

# Evolving healing method

Stem cell therapies for tendon injuries continue to show promise

by Robin Stanback

TENDON injuries are costly, and money is only the start of it. If the injury is such that the horse might be able to recover and return to racing, there is still the matter of lost training time and conditioning. Therapies and theories abound, none of which have been able to prove 100% efficacy, but one relative newcomer to the treatment arsenal—the use of a horse's own stem cells to aid in the healing process—shows promise.

One of the pioneers of stem cell research for equine tendon problems is Roger K. Smith, Ph.D. A professor of equine orthopedics in the Department of Veterinary Clinical Sciences at the Royal Veterinary College in Hatfield, England, Smith and his colleagues first brought this therapy to the equine market in 2002 when the college started VetCell Bioscience Ltd., a company through which to market their findings.

Since its inception, the veterinarians and scientists there have treated and followed more than 700 horses.

"The results have been encouraging," Smith said. "We have been comparing published reports of horses with tendon injuries that have been treated conventionally with those that we have treated with stem cells. For National Hunt horses, those that race and jump, there is about a 56% rate of re-injury to tendons treated with conventional methods. The horses that received the stem cells have about a 24% reduction in re-injuries to those tendons over the horses that received the other therapies. It does look like there is a statistically significant improvement with this therapy."

Smith said that tendon injuries often result in scar tissue forming in and around the tendon itself during the healing process. Scar tissue is not always as elastic or strong as the tendon it replaces.

A tendon that has sustained an injury and recovered might also not be aligned as well as the original, making the chances of re-injury to the tendon greater. Researchers hypothesized that if stem cells could be injected into the tendon tissue in greater numbers than are present normally, there would be an increased chance of the lesions healing correctly with less scar tissue.

## Equine differences

Unlike the more controversial stem cell research in human medicine that uses cells derived from human embryos, the cells used to treat tendon, ligament, and cartilage problems in horses come from the equine patient's own adult stem cells.

Mesenchymal stem cells (MSCs) can be harvested from bone marrow or adipose (fat) tissue, muscles, tendons, and cartilage. The unique properties of these cells were first reported in the 1960s when two researchers discovered the clonal nature of transplanted mouse marrow cells. In subsequent years, studies have shown that MSCs can differentiate into bone, cartilage, tendon, and fat cells as well as scar tissue. MSCs can make that differentiation during embryonic development or during adult life. The advantage to using an animal's own

adult stem cells in any type of therapy is that there is a decreased chance that the cells will be rejected.

To get the MSCs for equine therapy, researchers aspirate bone marrow from the sternum (breastbone) or the iliac crest near the hip bone and from fat cells pulled from adipose tissue at the tail head.

There are two different methods for the use of these cells once they have been harvested. One, using bone marrow aspirate, involves culturing the cells, a process that can take three weeks. The other method uses the aspirate from adipose tissue. The fat cells are separated, usually within about 48 hours, and the remaining aspirate that contains an estimated 2% MSCs is injected directly into the affected area using ultrasound technology to pinpoint the exact placement.

Duncan F. Peters, M.S., D.V.M., director of the Sport Horse Program at Hagyard Equine Medical Institute in Lexington, has used both types of stem cell therapies for horses with tendon injuries, but has come to favor the fat-derived source.

"There is a debate about the time factor in treating tendon injuries," Peters said. "Some people like to give the tendon time to quiet down. They want to treat the tendon with cold therapy, use anti-inflammatory medications, wrap it—give it time for the inflammation to reduce. When using stem cell therapy, however, an earlier treatment might be crucial. The stem cells will seek out the damaged tissue and attach to it. You might get a better attachment earlier in the process than you would by waiting for the inflammation to reduce. There is a need for a lot more research into this."

The most recent work done by scientists at the Royal Veterinary College suggests that the later the implantation of the MSCs occurs, the greater the chance for increased fibrosis.

Two groups of horses were studied by the scientists, and each had received stem cell therapy for tendon injuries. After the horses returned to work, those that re-injured their tendons were compared by ultrasound to those that had not. The horses that received stem cell therapy later in the course of treatment were the ones with more substantial



Bennett & Associates photo

## STEM SUCCESS

Stem cells harvested from Greg's Gold's own fat helped repair tendons in the gelding's right front leg and allowed the three-time graded stakes winner to return to the highest levels of racing

fibrosis present. This has led researchers to suggest earlier aspiration of bone marrow and culturing of cells. Thus, the implantation process can begin as soon as the inflammatory phase has diminished but before fibrosis begins. Ideally, they would like to see this happen within a month of the initial injury.

Smith sees the waiting period for culture of the bone marrow stem cells as a bit of a drawback.

"But," he said, "there are advantages to this therapy. When the cells are cultured, the result is a higher concentration of MSCs."

## No easy route

Whichever process is used, one thing is certain: There is no significant shortcut to tendon repair.

"It would be wonderful if this therapy could cut healing time by, say, 25%, but, unfortunately, if it cuts the time at all, it might be only about 10%," Peters said. "In the course of a year, how much time would you really be saving?"

Peters and Smith see stem cell therapy as an addendum to conventional methods of healing a horse with a tendon injury.

"This therapy complements what we have been doing in the past," Peters said. "It has the added advantage that we are not injecting

anything foreign into the horse. Oh, any time you inject anything into a horse there is a risk of a reaction or infection, but with this therapy, we are using the horse's own cells to help in the healing process, and there is a very small chance of infection, so small that I do not consider it to be a problem.

"We have learned a lot in recent years. You don't see too many people doing long stall rests or throwing a horse out in the pasture for a year off as the first choice for healing a tendon anymore. Instead, we have learned that we need to control the inflammatory process as much as possible, and then begin a process of physical therapy and controlled exercise to bring the horse back into condition.

"In some respects, the horse probably was doing the controlled exercise on his own when he was turned out in the pasture. He would run or walk around until something hurt, and then he would stop. It was self-regulating.

"Today we have improved ultrasound technology that allows us to monitor the tendon's condition. We can clearly see edema forming. So, we can begin a process of exercise and weight-bearing while monitoring the tendon. If a problem arises, we can catch it early and modify the

program."

Combining that carefully monitored program with stem cell therapy is something Smith sees as a real advantage.

"Right now, we know that those horses treated with this stem cell therapy have responded well, and fewer of these horses re-injure their tendons," Smith said. "The treatments have been well accepted by the industry and, encouragingly, by the insurance companies. Here in the [United Kingdom], many people have health insurance for their horses. The insurance companies have accepted stem cell therapy as an insurable treatment."

## Cost concerns

Expense remains a serious consideration for stem cell therapy. Peters said that the cost for a horse to receive stem cell therapy from fat tissue can be more than \$1,000 in the United States. In England the cost can be £1,600 to £2,000 for bone-marrow-derived stem cell therapy.

Stem cell research has come a long way in the six years that it has been commercially available.

Companies throughout the world have been refining their collection techniques and methods of isolating MSCs and delivering them to equine patients. The goal for researchers now is to continue refining the art of harvesting and separating MSCs.

"Ideally, we would like to do controlled studies measuring and comparing horses without tendon injuries, those with injuries treated conventionally, and those that receive the stem cell therapies," Smith said. "The challenge there is one of cost—it is very expensive to do this type of research. In that, we are very fortunate to have the support of the Horserace Betting Levy Board, an organization in the UK that collects contributions from bookmakers and the Tote and distributes those for the improvement of horse racing and the advancement of veterinary science and education." ♣



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## Stem cell purpose depends upon origin

Stem cells are found in most multicellular organisms. Through cell division, they have the ability to duplicate and differentiate into a specialized cell types throughout a lifetime. They can multiply numerous times and stay in an undifferentiated state.

Through cell cultures, stem cells can be grown and transformed into a variety of tissues such as ligaments, tendons, nerves, and muscles. Researchers collect stem cells from a variety of places within the body, and each has its own unique purpose and ability.

For equine tendon injuries, the best type of stem cell will come from the injured horse itself from either bone marrow or fat deposits. The different types of stem cells and their uses are:

**Embryonic stem cells (ESCs)** are found in aborted

fetuses. These cells are pluripotent, having the ability to form more than one tissue type. While the potential uses of ESCs for disease and injury therapy is great, ethically it presents complications.

**Hematopoietic stem cells (HSCs)** can be collected from bone marrow or umbilical cord blood. They have the ability to regenerate only blood cell lineages and can have long-term and short-term regeneration properties.

**Mesenchymal stem cells (MSCs)** are multipotent progenitor cells found in bone marrow and small amounts of skeletal and adipose tissue. These cells can differentiate into a wide variety of cells including bone, tendons, and cartilage. MSCs can differentiate during embryonic stages and during adult life.

## Have a question for a veterinarian?

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