Mesenchymal Stem Cells (MSCs)

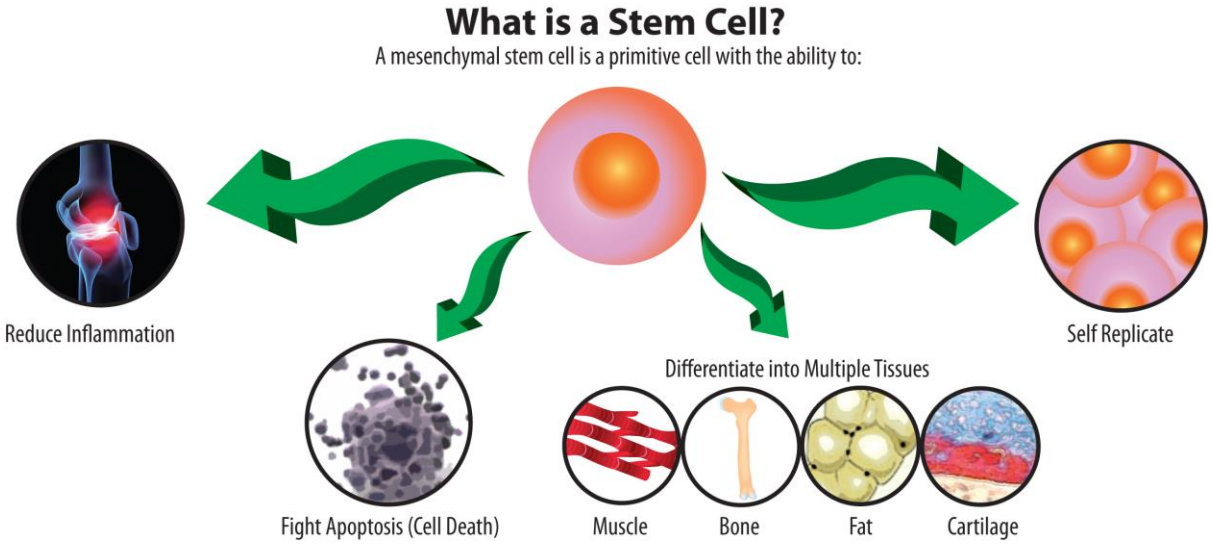
Stem cell therapy is one of an advanced, new class of regenerative treatments that aim to utilize the body's own powerful repair mechanisms to treat a wide range of diseases.

It is particularly useful in the management of joint conditions such as joint dysplasia, degenerative joint disease (DJD) and osteoarthritis (OA) but is showing potential in treating disease elsewhere in the body – wherever, really, that there is any damage to normal tissue structure or function.

This guide is intended to give a little more detail about treating your pet with stem cells – how it works, how it might help your pet and a few details about the procedure itself.

What are 'Mesenchymal Stem Cells'?

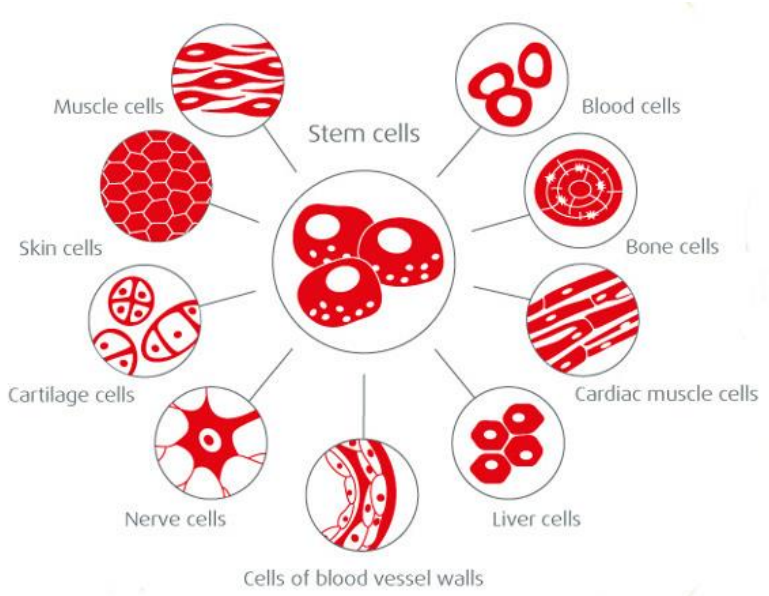
The stem cells used in this sort of treatment are known as 'Mesenchymal Stem Cells' (MSCs). Mesenchymal cells are basic structural cells which through growth and differentiation provide the fundamental architecture for most tissues throughout the body. They are effectively the body's own repair kit, acting to modulate tissue inflammation and encouraging protection, repair and regeneration of damaged tissue.
They are referred to as 'stem cells' when they are in their original, undifferentiated state. What they eventually become depends on local growth factors and where they are located within the body.



How do MSCs help in the management of diseases such as arthritis?

MSCs have the ability to do, or become, almost anything - they are 'omnipotent'. They are influenced by chemical signals ('growth factors') specific to the region of the body in which they are implanted to differentiate and behave in a way that is likely to benefit that area of the body. This can include reducing inflammation, providing building blocks for repair of joint tissues, improving joint fluid production and blocking the cells and enzymes that lead to

cartilage destruction. MSCs have an affinity for damaged tissues and once activated by local growth factors they will do what they can to resolve or improve matters. This does not mean that they can create a whole new joint or undo the extensive remodelling of joints that occurs with advanced arthritis but they can help patch things up, improve the way the joint functions and slow the pace of future degeneration.



At what stage is it appropriate to consider using stem cells?

Stem cells can be used at any age or stage of disease. Young dogs with elbow dysplasia often have quite marked degenerative change at only 6 months of age and early treatment is often recommended in these cases in the hope of minimising long-term joint damage. Likewise older dogs with severe end-stage arthritis and extensive remodelling (where a joint is physically deformed by the degeneration) are still good candidates; despite the advanced damage, the reduction in inflammation and improvement in joint fluid and cartilage health leads to reduced pain and significant improvements in mobility.

What are the side effects of treatment with MSCs?

MSCs are 'autologous' which means that they originate from the patient's own body. They therefore carry no risk of side effects or provoking an adverse reaction, unlike conventional anti-inflammatory drugs and painkillers. There are some small risks and aftercare considerations associated with the procedure to obtain and implant the stem cells but these are relatively minor and/or short-lived - see later.

How quickly after implanting are improvements seen and how long do the effects last?

This seems to be highly variable with some patients improved within a matter of days and others taking 6 weeks or longer before any benefits are seen. However by 12 weeks post-implantation nearly all patients can expect to be showing signs of improvement – this may be in the form of reduced lameness, decreased pain or stiffness (particularly after rest), improved mobility and a greater ability and willingness to exercise. It is worth trying to make

a checklist of your pet's symptoms prior to treatment and make a note of any changes in the weeks and months following MSC implantation to help assess how well your pet is doing.

In many cases, a single treatment has resulted in a sustained improvement such that repeat treatment has not been needed – this seems to particularly be the case in younger dogs with early degenerative joint disease. In other patients the beneficial effects have seemed to fade after 6 to 9 months of treatment. It is difficult to give an average figure as every patient seems to respond so differently but for most patients with moderate arthritis benefits appear to last around 12 to 18 months – sometimes a little longer, sometimes a little less.

Inevitably there are always a small proportion if animals who fail to respond significantly to treatment with MSCs. This may be due to the presence of generalised/systemic illness, overwhelming problems elsewhere (e.g. spinal/back pain) or other mechanical factors requiring surgical intervention (such as a ruptured cruciate ligament).

Can treatment be repeated?

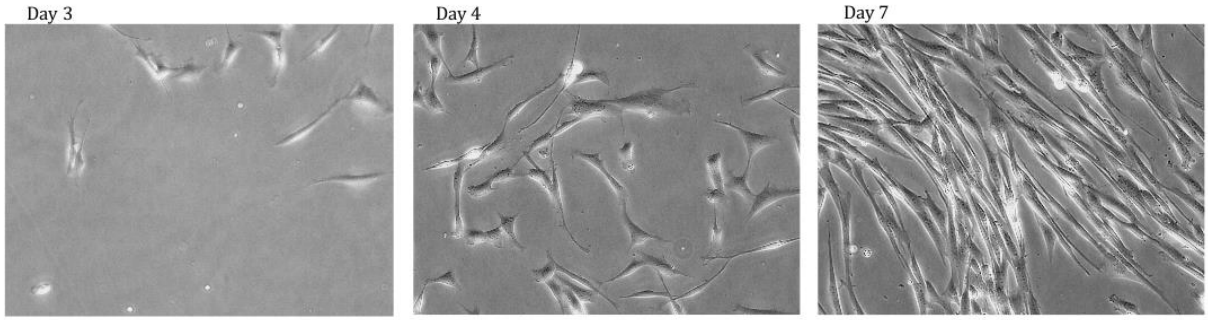
Treatment with MSCs can be repeated as often as needed throughout your pet's life. A sample of MSCs are cryogenically preserved by the lab and these can be used to culture more cells as needed. A further sample of your pet's blood may need to be sent to the lab to assist with the growth of new cells (see later). Repeat treatment with stem cells from the lab is done at a reduced cost. Note that storage of the 'reserve' stem cells at the laboratory is included in the initial treatment cost for the first three years – after this there will be additional storage fees to pay.

Can MSCs be used with other treatments?

Yes, MSCs are compatible with a range of conventional and regenerative treatments. Recent studies have shown how PRP therapy can help facilitate stem cells and certain class-4 laser treatments (such as K-laser) can work to activate the MSCs. Treatments which assist cartilage health such as pentosan polysulphate (eg Cartrophen) are also compatible and may be even more effective when used alongside MSCs and other regenerative techniques.

How are these stem cells obtained?

The stem cells are typically removed - or 'harvested' - from your pet via a simple operation to remove a teaspoon of stem-cell rich fat (adipose tissue) from underneath the skin. This is usually from an area of fat in the groin (inguinal fat) but can be from just inside the abdomen (falciform fat). These areas of fat are particularly dense in MSCs. The fat is then chilled and sent to the laboratory via same-day courier as it is imperative that the cells are kept alive (as with blood and organ donation). A sample of your pet's blood is taken and sent with the fat as this is used by the lab to help the stem cells grow and multiply. After a few weeks of growth and multiplication the lab will have grown sufficient stem cells (several million) to enable treatment. These cells are then concentrated into small vials and cryogenically preserved before being dispatched to the practice via same day courier in specially insulated boxes containing dry ice.



Stem cells multiplying in the lab

How are the stem cells implanted?

Implantation is relatively straightforward and usually performed under sedation. For joints, an area of 4-6 inches around the joint will need to be clipped of hair and then thoroughly cleaned to ensure complete sterility. The stem cells are then defrosted before being inserted into the centre of the affected joint using a long needle. In some instances stem cells may be used systemically via the bloodstream and in these cases the stem cells are given via an intravenous catheter (usually without need for sedation).

What aftercare is required after the stem cell 'harvest' procedure?

As the initial stem cell harvest procedure involves a general anaesthetic and a small operation, there is a little more aftercare required than the subsequent implantation.

The incision in the groin used to retrieve the fat sample may have dissolvable stitches or may have removable sutures that will need removing by a nurse after 10 days - you should be told which is applicable to your pet upon discharge. Either way, it is imperative that they are not allowed to lick the area so an elizabethan collar (or similar) should be used at all times to reduce the risk of self-trauma. Your pet should be kept in a clean, dry environment and kept rested for 10 days after the procedure. Short lead walks of up to 10 minutes are acceptable but do not do more than this until you have been given the green light to do so after a nurse has checked the wound and removed any stitches. Nurse checks are usually performed after 7-10 days (usually 10 days if stitches need to be removed).

The area of groin used for the harvest has a very rich blood supply and is subject to a lot of movement so it is not unusual for heavy bruising to appear in the days after the operation. This can be quite extensive in some cases but do not be alarmed as it is not unusual and will resolve over a week or so. If your pet will let you then a an ice pack applied to the area 3-4 times per day for the first 2 days can be quite helpful. If you are worried by the amount of bruising then do not hesitate to contact us for re-assurance (emailing a photo is useful)

You may also notice that an area of hair has been clipped from your pet's neck and there may be some bruising here too - this is because a reasonably large amount of blood needs to be obtained from your pet to help the lab culture the stem cells. If this area looks sore then apply a little arnica, aloe or antiseptic cream (savlon/sudocrem).

What aftercare is required after stem cell implantation?

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Aftercare following MSC implantation is usually very minimal though this does vary a little depending on the patient and area being treated. The injection sites are tiny and may not be visible but monitor the clipped area of skin for signs of bruising, swelling or discharge.

After being discharged, we normally recommend two days of complete rest in a warm, dry and clean environment – cleanliness is important to avoid the injection sites becoming infected. This should be followed by two weeks of gentle lead walks (up to 20 or 30 minutes twice daily) before resuming your pets normal exercise regime. It may be that we advise moderating this going forward to help assist with the management of your pet's condition.

There is no need for post-operative check following implantation though we normally recommend a check-up with your vet or orthopaedic surgeon about 6 weeks after implantation to review progress.