HEALTH ZONE

Stem Cells

BY HEATHER SMITH THOMAS / PHOTOS COURTESY OF DR. SCOTT McCLURE

New Techniques for Harvesting and Administering Stem Cells

Stem cell therapy can help heal tendon, ligament, and joint injuries

STEM CELL THERAPY has been utilized in horses to help heal tendon, ligament, and joint injuries for nearly a decade, and new uses for stem cells are continually being explored. At this point there are basically two sources of stem cells for clinical use—from bone marrow and from fat tissue. Allogeneic stem cells—from another (donor) horse—and preserved cells, such as from umbilical cord blood from newborn foals, are not commonly used.

Cells harvested from bone marrow are usually cultured and expanded, putting them back into the horse some weeks later. Cells harvested from fat can be collected and concentrated at a lab and sent back within about 48 hours for quicker administration. Now there is a way to obtain

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from Michael Matz...

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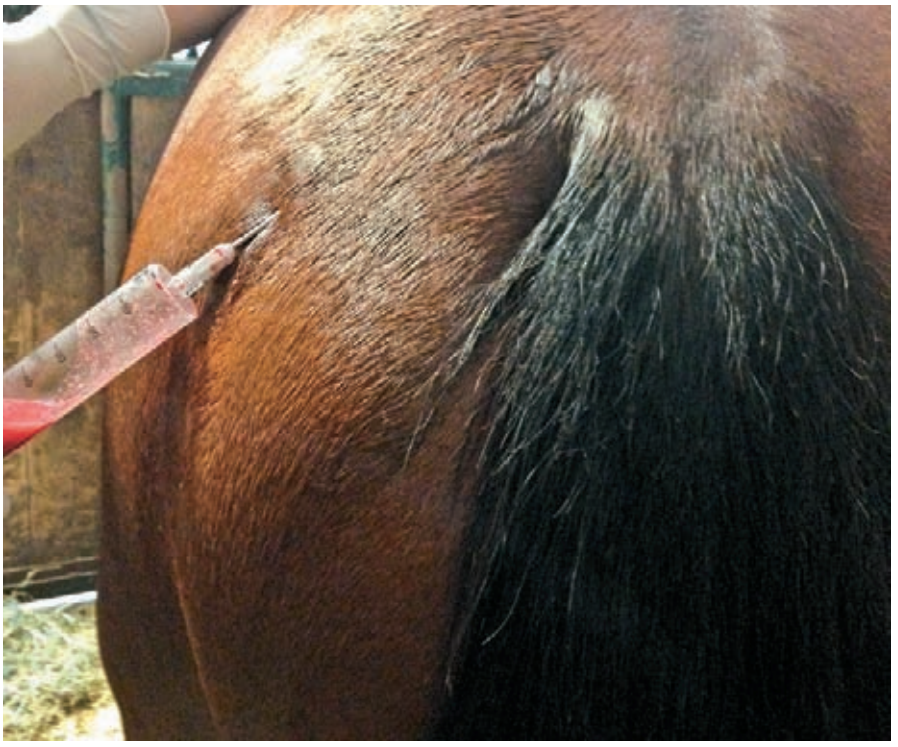

Fat can be taken from the tail head to be processed and ready to inject in two hours

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and use those cells within a much shorter time.

Dr. Scott McClure, associate professor of equine surgery, Iowa State University, is utilizing this new method.

"A research group has simplified the procedure for stem cell processing so that we can obtain them and inject them back into the horse wherever there's an injury, to stimulate healing," he said. "Stem cells are present throughout the body and have the ability to perpetuate themselves. They can also divide and differentiate into the appropriate cells for healing bones, tendons, ligaments, or whatever."

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It's helpful to have a population of cells to aid healing wherever there is damaged tissue.

"The body has a way of doing this, to some degree, but not always to an adequate degree to heal the tissue the way we'd like it to heal," McClure said. "We can add more stem cells to that area to speed optimal healing.

"We can utilize stem cells to treat specific injuries. We use autologous cells—from the patient's own body. We can harvest cells from bone marrow and send this material to a lab where it is cultured and the number of MSC (mesenchymal stem cells) are expanded to the number that we need. These are sent back for us to place into the injury to be treated," he said.

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"The other way is to harvest some adipose (fat) tissue from the patient and send it to the California laboratory (VetStem). They isolate the cells and ship them back within about 48 hours. In the past couple of years, there has been some interest in trying to find a way to harvest and inject these cells the same day, while the patient is still there in the clinic or hospital.

"We could potentially maintain a pool of embryonic stem cells (which are not autogenous) like a drug on the shelf to inject into any patient," he continued. "Embryonic cells are fairly flexible, but there is always the possibility of reaction (and rejection) by the patient since these are not from the horse's own body. Another option would be to have fetal blood or umbilical cord MSCs saved for each horse (at birth) to use at a later date, but this is not commonly done.

"So we've been looking at possible things we might do to obtain rapidly derived autologous stem cells—looking at what we can take from the horse today and put back into that horse today. We can process those cells while we are doing surgery for instance and put them right into that injury," McClure said.

This technology has already been used in humans and is now being used in veterinary medicine.

"I can harvest some fat from a horse standing here right now, and in two hours I can have a stromal vascular fraction to inject," he said. "This is in contrast to what we get when we culture stem cells in a petri dish for a period of time. If we culture the cells, all we have are pure MSC. If I take some adipose tissue and process it right now, however, I have a population of stem cells, a population of fibroblasts and other cells, and some very small embryonic-like cells. It's actually a mixture of cells; there are stem cells along with some other cells that also aid healing," he said.

Some of those cells are very beneficial.

"We can have that population of cells available to re-inject within about two hours," McClure said. "We don't have to send a sample off to a lab and wait 24 or more hours. We can do it right here on the counter in the clinic or hospital with what we have available now for equipment and technology.

"For instance, I can diagnose a horse with a tendon injury today, liposuction some fat from his tail head or wherever there's a good source of adipose tissue on that horse, and be ready to inject these cells in two hours. We are still in the early stages of this technology, but we know it works. We've done it enough times now, in enough horses, to know it is effective. There are still some questions because we don't know yet if we are better off to put in five million of the mixed stromal vascular fraction today or 10 million pure cultured cells 2½ weeks later. If we put in 2½ to 5 million today, they are already there and have gone to work," he said.

"There are many things to evaluate, but it clearly appears that treating horses early with the stromal vascular fraction has clinical benefits. This technology has been used in humans and other veterinary species. It's unique and simple. With this technique the fat tissue is digested with a group of enzymes and then the cells are concentrated, spun out, rinsed, and re-injected," explained McClure.

"Many people in medical and engineering fields have worked on this technology to get it to this stage," he said. "We use a centrifuge-type device that also serves as an incubator. It heats, agitates, spins, and allows us to do this very easily. The research to create this process took a lot of labo-

ratory steps and has been able to compress them, utilizing a device to make it functional on a countertop in a hospital."

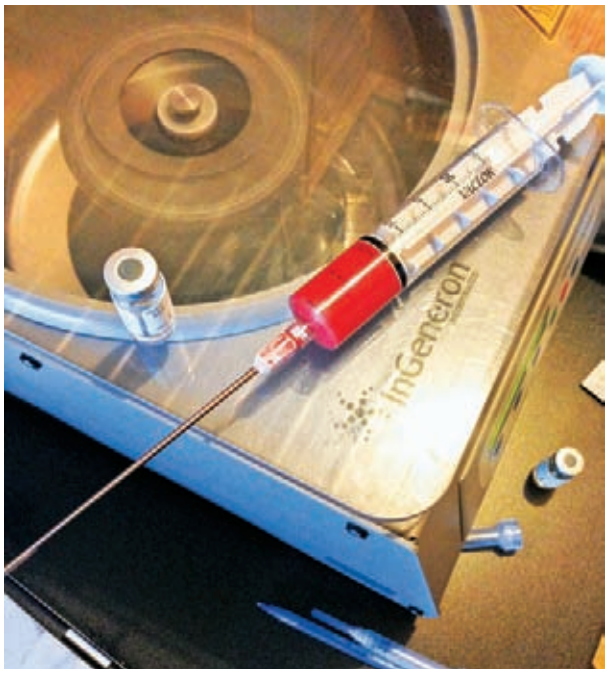
This technology is available now in a growing number of veterinary facilities.

"Some of the advantages are due to the fact that there is a large population of MSC in adipose tissue, and since horses have a large supply of adipose, we have the opportunity to obtain a lot of MSC," he said. "We are starting with a reasonably large population, to derive our subsequent population of cells.

"I've been doing this more than two years, and I feel the advantages are multiple. We are able to treat these cases earlier—on the same day we harvest the cells—and treat more cases. When the decision is made, we can do it effectively and efficiently. We don't have to be hauling horses back and forth and waiting a number of weeks," he continued.

"Another beneficial aspect is that the cells are being put back into the horse fresh. In some of the research we've done, we found that adipose-derived MSCs that are this fresh divide more rapidly than cells that have been cultured a number of times. Thus, we can utilize cells that have a large colony-forming unit potential."

There are some phenotypic differences regarding what these MSCs want to do, based on their source.



A centrifuge-type device (above and at left) also serves as an incubator

"It's been shown that cells derived from adipose tissue tend to differentiate very well toward becoming bone, versus the cells derived from bone marrow (that are cultured), which differentiate well toward chondrocytes," McClure said. "In the laboratory, in culture, there are some differences in what these cells want to do, but in that scenario we are counting on laboratory stimulation; we are putting some things in with these cells to differentiate them. However, if you put them into a certain environment—such as a bone formation—this will influence how well they will take that route.

"We can't say that the exact same things occur in the body as occur in the lab," he explained. "When we inject these cells into a defect in a tendon, that environment will be much more tenogenic (influencing the cells to become tendon tissue) than what we would be able to do in the laboratory. If you inject some cells into a fracture callus in a leg, that would be an environment where they would be much more likely to form bone than they would in the environment of a laboratory dish.

"There are still some areas where people debate what's best, one way or the other. They can make legitimate arguments on which might be better (cultured cells or fresh ones), but this new technique is an available option," McClure said.

A staple closure is performed after bone marrow aspiration

> With new technology, it is nice to be in the forefront, but one has to be cognizant of not making mistakes

This method will probably be used more and more in the future.

"In my experience to date, I've found it to be an effective method," he said. "We've treated some tendon and ligament injuries here, and some joints, and this is as effective as any other source of stem cells."

The first horse McClure treated had a hole in a suspensory ligament branch, and now that horse is back to barrel racing and doing well.

"This horse belonged to a personal friend," McClure said. "I didn't know how well this system would work, so I tried it on that horse as an experiment. With new technology like this, it's nice to be in the forefront and trying it early on, but you also don't want to be making mistakes. We have to be a bit cautious. The horses I treated early did well, however, and I've been pleased with their healing progress, so I am now using this on a growing number of cases." BH