fat is not difficult; however, people should be aware of the fact that there simply isn't a lot of fat, even at the tail head, in a fit racehorse.

Fortunately, stem cells are very concentrated in fat so only a small sample is needed. Once the fat is collected there are different ways to get the stem cells depending on which company your veterinarian uses. One option is to ship the fat in a sterile container to a commercial laboratory for processing.

Dr. Robert Harman, DVM, MPVM, CEO and founder of Vet-Stem, Inc. describes how his laboratory processes the cells.

"After we receive the shipment in a refrigerated collection box, the laboratory does quality evaluation of the sample and then extracts the stem and regenerative cell population from the fat using enzymes and high-speed spinning. Repeated rinsing of the cell mix to remove the enzymes and any other contaminants is done in addition to quality control evaluations of the cell mix and automated accurate cell counting.

Sterile syringes are filled with the appropriate number of cells for each dose needed, which are shipped back immediately (i.e., the same day) to the veterinarian for treating the horse. We believe that a central laboratory is the only way to ensure the quality and safety of the cells for the veterinarian."

A second option is to purchase a kit so the treating veterinarian can collect, process, and activate the cells "in-house" (e.g., the surgery suite) then inject the cells into the injury the same day.

According to Jeremy Delk, Managing Director of MediVet America, their kit yields a very high number of cells from only a small amount of fat.

Once the stem cells are injected, the exact

### READY, SET, ACTIVATE!

"Adipose-derived stem cells help the body do its job better. One way that we do this is by 'activating' the cells with platelet-rich plasma (PRP), which is also full of growth factors, cytokines, and chemokines, and with photobiostimulation using LED technology," relays Jeremy Delk, Managing Director of MediVet-America. Sound crazy? You're not alone, but as Delk says, "a few years ago people laughed at the thought of PRP and now look at how popular it is. Activation of these cells combined with the very high cell numbers in my opinion is key to achieving a successful long term treatment."

Data provided by Delk shows that cells collected from fat have a much higher viability being activated with PRP and an LED light. In fact, there were twice as many regenerative cells in the activated colonies after 48 hours than the controls.

**MORE TO STEM CELL THERAPY THAN JUST STEM CELLS**

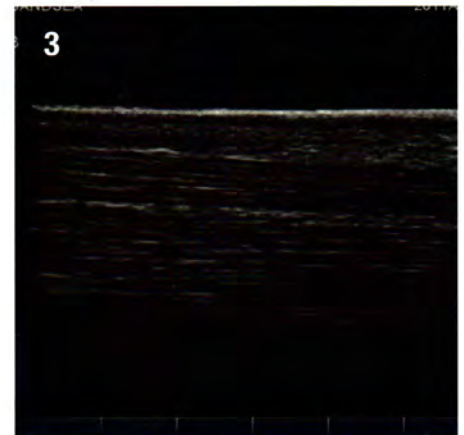
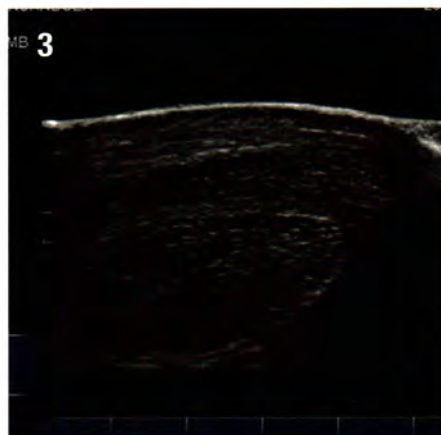
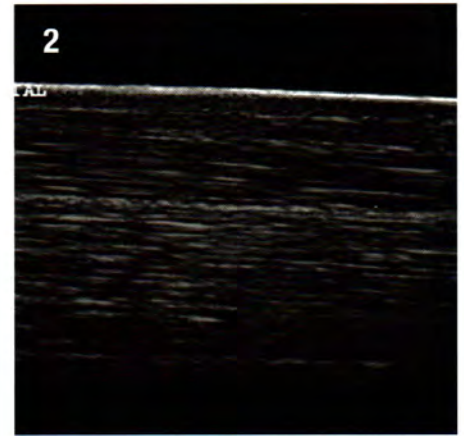
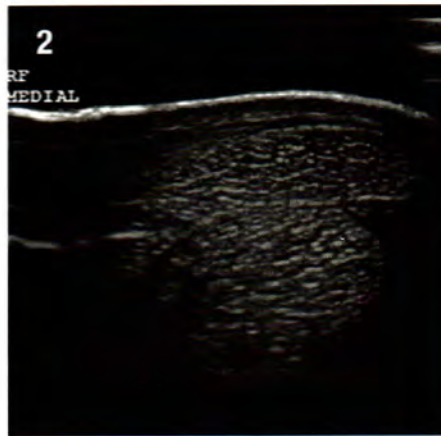
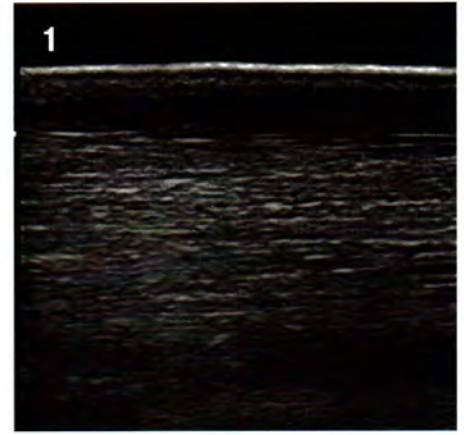
One point that Delk emphasises is that not all of the cells generated by processing a fat or bone marrow sample are “stem cells”.

“They are regenerative cells, but only 2-4% of the cells are actually true stem cells that have the ability to differentiate,” explains Delk.

Don't be deceived, however; the remainder of the sample is not “junk,” but actually contains other proteins, cells, and growth factors that are as potent and important as the stem cells themselves.

Examples include thymosin beta-4, osteoclast-1, ephrin A1, connective tissue growth factor, and transforming growth factor beta-2.

Delk adds, “Unlike bone marrow, adipose-derived stem cell therapy and the stromal vascular fraction act as a multipotent delivery system. The power of this stromal vascular fraction is just as, if not more, important of what these cells actually secrete in order to promote this repair.”



A series of scans showing the improved tendon development from 1. pre-injection, 2. after two weeks and 3. after four weeks

course of events that lead to regeneration of the injured tissue are not precisely known. Studies suggest that stem cells themselves can become tendon cells, for example, and help regenerate the damaged tissue. Alternatively, the stem cells can signal other stem cells in the soft tissues and stimulate those “resident” stem cells to regenerate the damaged tendon tissue.

Harman adds, “Stem cells from marrow or fat also reduce inflammation and pain in the injured area, stimulate growth of new blood vessels, and help prevent damaged cells from dying. They are truly paramedics!”

**Does Stem Cell Therapy Work?**

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Joseph Yocum DVM, ABVP

use of multi-potent cells for a variety of conditions in the horse,” relays Joseph Yocum, DVM, ABVP, an equine practitioner at Green Tree Veterinary Services in Kentucky and founder of The Center for Regenerative Medicine.

Yocum recently spoke at the second North American Veterinary Regenerative Medicine Conference held June 2-4, 2011, in Lexington, on the virtues of adipose-derived stem cells in equine practice and relayed that besides tendon injuries, stem cells reportedly can be used in subchondral bone cysts, laminitis, and fractures.

“I have also used stem cells in joints to treat a couple of severe OCD lesions. I administered three-to-four treatments one month apart and had a pretty good response.



Tom Bush (with his Grade 1 winner Get Stormy) has used stem cells in several horses

*“It is a pretty standard treatment with me. One of the tendons we treated with stem cells was only a minor lesion, but we did it anyway because we wanted to do everything we could. It was done one year ago and the horse has come back well”*

Tom Bush

This is not a controlled study by any measure, and the results are anecdotal, but I was still pleased with the outcome,” adds Yocum.

In addition to these anecdotal reports, some

“hard” evidence supporting stem cells in horses has been published. For example, one study on adipose-derived stem cells concluded that this therapy “appears

warranted” for superficial digital flexor tendon injuries. The researcher team, led by Dr Alan Nixon, a board-certified surgeon and professor at Cornell University’s College of

# VetCell

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**TOO GOOD TO BE TRUE?**

Stem cells are relatively easy to collect and inject, and appear to be beneficial for horses, but like any medical or surgical intervention, there are pros and cons associated with the procedure. For example, swelling and inflammation can develop after a stem cell injection. Joints appear particularly susceptible and a "joint flare" can occur after the injection. In most cases, horses respond to medical treatment. Cost may also be an issue as the procedure is approximately €1400 –€2000. While this may seem excessive for some owners, Bush says, "The cost is not that outrageous when you look at the cost of laying the horse up for six-or-seven months."

Finally, before embarking on a stem cell journey, consider the lack of data regarding if and how stem cells work and how horses do in the long run. Dyson concurs and adds, "I think that it is very early days at the moment. I am pretty sure that the soup that we inject – mesenchymal progenitor cells, growth factors, etc. – has a positive effect in some horses for management of tendon and ligament injuries. We still don't know how long the cells survive for or what they actually achieve, we don't know what types of injuries are best to treat or at what stage, what the optimum number of cells is or the optimum concentration of the other goodies, such as growth factors."

Veterinary Medicine, found that although there was no difference in the appearance of the tendon after scanning (ultrasounding) compared to horses that were not injected with stem cells, treated tendons were more "organised" and had better "architecture" than untreated tendons.

Data generated by two commercial laboratories also make stem cell therapies appear promising. At the first North American Veterinary Regenerative Medicine Conference held in March of 2010 in California, Harmann from Vet-Stem reported that 64.7% of horses with a tendon injury treated with adipose-derived stem cells went back to race one or more times.

Similarly, 70.7% of the horses treated for a ligament injury raced one or more times after stem cell therapy. Only 42.4% and 39.7% of the 197 horses with tendon and ligament injuries, respectively, raced three or more times.

A UK-based company, VetCell, which uses bone marrow-derived stem cells, has data from 495 horses – from an original study of 579, with a number of these horses still in the rehabilitation phase and others presented without verifiable names – posted on their website. Of these, 76.6% have returned to racing post-treatment, 55 of them having started greater than ten times.

But hold on: a separate study reported that 71% of horses subjected to only a controlled exercise program after injuring a tendon or ligament returned to racing. This data indicates that a carefully designed rehabilitation program can get horses back to the races as well as stem cell therapy.

The "secret" lies in the reinjury rate and there are two specific peer-reviewed journals that have studied this. One, by Dr Sue Dyson at the Animal Health Trust, showed that approximately 57% of horses treated by conventional therapies sustain a reinjury.

In contrast, data published in 2011 by a group of researchers at the Royal Veterinary College in Hatfield, UK, show that stem cell implantation using VetCell's technique reduces this reinjury rate to 27%. Both studies collected follow-up data on more

than 100 national hunt horses that had sustained a superficial digital flexor tendon injury.

**Stem Cell Therapy a "Valuable Addition"**

While researchers and veterinarians are trying to gain a better understanding of how stem cells really work and where they go after they are injected, trainers like Harty are embracing stem cells for treating their horses' soft tissue injuries.

"I don't want to know how it works or why it works, I just want to know that it does work, and in my experience, stem cells really seem to be effective. It was phenomenal how the horses came back," says Harty.

Although Bush reports a more modest success rate than Harty, Bush is still a proponent of the treatment.

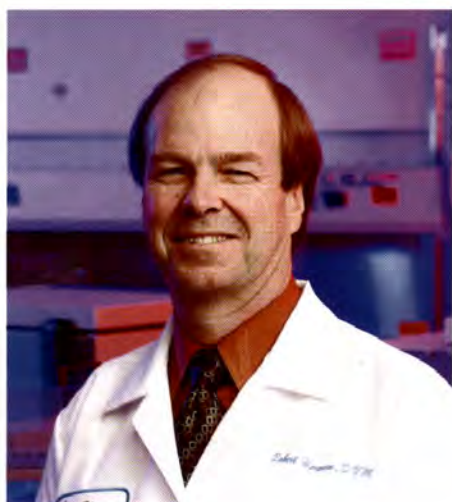
"It is a pretty standard treatment with me. One of the tendons we treated with stem cells was only a minor lesion, but we did it anyway because we wanted to do everything we could. It was done one year ago and the horse has come back well," relays Bush. "The horse we did with a very high suspensory did not do as well, but we weren't that surprised because it had a poor prognosis to start with."

Bush also says that he realises the verdict is still out on the efficacy of stem cell therapy but in his opinion, "It has a lot of merit. I think it will become a very popular and beneficial treatment for these soft tissue injuries."

**Maximizing your Chances of Success**

To get the best possible outcome following stem cell therapy, Hughes reminds us, "The goal of stem cell therapy is to improve the quality of tendon healing, not increase the speed of healing. The tendon may ultimately heal more quickly, getting the horse back into training sooner, but this is not the main goal of stem cell therapy."

Yocum concurs and adds, "Trainers try to get their horses back as fast as possible. My goal is to get better, not quicker, healing. To do this, stem cells need to be used in addition to the regular rehabilitation programs." ■



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Dr. Robert Harman, DVM, MPVM, CEO and founder of Vet-Stem, Inc.