New and Emerging Pain Treatments: Stem Cells, PRP, and Beyond

Michael C. Petty, DVM, CVPP, CVMA, CAAPM, CCRT
Canine Rehabilitation Institute, Inc.
Wellington, FL

Stem cell therapy

Not exactly new but not mainstream either. Stem cell therapy is an FDA approved procedure using autologous stem cells derived from mesenchymal cells. Vet Stem is the original and best known. There are some do-it-yourself companies out there also where you process the samples yourself. Stem cell therapy's most common use is to treat osteoarthritis, tendonitis and polyarthritis. It has other uses in veterinary medicine including inflammatory and immune mediated diseases. It will probably be many years before all the benefits and limitations of this treatment is known. Research in stem cell therapy in veterinary medicine has mostly involved mesenchymal cells from adipose tissue. They are easily harvested and can become one of several cell lines including cartilage. Other sources are bone marrow, periosteum, trabecular bone, synovial, skeletal muscle and deciduous teeth. Since stem cells are not specialized, they can renew themselves for long periods through cell division. They can also be induced to become specialized cells which seem to differentiate into the types of cells they are needed to be. Commercial labs have a decided advantage. Cells can be banked without the need for additional surgery to harvest new cells. Cell counts are done and you know how many cells there are per injection. They can be checked for infection. They can be diluted for IV injections. Current results: 80% of dogs have significant improvement in the pain from OA which lasts 3-24 months. Contraindications and concerns. They cannot be harvested from dogs with cancer, infection or from lipomas. There have been studies done that look at post-mortems of dog joints that have had therapy and what is found is not really cartilage that has grown back.

Platelet Rich Plasma has been quite popular in the equine field but is still young in the small animal field. Platelets release cytokines, and three different growth factors. Recent research results in human medicine have shown some disappointing results. However there is great research in equine medicine with really good results. Few studies in dogs have been done with good results. One recent one found that platelets are prematurely activating and pretreatment with prostaglandin E1 may stop that. Future studies utilizing this method are needed. There is nothing in platelets that stop pain, but rather pain is stopped secondary to rapid healing and return to function. Blood clots also promote healing but platelets have been shown to be superior.

Magnet therapy

There are two types of magnets, static and pulsed electro magnetic field (PEMF). Static magnets have little to no known effect on the reduction of pain. PEMF studies have shown mild decreases in pain. One human study showed they worked best when used a minimum of 4 hours daily for 6 weeks. Not practical for anyone. Clinical and anecdotal evidence seems to show that they do work in some cases. The Assisi loop is probably the device most studied. I am still waiting for some good research. It should not be hard to do which makes me wonder about them. There are also blankets and mats for the dog to rest on. No studies found.

Glial cells

These are immune cells found within the neural system. They were long thought not to have any neuronal activity as they have no axons or dendrites. Research over the past two decades has clearly shown their relationship with nerves and the spinal cord. They both create and maintain pathological pain states and dysregulate the action of opioids. There was probably some advantage for the immune system to talk to the brain during times of immune challenge. This was probably either some evolutionary advantage or, more likely, a dysregulation of ancient survival circuitry. The result is that the immune and nervous systems do not operate independently of one another. The brain can dymanically regulate the immune system and the immune system can effect the brain with proinflammatory cytokines. This means that we can get sickness induced hyperalgesia, for example when we get the flu and it comes with aches and pains. There is a special interaction between glial cells and opiates. Opiates activate glial cells to release interleukin 1. Glial cells also dysregulate opioids. The resulting pain control is a balance between these two interactions. In the case of chronic opioid administration, it can favor the glial side causing more pain. There are some new treatments in the works where we can get glial cells out of the way using glial blocking drugs. The problem can also be avoided by using opiate isomers that glial cells can't see: All opiates have positive and negative isomers. Only the negative are active against pain. This is also true of the opioid antagonists such as naloxone. Glial cells are not stereoselective, therefore they could be blocked by a (+) naloxone which would have no effect on the opioid receptors for pain which would only see (-) naloxone. There are several drugs in the works that would do this.

TRPV1 receptors are one of the main chronic pain receptors

This is also the receptor that is activated by capsaicin, the "spicy" in chili peppers. These receptors are sensitized and activated by many endogenous inflammatory products. However, when capsaicin is used on these receptors, there is a paradoxical reaction of nociceptor activation followed by subsequent analgesia. This comes about as a result of receptor desensitization, nociceptor

dysfunction, neuropeptide depletion and nerve terminal dysfunction. This is why the more spicy foods you eat the less it burns over time. Resiniferatoxin is an artificial TRPV1 agonist that is being used to treat intractable pain from bone cancer and end stage OA. It is injected into the spinal cord dorsal horn that is responsible for input from the painful limb. There have been some encouraging results with reductions of 70-90% of pain over pre-treatment measures, and the results last for months.

Substance P Saporin

Substance P is an inflammatory substance which activates the NK1 receptor and causes pain. It is one of the players involved in chronic pain. Substance P Saporin is a toxin that inactivates the NK1 receptors. At the University of Pennsylvania, research is being done where an intrathecal injection of SP-SAP causes loss of NK1 cells and dendrites in Laminae I and II in the dorsal horn. A significant reduction of pain similar to the studies using resiniferatoxin is being seen.

Prolotherapy also known as PrT and Proliferative therapy is an alternate injection based therapy for chronic musculoskeletal disorders. It is most often used to treat tendinopathies. The theory is that after an injection of an inflammatory substance is injected into an injured area, inflammation or cell death occurs which then activates a healing cascade. There are wildly mixed results and many of the good studies show short term benefits with long term detriment.