Sometime around when “Ursa,” a domestic shorthaired cat, turned 13 years old, she began struggling to jump on the couch. She started bunny hopping with her rear legs to climb stairs. Her stiff-legged gait and decreased range of motion became obvious.

Ursa’s owner recognized the signs of degenerative joint disease (DJD) in her cat. A board-certified veterinary behaviorist, Margaret E. Gruen, DVM, PhD, DACVB, was working at the Comparative Pain Research and Education Centre at North Carolina State University (NC State) in Raleigh, where she studied chronic pain in cats with DJD and investigated treatments to help them deal with the pain associated with the disease.

“It took a while for me to put together all the signs Ursa was showing and recognize how much less she was able to do,” Dr. Gruen says. “The most remarkable one was that she stopped jumping up to the bathroom sink in the morning, though she would make an intermediate jump to get there. She would still jump up to sit with me on the couch, but she stopped being able to cleanly clear the jump with her back legs. The changes were very subtle at first, and it really brought home for me how difficult it can be for owners to detect pain in their cats.”

A clinical trial was underway at NC State’s Veterinary Hospital to evaluate an anti-nerve growth factor antibody for the treatment of DJD-associated pain, so Dr. Gruen enrolled Ursa. To confirm a diagnosis of DJD, an orthopedic exam was performed. During the orthopedic exam, Ursa reacted strongly, pulling away and meowing when her rear legs were extended. Next, radiographs were taken to confirm the clinical suspicion of the disease, which can show up as changes, such as osteophytes or bone spurs, in the outline of the bones making up the joint, and as mineralization or calcification of tissues near the joint.

Ursa’s diagnosis of DJD was confirmed. Her radiographs showed the presence of osteophytes around the hip and thickening of the head of the femur, the part of the bone that makes up the “ball” of the hip’s ball-and-socket joint. Her radiographs matched the findings from her orthopedic exam, as well as the clinical signs she was showing at home. In many cats, as well as in dogs and people, clinical signs do not always match radiographic evidence or orthopedic exam findings, thus overlapping evidence from all three was required for participation in the study.

“Ursa was eligible for the study, and was fitted with an activity monitor to objectively measure the distance she traveled in order to obtain a baseline reading of her overall activity and activity pattern,” says Dr. Gruen. “Along with changes to subjective outcomes of clinical metrology instruments, such as standardized questionnaires used to track progress in the study, it was expected that Ursa’s overall activity would increase if she received the active treatment.”

The most common disease in cats, DJD, is believed to affect up to 92 percent of felines.¹
apparent cause. Osteoarthritis, an age-related condition seen in older cats, is the most common form of primary DJD. Secondary DJD is the result of trauma or other underlying condition, such as hip dysplasia, nutritional deficiencies or breed-specific cartilaginous disorders such as in Scottish Fold cats.

DJD results in the progressive destruction of joints, affecting synovial and cartilaginous joints. Synovial joints have hyaline cartilage covering the ends of bones, and the bones are joined by a fibrous joint capsule and ligament. The joint is filled with synovial fluid produced by an inner lining of cells, the synovium, inside the joint capsule. These characteristics allow normal, smooth, pain-free motion of synovial joints, but when DJD occurs, all the components of the joint start to degenerate, resulting in poor function and pain. Hips, stifles (knees) and elbows are the most commonly affected synovial joints in cats. Degeneration of cartilaginous joints, which are connected entirely by fibrous cartilage, also occurs and can be associated with pain.

“Surprisingly, little is known about DJD in cats. We need to better understand the prevalence of DJD, and whether it relates to age, breed, sex, or a cat’s indoor/outdoor status,” says B. Duncan Lascelles, BSc, BVSc, PhD, DSAS(ST), DACVS, DECVS, professor of small animal surgery and pain management at NC State’s College of Veterinary Medicine, and the principal investigator at the Comparative Pain Research and Education Centre.

Although several features of DJD are similar in cats and dogs, differences include the radiographic presentation of the disease. For example, cats frequently develop bilateral disease, affecting the same joint on both sides of the body, and thus overt limping or lameness may not be seen. Instead, there may be a gradual decrease in the ability to perform some of the activities a cat used to do easily and smoothly.

Owners don’t typically interact with cats in the same way as with dogs, which could impact their ability to detect reduced activity and mobility. For example, most cats don’t go for walks with their owners or jump into the back of a car.

“Treatment options are lacking, in part, due to the difficulty in accurately assessing pain and disability in cats,” Dr. Gruen says. “There is a critical need for safe and effective analgesics to treat the pain associated with DJD, particularly in the high percentage of cats with chronic kidney disease (CKD) in which certain treatments may not be tolerated. The biggest problem in developing analgesics in cats has been in measuring their pain.”

Detecting pain in cats with DJD is challenging. Owners have difficulty determining whether their cats’ lack of jumping and decreased jumping heights
are due to normal aging or musculoskeletal pain. Until recently, there has been little information about what behaviors should be evaluated and about what input owners can provide to help determine whether their cats are experiencing chronic pain associated with DJD.

Identifying Biomarkers of DJD

Better understanding pain in cats with DJD was the goal of a study led by Dr. Lascelles in 2014. Funded by the Winn Feline Foundation, a nonprofit organization that supports feline health research, the study aimed to measure inflammatory mediators in the blood of cats with DJD and in cats with DJD and CKD to identify biomarkers, or a biomarker profile, associated with DJD.

“We believed that cytokine/chemokine profiles in the blood could lead to novel targets for developing effective, safe analgesics in cats, especially for those with concurrent DJD and CKD,” explains Dr. Lascelles. “The evidence suggested that DJD pain in cats is due to an altered state of immune function resulting in inflammatory mediators, cytokines and chemokines, building up in the body and producing pain. This essentially would be a blood test to determine chronic pain.”

The study included cats being treated at NC State’s Comparative Pain Research and Education Centre. Veterinary physical, orthopedic and neurological evaluations were performed on all cats, and radiographs were taken of each joint and spinal segment to determine the overall radiographic burden of DJD in each cat. During the orthopedic examination, joints were evaluated for pain and scored using a standardized pain scale.

“The results of the orthopedic and radiographic evaluations allowed us to generate orthopedic pain scores, which were the sum of scores for individual joints, and radiographic DJD scores, the sum of standardized scoring for individual joints,” Dr. Lascelles says. “We were then able to categorize cats according to their severity of pain and radiographic DJD.”

One of the first veterinary studies to examine the inflammatory aspect of chronic pain, this research provided insights about cytokine and chemokine concentrations in cats with and without DJD. “Ultimately, this work was a launching point for further research,” says Dr. Lascelles.

“Dr. Gruen led the analyses and evaluated the concentration of these cytokines and chemokines in blood samples from 186 cats,” he continues. “In total, these cats represented a broad range of severity on radiographic and orthopedic evaluations and as categorized by DJD scores and pain scores.”

The study, published in the January 2017 issue of *Veterinary Immunology and Immunopathology*, reported the results. “Our findings suggest there are measurable changes in cytokine concentrations in cats with DJD that reflect their association with DJD burden and pain,” Dr. Gruen says. “However, further work is needed to determine if combinations of cytokines help us distinguish between cats with painful DJD and normal cats.”

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Margaret E. Gruen, DVM, PhD, DACVB, a board-certified veterinary behaviorist
Investigating Possible Pain Treatments

Among the challenges in treating cats for chronic pain associated with DJD is a lack of knowledge about safe, effective drug therapies and a lack of clinical screening tools to identify cats with DJD mobility impairment. The use of nonsteroidal anti-inflammatory drugs (NSAIDs) to manage pain has been effective for treating many diseases involving chronic pain; however, in cats, only one NSAID, meloxicam, is approved for long-term use, but its use is limited to Europe, Canada and Australia.

“There are concerns about the long-term use of NSAIDs in cats, especially since the majority of cats with DJD-associated pain also have chronic kidney disease,” Dr. Gruen says. “However, administration of NSAIDs in cats with CKD is typically well-tolerated unless their appetite is decreased or they become dehydrated.”

Dr. Gruen was the lead investigator of research, published in PLOS ONE in July 2015, to evaluate the effectiveness of a low-dose oral meloxicam to improve mobility in cats with DJD-associated chronic pain. The study included 66 cats with DJD whose owners had noted their impaired mobility. Cats were given a placebo or meloxicam for 21 days, followed by a placebo for 21 days during a washout period, and then the reverse treatment of a placebo or meloxicam for 21 days. The cats wore activity monitors throughout the study and owners completed questionnaires noting behavioral differences in their cats’ ability to perform a variety of behaviors that are frequently impaired in cats with DJD activity levels. “We hypothesized that a low-dose of oral meloxicam given once daily would increase activity, but activity would significantly decrease following withdrawal of meloxicam,” she says.

The study also helped evaluate the validity of the Feline Musculoskeletal Pain Index (FMPI), a questionnaire developed at NC State in which owners assess the effects of chronic pain in their cats based on its impact on their everyday behaviors. Other tools used to determine the effectiveness of meloxicam were the Client-Specific Outcome Measures (CSOM) questionnaire, in which owners described changes in their individual cat’s behavior related to treatment, and assessed their cat’s quality of life and temperament.

“We saw significantly higher levels of activity in the meloxicam-treated cats,” says Dr. Gruen. “Thus, we considered the low-dose oral meloxicam, about two-thirds of the dose approved in Europe, as effective in managing DJD-associated chronic pain. Although we enrolled cats with mild-to-moderate renal insufficiency, overall changes in creatinine and blood urea nitrogen were not observed.”

A more recent pain-management study, one that Dr. Lascelles describes as “the biggest leap forward in chronic pain

Tips on Caring for Cats with DJD

Degenerative joint disease (DJD) is the most common disease in cats. It is readily recognized as changes in the ability to move vertically, or jumping up and down, and a loss of the normal, fluid movement cats have, with their movement becoming stiff or stilted. Experts offers these tips to help breeders and owners care for cats with DJD.

- **Seek a veterinarian with expertise in understanding and treating DJD** to help find the best therapy for your cat. There may be medications, nutritional diets, nondrug therapies, and environment modification options to help decrease the impact of chronic pain.
- **Prompt treatment is important** in maintaining mobility by helping to minimize the widespread negative impact of pain on the musculoskeletal system, and the affective system related to feelings and anxiety.
- **Ask your veterinarian** whether a diet rich in omega-3 fatty acids might help decrease inflammation in your cat.
- **Keep your cat in ideal body condition** and encourage activities that promote exercise. Healthy weight is important in reducing the progression of disease. In dogs and humans, there is evidence that maintaining good body condition can dramatically reduce the risk of developing DJD, as well as the severity of DJD.
- **Take steps to make sure everyday items are accessible.** Use stools or steps to help your cat reach favorite areas, place food and water bowls in convenient locations, and be sure the litter box is handy. Some cats with DJD may not be able to maneuver the litter box easily, so modifications to the front of the box may be needed to make sure your cat can easily get in and out of the box.

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management in cats,” involved using a feline-specific anti-nerve growth factor (NGF) antibody, called NV-02, now designated as frunevetmab (made by NexVet Biopharma), to help improve mobility in cats with DJD-associated pain.

Dr. Gruen, who led the study of 34 client-owned cats, says, “We found that a single dose of anti-NGF antibody would alleviate pain and improve mobility for up to six weeks, allowing owners to notice improvements reflected in their scores on their questionnaires. NV-02 appears to offer great promise as a treatment for long-term pain alleviation in cats with chronic DJD-associated pain.”

This was the study that Ursa participated in, though Dr. Gruen was blind to what treatment her cat received during the study. “I was so worried about being wrong, as I know about the dramatic placebo effect that occurs in these studies, and didn’t want to be imagining her improvements,” Dr. Gruen says. “I would take video and compare it to before treatment to be sure, but the changes were undeniable.”

“The beneficial effects seen with the anti-nerve growth factor antibody were large enough to overcome the very strong caregiver placebo effect seen in chronic pain studies in cats, and certainly the most effective therapeutic we have evaluated to date,” Dr. Lascelles says.

Despite the challenges treating DJD in cats, considerable progress has been made in the past 10 years, thanks to the work being done at NC State’s Comparative Pain Research and Education Centre. Hopefully, in the future, the most common disease in felines may become one in which effective clinical treatment is commonplace as well.

Meanwhile, Ursa continues to receive pain management. She has even begun successfully jumping up to the bathroom sink and the couch. “Once you see how big a difference pain therapy can make, you never want them to go back to how they were before,” says Dr. Gruen.


Purina appreciates the support of the Winn Feline Foundation, and particularly Glenn A. Olah, DVM, PhD, DABVP (feline), president, in helping to identify this topic for the Purina Pro Plan Cat Update newsletter.
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