



The new
science of
tissue
engineering

could hold the key to a breakthrough in the treatment of tendon injury in horses.

SEAMOUR RATHORE

talks to Dr Roger Smith MRCVS (above)

IT is almost the stuff of science fiction: tissue engineering — one of the techniques pioneered to provide “new parts for old” in human medicine — could form the central plank in the future effective treatment of tendon damage in horses.

“The issue is this; can we take the tendon and repair it in such a way that it is new again?” says Roger Smith MRCVS, orthopaedic and tendon specialist at the Royal Veterinary College (RVC), University of London.

Up until now, the only treatment for a horse with tendon damage has been months of rest and controlled walking, known prosaically as “a double helping of God and time”.

Thankfully, the ancient procedure of firing — ie burning weals into the tendon with hot irons, to create massive amounts of scar tissue — no longer has a place in veterinary science.

Even so, the horse’s natural healing process results in scar tissue being generated to repair the damaged tendon, rather than the infinitely more desirable tendon tissue.

“The tendon is good at laying down scar tissue but this fibrous tissue is not tendon and will not work optimally in the future. Therefore, the horse is always at risk of re-injury,” explains Dr Smith.

So, is it possible to regenerate tendon tissue rather than repair it with scar tissue? The answer is maybe.

“Tissue engineering has considerable potential across a range of human medical problems — from offering a way to grow organs such as heart, liver, kidneys and brain to therapeutic solutions that could enable the Christopher Reeves of this world to be walking people again. But, so far, the benefits have only been shown experimentally,” says Dr Smith.

How can these completely new tissues be made in the adult? Two possible approaches exist — the use of growth factors (see boxed item) or stem cells.

Scientists have only recently discovered

Whole again?



Pictures by Trevor Meeks, Karen Coumbe and Roger Smith



A severely bowed tendon
Main picture: tendon injuries are a serious risk for top sport horses as well as racehorses

the potential of stem cells. These are cells that are capable of differentiating into many different tissues. There are two types of stem cells – those derived from embryos and those derived from adult skeletal tissues. The latter concern us here. These stem cells can differentiate into a spectrum of tissues, ie they could potentially become bone, make cartilage or in this case, make tendon tissue.

While all tissues in the body contain a small number of stem cells, these special cells are thought to be particularly abundant and easier to recover in bone marrow.

Accordingly, a Californian vet, Dr Doug Herthel, has already taken bone marrow from a horse's sternum (breast bone) and injected it straight into the same horse's damaged suspensory ligament.

His work was first published by the American Association of Equine Practitioners (AAEP) Annual Conference in November 2001.

The substance taken from the bone marrow contains stem cells along with large volumes of things such as blood, including red and white blood cells, and fat.

So far, the American vets have not claimed that this process produces tendon tissue, but that it does produce "a better heal" for the tendon.

As a result it has become a popular treatment in the US for ailments such as suspensory ligament damage.

"This work needs more proof and I worry about the crudeness of the technique," says Dr Smith. "There are very few stem cells in the bone marrow fluid and very large volumes of this liquid are injected into the tendon: there is a real danger of damaging it further and making it scar more."

So, Dr Smith, together with Prof Allen Goodship and his colleagues at the RVC, have come up with a novel project which they hope will be a better way of using this technique while avoiding some of the disadvantages.

Dr Smith plans to combine a series of techniques which will involve the recovery

of stem cells from the horse's bone marrow, multiplying them up in the lab and subsequently injecting them into the damaged tendon of the same horse.

"This is really exciting as it provides an avenue of potential improvement in the way we manage tendon disease," says Dr Smith.

"Early results have shown that this

❖ The issue is this: can we take a tendon and repair it in such a way that it is new again? ❖

technique is feasible and does not damage the tendon. We've already tried it on one 11-year-old polo pony with an injury to the superficial digital flexor tendon."

This work was first published in the *Equine Veterinary Journal* last month.

"I am not claiming at this stage that it is efficacious, only that it has potential – a lot

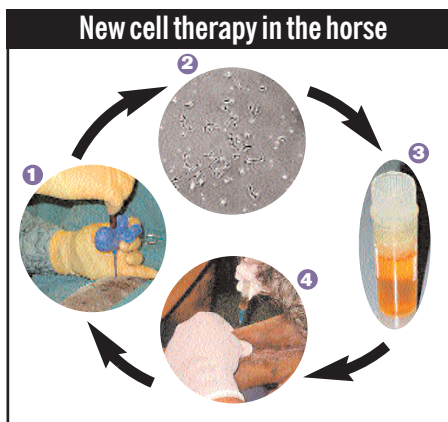
more work needs to be done, and we have applied for funds to continue this research" he adds.

At the same time, along with a commercial partner, the RVC is planning a lab facility to process bone marrow samples from around the country and a rehabilitation centre. Rehabilitation will be a key element because successful use of these cells will also depend on an appropriate and carefully followed rehabilitation programme which will encourage the

stem cells to differentiate into tendon cells and make new tendon tissue.

A nationwide clinical trial is planned for treatment of a certain type of tendon injury. Details of this trial will be sent to veterinary practices in the near future.

"The considerable potential of stem cells already recognised in human medicine warrants further investigation in the equine field. Ultimately, we want to improve the treatment of tendonitis," says Dr Smith. **H&H**



Steps to treatment: 1. the bone marrow is collected from the horse's sternum; 2. the stem cells are isolated from the fluid; 3. growing the stem cells; 4. injecting the stem cells in the tendon

WHAT ON EARTH ARE GROWTH FACTORS?

■ GROWTH factors have been recognised for a number of years. They are substances that may help generate certain types of tissue.

The growth factor, TGF beta for example, is being trialled to promote scarless healing in burn victims.

In equine medicine, vets have already injected various growth factors such as IGF 1

(insulin-like growth factor) straight into the damaged tendon or EST (equine growth hormone) into the muscle to promote healing.

"My concern is that injecting tendons with single growth factors may only serve to increase the amount of scar tissue rather than regenerate tendon tissue," says Dr Smith.

He feels that the best hope may lie with a combination of

growth factors, or manipulating the balance of different forms of TGF beta, thanks to work by Prof Mark Ferguson at Manchester University.

Prof Ferguson found that types of TGF beta in foetal skin (where scars do not form after injury) were present in a different balance than in the human adult skin, which obviously does scar.