

About 40% of all cats have clinical signs of osteoarthritis but often these signs are infrequently recognised and, as a result, the condition is underdiagnosed. In part two of a two-part series, Sorrel Langley-Hobbs MA BVetMed DSAS(O) DipECVS FHEA MRCVS, chair in small animal orthopaedic surgery, RCVS specialist in small-animal surgery and Dr Edwina Gildea MVB MRCVS, Zoetis companion animal veterinary lead, outline the treatment, pain-management options and what the future hold for cats with osteoarthritis

## TREATMENT

Once you have established that a cat does have osteoarthritis (OA), a treatment plan needs to be formulated. The aims for treatment are to treat the primary problem (pain), maintain mobility, and limit progression of the disease. A multimodal approach to management should be considered while also factoring in the burden of care and the relative impact on owner compliance. The following categories form the structure around a comprehensive management programme:

- Pain management therapy
- Dietary modulation
- Weight loss if required
- Physical therapy
- Exercise
- Environmental modification
- Surgery

## PAIN-MANAGEMENT THERAPY

Pain-management therapy is the pivotal point around which all other supportive management is implemented. For this reason, it is essential to not only diagnose the condition but to treat the associated pain with clinically effective medication. In comparison to dogs, there are limited drug therapies licensed for use in cats. Furthermore, not all therapies are licensed in all countries. As such, many medications used by veterinarians today do not have safety and/or efficacy data to support their use in the cat. Non-steroidal anti-inflammatory drugs (NSAIDs) are the main treatment modality in most species, and the cat is no different. Although robenocoxib and meloxicam are the only NSAIDs licensed for long term use in the cat, they are not licensed in every country.

Multimodal analgesic therapy can be applied, but consideration needs to be taken to recognise what is licensed as well as what is feasible for the owner to implement for a condition that requires long term management daily. Oral delivery of medication may be difficult for pet owners whether liquid or tablet/pill. In fact, difficult treatment paradigms may disrupt the human-animal bond. Evidence based medicine suggests veterinarians should choose a pain medication with high- level evidence to support use, ideally, with efficacy and safety proven in the cat in multicentre controlled trials. Pain medication that is easy-to-deliver is another important consideration for selecting a pain management treatment for cats with OA.

## NSAIDS, OLDER CATS AND RENAL DISEASE?

Older cats with OA may have concurrent disease that may be of concern to vets when considering administering drug therapy, particularly as it may need to be given long term. Routine blood and urine analysis is recommended prior to starting NSAID therapy to investigate for renal or hepatic problems. It is also advisable to measure blood pressure as inhibition of cyclooxygenase (COX) in the kidneys can exacerbate preexisting hypertension. If cats are diagnosed with chronic kidney disease (CKD), then NSAIDs can still be used with appropriate checks and follow-ups.<sup>13</sup>

## NUTRACEUTICALS AND DIETS

Nutraceuticals are food supplements with potential health benefits. The claims for these products include antiinflammatory properties, cartilage regeneration and delayed cartilage degeneration, with the potential to improve mobility and decrease stiffness in animals. However, there is currently no definitive, unbiased *in vivo* measurable evidence that they work, and there is little evidence available for evaluating long-term impact. Diets rich in omega-3 fatty acids are recommended for cats with degenerative joint disease (DJD).<sup>14</sup> Studies have provided evidence that n-3 fatty acid supplementation can reduce the inflammatory and matrix degradative response elicited by chondrocytes during OA progression.<sup>15</sup> These diets may also assist with weight loss.

## WEIGHT REDUCTION IF NEEDED

While obesity has not been proven as a risk factor for OA in cats, it is notable that approximately 14% of older cats suffering from OA are obese.<sup>16</sup> Adipose tissue secretes a mixture of cytokines that circulate throughout the body, contributing to the pathology of many diseases, including DJD, and to the hypersensitisation process in general. Either maintaining or regaining a lean body condition score is central to the treatment of chronic pain.<sup>17</sup> Weight loss in overweight or obese cats with OA should be encouraged by the use of low-calorie diets and encouraging exercise. The latter might be improved by environmental modification. Regular monitoring by revisits including weight measurement is recommended to maintain motivation.

#### EXERCISE

Encouraging the cat to move around more can be achieved using toys, feeding puzzles, playing chase games and cat nip toys. A cat tower/scratcher with different levels that are easily accessible may encourage more activity. Owners should try to interact with their cats and encourage play several times daily. Establishing a baseline of 'normal' for each cat also acts as a reminder to the cat owner of what their cat used to enjoy doing, so they can find ways to continue to provide that as part of their cat's OA therapy.

#### **ENVIRONMENTAL MODIFICATION**

Altering the cats' environment to accommodate its disability associated with osteoarthritis can have beneficial effects. Cats are creatures of routine and masters of their territory: cat owners can help to restore their cats' routines disrupted by OA pain. Modifications to the environment can be achieved by ensuring the cat has easy access to its food and water bowls, sleeping area and litter tray, and if this is not the case, providing access by means of steps or a ramp. A litter tray with a low side can aid entry and prevent accidents in the house. In houses with multiple floors, consider multiple litter trays so the cat doesn't have to tackle the stairs to get to the litter tray. Ensure the cat flap/door is easily accessible both from inside and outside. These slight modifications may lead to less effort on the cat's part for activities of daily living and improve their life quality overall.

#### PHYSICAL THERAPY

Physiotherapy and hydrotherapy will not suit every cat, but with an amenable animal these therapies can have advantageous effects. Where possible, a programme should be designed, implemented, and monitored by a qualified veterinary physiotherapist. Passive range of motion exercises and massage can be performed at home and be useful at reducing muscle pain.<sup>14</sup> Cold and heat therapy, laser, ultrasound, and shock wave are other therapies that could be considered, although there is little evidence published about their usage in cats. Acupuncture can be beneficial and has been used in cats with arthritis. It may take several sessions before an improvement is seen and then intermittent top up treatments can be used for maintenance. Acupuncture can be used in combination with analgesic drugs.

## SURGERY

There may be an underlying condition that is causing or predisposing a cat to osteoarthritis such as cranial cruciate ligament rupture, elbow dysplasia, patellar luxation, hip dysplasia and traumatic injury. Underlying problems with the joint lead to degeneration and inflammation causing synovitis, loss of cartilage and sclerosis of the subchondral bone. Elimination of these underlying problems can be an important part of managing or preventing and limiting osteoarthritis formation. Surgical correction of joint stability, removal of osteochondral fragments, and correction of inappropriate loading of the joint is often needed to slow the progression of osteoarthritis and give the best outcome. Salvage surgery by joint fusion, replacement or excision can all be performed in the end stage joint where medical management and environmental modification are no longer deemed effective.

## WHAT DOES THE FUTURE HOLD FOR CATS WITH OA?

As previously discussed, the multimodal management of OA relies on effective analgesia. Although current analgesic options are effective, current therapeutics may be difficult for pet owners to administer to a cat, there remains some limitation around the availability of licensed medications in different countries, and safety considerations may limit long term use or use in the face of concurrent disease, eg. CKD. A new analgesic approach shows potential – a therapeutic antibody that targets a novel driver in the pain pathway – nerve growth factor (NGF). Research into NGF and its interaction with receptor tropomyosin receptor kinase A (TrkA), has led to some interesting findings that could see pain management move into a new era for cats. It is interesting to note that this is a different mechanism than the more commonly known prostaglandin pathway targeted by NSAIDs, including EP4, 'piprant' NSAIDs. This is the first novel OA pain pathway showing promise for new therapeutics in several decades.

## NGF - A KEY DRIVER IN THE PAIN PATHWAY

Studies have identified a new key player in the transmission of pain associated with osteoarthritis (OA) in people, dogs and cats.<sup>18</sup> In adults, Nerve Growth Factor (NGF) plays a significant role in pain signalling. NGF is an integral component of central sensitisation (wind up), spinal cord plasticity and maladaptive pain signalling which inevitably results in hyperalgesia (wind up).<sup>19</sup> As a result of these research findings, several anti-NGF/ TrkA signalling strategies have been investigated for their efficacy and safety in modifying pain. Therapeutic antibodies (also called monoclonal antibodies (mAbs)) that bind to NGF and thereby block the pain signal are leading the way within this new field with pilot safety and efficacy studies showing promise in cats.<sup>20</sup>

## NGF INTERACTS WITH IMMUNE CELLS IN THE JOINT

NGF is elevated in osteoarthritic joints in the dog.<sup>21</sup> Not only is it released from damaged tissues, but it is also found in some immune cells associated with pro-inflammatory mediators.<sup>22</sup> The same receptor, TrkA, also appears on these cells.

# THERAPEUTIC ANTIBODIES ARE FUNDAMENTALLY DIFFERENT

Therapeutic antibodies are metabolised differently to drugs and, generally, have different safety profiles. They are broken down within cells into amino acids and peptides and therefore are not metabolised in the liver or kidneys, converted into reactive or toxic metabolites, or excreted in urine. Thus, they are unlikely to cause drug-drug interactions or to induce liver or kidney toxicity.<sup>18,23</sup> Monoclonal antibodies are cleared via multiple potential pathways:

- 1. Binding to target
- 2. Antidrug antibodies in circulation
- 3. Flow out of capillaries into interstitial space, taken up by cells and catabolised

#### **SUMMARY**

Feline OA is very common and there is opportunity to diagnose this painful condition in more cats. Screening cats early establishes a baseline for 'normal' for that cat. Check lists can help to identify signs of osteoarthritis in cats. There are many opportunities for intervention including analgesics, environmental adjustments, activity, and surgery as needed. There are also new antibody therapies on the horizon. With prolonged duration of activity (~1 month) and easy administration to cats with a subcutaneous injection, this new therapeutic antibody approach may be the solution that veterinarians, cat owners and cat suffering from OA have been waiting for.

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