# Cognitive Dysfunction in Cats: Clinical Assessment and Management

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### **Key Points**

- Increasing numbers of cats are living to old age, and they commonly develop behavioral changes.
- The behavioral changes reported most frequently are loss of litter box training and crying loudly at night.
- The most typical causes of these problems are cognitive dysfunction syndrome (CDS), osteoarthritis, systemic hypertension (commonly secondary to chronic kidney disease or hyperthyroidism), hyperthyroidism (even without hypertension), deafness, and brain tumors.
- Almost one-third of cats 11- to 14years of age develop at least one geriatric-onset behavior problem that appears to relate to CDS, increasing to over 50 percent for cats 15 years of age or older.

### Introduction

With improvements in nutrition and veterinary medicine, the life expectancy of pet cats is increasing. The number of aging cats seen by veterinarians has increased considerably in recent years. For example, there has been a 15% increase in cats over 10 years of age seen at veterinary clinics in the United States.¹ Currently, it is estimated that there are over 2.5 million senior cats in the United Kingdom,² while between one-third and one-half of pet cats in the United States are 7 years of age or older.³ Hence, good management of these individuals is becoming an increasingly important consideration for small animal veterinary practitioners.

Unfortunately, accompanying this growing geriatric population are increasing numbers of pet cats with signs of altered behavior and apparent senility. Behavior changes may result from many different disorders (Figure 1) including systemic

### Glossary of Abbreviations

CDS: Cognitive Dysfunction Syndrome

**CKD:** Chronic Kidney Disease **CT:** Computed Tomography

**DM**: Diabetes Mellitus

ECG: Electrocardiogram

FeLV: Feline Lukemia Virus

**FIP:** Feline Infectious Peritonitis **FIV:** Feline Immunodeficiency Virus

**FLUTD:** Feline Lower Urinary Tract Disease

GI: Gastrointestinal

MRI: Magnetic Resonance Imaging

OA: Osteoarthritis

UTI: Urinary Tract Infection

illness, organic brain disease, true behavioral problems, or cognitive dysfunction syndrome. Diagnosis involves a full investigation looking for underlying illness (Figure 2) and assessment for behavioral problems. Once these have been ruled out, CDS should be considered, although ante-mortem this is a diagnosis of exclusion. The most commonly seen behavioral changes include spatial or temporal disorientation, altered interaction with the family, changes in sleep/wake cycles, housesoiling with inappropriate urination/defecation, changes in activity, and/or inap-

propriate vocalization (often displayed as loud crying at night) (Figure 3).

# Potential Causes of Behavioral Changes in Geriatric Cats

Perhaps the most common causes of behavioral changes in older cats are CDS, osteoarthritis (OA), systemic hypertension, hyperthyroidism, deafness, and brain tumors. Much has been written elsewhere about the diagnosis and treatment of other potential causes of behavioral disorders in old cats so this paper will concentrate on CDS.

## Cognitive Dysfunction Syndrome

Cognitive dysfunction syndrome is the term applied to agerelated deterioration of cognitive abilities, characterized by behavioral changes (Figure 3), where no medical cause can be found.<sup>4-7</sup> A survey looking at older cats (7- to 11-years of age) revealed that 36% of owners reported behavioral problems in their cats, and this increased with age to 88% in cats between 16 to 19 years of age.<sup>8</sup> A more recent study suggests that 28% of

## Figure 1: Potential Causes of Behavioral Changes in Geriatric Cats

- Cognitive Dysfunction Syndrome (CDS)
- Osteoarthritis (OA)\*
- Systemic Hypertension (high blood pressure may either be primary or secondary to hyperthyroidism, chronic kidney disease or possibly, diabetes mellitus, acromegaly or hyperadrenocorticism)
- Hyperthyroidism
- Chronic Kidney Disease (CKD)
- Diabetes Mellitus (DM)
- Urinary Tract Infection (UTI)
- · Gastrointestinal (GI) Disease
- · Liver Disease (hepatic encephalopathy)
- · Reduced Vision or Hearing
- Brain Tumors (e.g., meningioma, lymphoma)
- Neurological Defects (either sensory or motor deficits)
- Infectious Disease (e.g., FIV, FeLV, toxoplasmosis, FIP)
- Pain and/or Inflammation in General (e.g., dental or periodontal disease)
- · True Behavioral Problems, Stress
- \* The importance of OA should not be overlooked.<sup>29</sup> Radiographic evidence of degenerative joint disease is present in 70 to 90% of cats over 10 years of age.<sup>30-32</sup> Associated pain and/or dysfunction can result in reduced activity and mobility, aggression, altered interactions with the family, and/or loss of litter box training. Owners can help their arthritic cats by adjusting their house; for example, by moving food and water bowls to lower surfaces, adding ramps to allow easier access to favored sleeping areas, providing deep comfortable bedding that will support and protect the cat's joints (heated beds can be particularly soothing), and placing low-sided litter boxes within easy reach of the cat.

pet cats aged 11- to 14-years develop at least one geriatriconset behavior problem that appears to relate to CDS, and this increases to over 50% for cats 15 years of age or older. Excessive vocalization and aimless activity are the most common problems in this older age group.<sup>7,9</sup>

The cause of the syndrome is still unknown, but 1) compromised cerebral blood flow, and 2) chronic free-radical damage are both believed to be important. Numerous vascular changes can occur in the brains of old cats, including a decrease in cerebral blood flow, the presence of small hemorrhages around the blood vessels, and a form of arteriosclerosis. In addition, the brain of an elderly cat also may be subject to compromised blood flow and hypoxia due to heart disease, anemia, blood-clotting defects or hypertension.

Chronic free-radical damage also can occur as cats age. A small amount of the oxygen that is used by cells in energy production is normally converted to free radicals. As cells age they become less efficient, producing less energy and more free radicals. (As a simile think of increasing emissions as a car engine ages and becomes less efficient.) Normally these free radicals are removed by the body's natural antioxidant

defenses, including a number of special enzymes and free radical scavengers, such as vitamins A, C and E. The balance between the production and removal of free radicals can be upset by disease, age and stress. An excess of free radicals can lead to damage, and the brain is particularly susceptible because it has a high fat content, a high demand for oxygen, and a limited ability to repair.<sup>6,11</sup>

Ultimately, chronic damage can eventually lead to disease processes similar to those seen in humans suffering from Alzheimer's disease, with alteration of proteins within nerve cells (e.g., tau hyperphosphorylation) and deposition of protein plaques outside the nerve cells (made from  $\beta$ -amyloid protein). In humans and dogs, genetics, diet and lifestyle choices have all been found to influence the prevalence and pattern of neuropathological changes (particularly  $\beta$ -amyloid plaques) and the nature of the cognitive dysfunction. While these relationships have still to be determined in cats, it is likely that they will be similar.

# Diagnosis and Management of Older Cats with Behavioral Disorders

Gaining a correct diagnosis involves a full investigation (Figure 2). Unfortunately, the diagnosis and management of older cats is often complicated by the concurrent presence of multiple interacting disease processes. In some cases, interacting conditions may worsen clinical signs. For example, OA, chronic kidney disease (CKD) or other causes of polyuria, plus or minus increased fecal urgency with chronic gastrointestinal (GI) disease, or difficult defecation with constipation may each exacerbate apparent loss of litter box training. Concurrent hyperthyroidism and diabetes mellitus (DM) can be very confusing as the clinical signs can be similar and because each condition can affect laboratory findings for the other. For example, DM may suppress the serum thyroxin concentration to within the reference range, 12,13 while the increased protein turnover associated with hyperthyroidism can reduce the serum fructosamine to a lower level than would be expected in a cat with uncomplicated DM.14,15 In some cases, the treatment of one disease may worsen another. For example, treatment of hyperthyroidism can unmask the severity of CKD. 16 Prompt and full investigation is therefore essential if management is to be effective.

It is not always easy for owners to recognize signs of ill health in their cat as they often do not know what signs to look for. Veterinarians need to educate owners as to what they should monitor and encourage them to report any changes in their cat. Owners need to understand that the changes they see are not "normal" and that they may represent the presence of treatable disease. Owners need to monitor their older cats for changes in food and water consumption, body weight, production of urine and feces, and behavior.

The implementation of Senior Health Care Clinics can be

beneficial. While the clinics do need to be tailored to individual cats, in general they should include regular and thorough physical examinations including assessment of body weight, calculation of percentage change in body weight, body condition score, systemic blood pressure, and retinal examination. Ideally, the evaluation also should include in-practice mobility assessment plus full orthopedic and neurological examinations, which can be challenging to perform in cats as they need time to relax and move about on their own volition, preferably on a floor surface that gives them sufficient grip without catching their nails. A blood sample should be collected for biochemical screening, thyroxin concentration and hematology and, where appropriate, serological testing for feline lukemia virus (FeLV) and/or feline immunodeficiency virus (FIV). A urine sample should undergo routine analysis, urine protein to creatinine ratio and, wherever possible, bacterial culture. Initially, most cats will only need to attend a clinic once or twice a year. However, those cats showing significant aging changes may need to attend more frequently for repeated reassessment, monitoring and treatment.

## Management of Cats with CDS

While there are no published studies relating to the treatment of cats with CDS, it is possible to consider potential treatment options by extrapolation from studies of humans with Alzheimer's disease and dogs with CDS. Potential interventions include dietary modification, environmental management and drug therapies.<sup>17</sup>

### Dietary Modification and Environmental Management

Diets enriched with antioxidants and other supportive compounds (e.g., vitamin E, beta carotene and essential fatty acids) are believed to reduce oxidative damage, thus reducing  $\beta$ -amyloid production and improving cognitive function. In humans, studies have shown that high intake of fruits, vegetables, vitamins E and/or C, folate and/or B12 may improve cognition. In addition, alpha-lipoic acid and l-carnitine enhance mitochondrial function, and omega-3 fatty acids promote cell membrane health and have, in humans, been found to be beneficial in the treatment of dementia. Unfortunately, excessive intake of some of these compounds can be harmful. In general, combinations of these compounds are believed to work best.

There have been a number of studies investigating the potential benefit of various supplements in dogs with CDS. <sup>11,17-19</sup> For example, a study of dogs over 6 years of age, when given a supplement containing omega-3 fish oils, vitamins E and C, L-carnitine, alpha-lipoic acid, coenyzyme Q, phosphotidylserine and selenium (this supplement is sold in the United Kingdon as Aktivait® from VetPlus) over a twomonth period resulted in significant improvements in signs of disorientation, social interaction, and housesoiling. <sup>20</sup> Unfortunately, a different formula is needed for cats as alpha-lipoic

## Figure 2: Investigation of Behavioral Changes in Older Cats Should Include:

- Full history, including the possibility of previous trauma (which may have led to OA), any potential exposure to toxins or drugs, and any recent environmental changes (in the household, family members, diet, etc.). Asking specific questions about alterations in the cat's behavior can help determine how the cat has changed (see below Mobility/Cognitive Dysfunction Questionnaire).
- Full physical examination (including body weight, calculation of percentage change in body weight, body condition score, and retinal examination).
- Assess systemic blood pressure (this is important as hypertension occurs commonly in older cats and produces many of the same signs as CDS).
- Mobility assessment, plus neurological and orthopedic examinations, which can be challenging in some cats.
- Assess hematology and serum biochemistry, including thyroxin level.
- Urine analysis (including urine protein to creatinine ratio and bacterial culture).

Further investigation may include:

- Where appropriate, serological testing for FeLV, FIV, toxoplasmosis or FIP.
- Thoracic, abdominal or skeletal radiography, abdominal ultrasound examination, electrocardiogram (ECG), echocardiography, intestinal endoscopy/exploratory laparotomy, and biopsy collection, as indicated from initial findings.
- Head computed tomography (CT) or magnetic resonance imaging (MRI) testing.

Mobility/Cognitive Dysfunction Questionnaire*					
My cat	Yes	Maybe	No		
Is less willing to jump up or down					
Will only jump up or down from lower heights		٥	۵		
Shows signs of being stiff at times					
Is less agile than previously					
Shows signs of lameness or limping					
Has difficulty getting in or out of the					
cat flap					
Has difficulty going up or down stairs					
Cries when picked up					
Has more accidents outside the litter tray	/ 🗖				
Spends less time grooming					
Is more reluctant to interact with me					
Plays less with other animals or toys					
Sleeps more and/or is less active					
Cries out loudly for no apparent reason					
Appears forgetful					

\*Ensure there have been no environmental reasons for the change(s). It can be difficult to differentiate between many of the changes caused by CDS and/or other behavioral/neurological diseases in old cats, and those caused by OA. In addition, it is not unusual for an individual cat to have multiple interacting conditions.

## Figure 3: Common Behavioral Changes That Can Be Seen in Older Cats

- Spatial disorientation or confusion, e.g., getting trapped in corners or forgetting the location of the litter box (housesoiling is the most common reason for referral of old cats to behavioralists).
- Altered social relationships with owners or other pets in the household, e.g., increased attention seeking or aggression.
- Altered behavioral responses, e.g., increased irritability or anxiety or decreased response to stimuli.
- Changes in sleep/wake patterns.
- Inappropriate vocalization, e.g., loud crying at night.
- Altered learning and memory, such as forgetting commands or breaking housetraining.
- Changes in activity, e.g., aimless wandering or pacing, or reduced activity.
- Altered interest in food, either increased or, more typically, decreased.
- · Decreased grooming.
- Temporal disorientation, e.g., forgetting they have just been fed.

acid is toxic in this species,<sup>21</sup> so products containing it should not be given. While the new feline-safe version of Aktivait is on the market, trials in cats still need to determine its efficacy.

Environmental enrichment can lead to an increase in nerve growth factors, the growth and survival of nerves, and an increase in cognitive function. The combination of environmental stimulation (e.g., toys, company, interaction and food hunting games) and a diet enriched with antioxidants is believed to have a synergistic action in improving cognitive function. In aged dogs, a two-year study on the use of an antioxidantenriched diet (e.g., vitamins E and C, selenium, fruit and vegetable extract [beta carotene, other carotenoids, flavinoids]), mitochondrial cofactors (dl-lipoic acid and l-carnitine), and essential fatty acids (omega-3 fatty acids), plus environmental enrichment (e.g., toys, kennel mate, walks, and cognitive experience testing) revealed rapid (two to eight weeks into treatment) and significant improvements in learning and memory. Interestingly, while there was no reversal of existing pathology, the antioxidants did appear to prevent the deposition of more  $\beta$ -amyloid while the environmental enrichment did not.<sup>22,23</sup>

While a similar study showing improvement of CDS in cats in response to dietary supplementation is not yet available, a five-year study feeding healthy old cats (7- to 17-years-old; n=90) a diet supplemented with antioxidants (vitamin E and  $\beta$ -carotene), essential fatty acids (omega-3 and -6 fatty acids) and dried whole chicory root (which contains the prebiotic inulin to modify intestinal flora) resulted in the supplemented cats living significantly longer (and more healthily) than the

unsupplemented ones.<sup>24</sup> Another diet, designed for cats with OA, is supplemented with a mixture of antioxidants (e.g., vitamins C and E, and beta carotene), essential fatty acids, chondroprotectants (e.g., methionine, glycosaminoglycans, glucosamine and chondroitin sulphate), and L-carnitine and lysine. In a two-month study in which this diet was fed to 75 cats 12 years of age or older that were not selected for signs of CDS (or OA), owner-completed questionaires indicated >70% improved in one or more signs of cognitive function (and >50% improved in one or more signs of mobility).<sup>25</sup>

Unfortunately, once cats develop significant clinical signs of CDS, instigating environmental change can actually have a negative effect. This is because affected cats often become stressed and cope poorly with change whether in their environment, their daily routine, their diet, or the members of the household. The cat's response to this stress is to show more obvious signs of CDS (e.g., anorexia, hiding, and/or upset of toileting habits). 26 For these cats, whenever possible, change should be kept to a minimum; when it cannot be avoided, change should be made slowly and with much reassurance. Some cats may be so easily disorientated and cope so poorly with change that they may benefit from having their area of access reduced in size to a single room containing everything they need, i.e., the key resources for cats: food, water, litter box, resting places, somewhere to hide and/or some way of escaping, and companionship (as dictated by the particular needs of the individual cat). This core territory can then be kept safe and constant. Environmental application of synthetic feline appeasement pheromone (Feliway®; Ceva) can also help in reducing feline anxiety.

#### Potential Drug Therapies

There are a growing number of possible drug options for Alzheimer's disease. These include various cholinesterase inhibitors (to increase the availability of acetyl choline at the neuronal synapses), selegiline (to manipulate the monoaminergic system), antioxidants (e.g., vitamin E), and non-steroidal anti-inflammatory drugs (to reduce neuronal damage). While there are no drugs licensed for the treatment of CDS in cats, a number of drugs have been used "off label." 6,17,27,28 These include selegiline (Selgian®; Ceva: Anipryl®; Pfizer: suggested dose 0.25 to 1.0 mg/kg PO q24h), propentofylline (Vivitonin<sup>®</sup>; Intervet: suggested dose 12.5 mg/cat PO q24h), and nicergoline (Fitergol®; Merial: suggested dose quarter of a 5mg q24h), all of which have been used in cats with varying degrees of success. For example, a small open trial using selegiline showed a positive effect, 17 and the American Association of Feline Practitioners supports the use of this drug for the treatment of CDS. Other drugs that have been used to treat particular signs of CDS in cats include anxiolytic drugs, such as a number of nutraceuticals (e.g., Zylkène®; Intervet Schering

## Case Report — "Sally"



History: "Sally," a 16-year-old neutered female domestic shorthaired cat was presented with a two-week history of crying loudly at night and a six-month history of urinating around the house, which was now occurring with increasing frequency. However, she was still defecating in her litter box. Sally had always had a "picky" appetite, but her owner reported that she had become very fussy with her food, had lost weight, and stopping grooming. Overall, they felt Sally had "aged" considerably in the last two years. Sally was an indoor/outdoor cat, the only pet in the household, and was fed dry and wet cat food.

**Physical Examination:** Sally was bright and alert, but thin (body condition score 2 to 3 of 9). Her coat was ill-kept and matted, and she appeared slightly dehydrated. Her heart rate was 190 beats per minute, with a grade II of VI systolic murmur, loudest over the sternum, and occasional gallop sounds. Her respiratory rate was 40 breaths per minute. Her left thyroid gland felt slightly enlarged, and there was considerable bony enlargement of both elbows and stifles (consistent with OA).

#### Q.What is the major problem list for this case?

• 1) inappropriate urination; 2) night crying; 3) tachycardia, cardiac murmur and occasional gallop sound; 4) OA.

#### Q. What are the major differentials for the problems?

- Inappropriate urination 1) feline lower urinary tract disease (FLUTD); 2) polyuria/polydipsia (e.g., CKD, DM, hyperthyroidism, liver disease, hypercalcaemia, etc.); 3) neuromuscular/orthopedic disease (e.g., OA); 4) CNS/ behavioral problems (see Figure 1).
- Night crying (see Figure 1).

- Tachycardia, cardiac murmur and occasional gallop sound
   — Primary cardiac disease (which is unlikely in a cat of
  this age); secondary cardiac disease (e.g., due to hyperthyroidism, hypertension, CKD, DM, etc.).
- OA Idiopathic or secondary to trauma, infection, obesity or developmental defects.

#### Q. What is your diagnostic plan?

See Figure 2, including ECG, echocardiography, chest radiography, and head MRI.

Results:		_	
Serum Biochemist	ry:	Reference Range:	
Albumin	28 (2.8)	28-39g/l (2.8-3.9g/dL)	
Globulin	32 (3.2)	23-50g/l (2.3-5.0g/dL)	
ALT	64	15-60u/l	
ALP	112	10-100u/l	
Bile acids	8.0	(0.0-7.0 umol/l)	
Creatinine	180 (2.0)	140-177umol/l (1.6-2.0mg/dL)	
Urea	11.2 (31.4)	5.5-10.5mmol/l (15.4-29.4mg/dL)	
Glucose	7.6 (138)	3.3-5.0mmol/l (60-90mg/dL)	
Ca	2.2 (8.8)	2.1-2.9mmol/l (8.4-11.6mg/dL)	
PO <sub>4</sub>	2.5 (7.7)	1.4-2.5mmol/l (4.3-7.7mg/dL)	
K	4.0	4.0-5.0mmol/l (mEq/L)	
Na	148	145-156mmol/l (mEq/L)	
Thyroxin	60 (4.7)	19-65nmol/l (1.5-5.0ug/dL)	
Systolic BP:	150 120-180 mmHg		
Eall/Ell/ Tests	Magativa		

FeLV/FIV Tests: Negative

**Urine:** SG 1.035 (ref. >1.035), pH 7.8,

(collected by glucose negative, ketones negative, protein

cystocentesis) positive, sterile Hematology: Unremarkable

Thoracic Radiographs, Abdominal Ultrasound and Head MRI:

Unremarkable

**Echocardiography:** Moderate cardiac hypertrophy with a basal

septal bulge

ECG: Tall QRS complexes

### Q. What is your interpretation of these findings?

- Marginal renal insufficiency Slightly increased serum urea and creatinine concentrations (in a cat that has very little muscle mass and has not been fed for 12 hours), with a urine SG just within normal limits (but she is slightly dehydrated and a reasonable proportion of her diet consists of dry cat food so her urine SG should be higher than this).
- Possible early hyperthyroidism Serum thyroxin is at the top of the reference range, but Sally is an old, ill cat who might be expected to show thyroxin suppression; there are also slight increases in her liver enzymes and bile acid concentration.
- Stress Slight increase in blood glucose concentration.
- **Increase in urine pH** This can be caused by stress (hyperventilation), diet, urease-producing UTI, old urine, etc.

Case Report — "Sally," continued

 Moderate cardiac hypertrophy – This could indicate either primary cardiac disease or (perhaps more likely in a cat of this age) cardiac disease secondary to hyperthyroidism, hypertension, CKD, DM, etc.

#### Q. What is your diagnosis?

 CDS, OA (elbows + hips), moderate cardiac hypertrophy, marginal renal insufficiency, and possible early hyperthyroidism.

#### Q. How would you manage this case?

- CDS Environmental modification, diet change or supplementation, drugs?
- OA Environmental modification, diet change or supplementation, NSAIDs?
- Monitor cardiac hypertrophy
- **Regularly reassess** Monitor renal function, blood pressure, serum thyroxin concentration, etc.

Follow-Up: Sally was initially managed with environmental modification. This involved ensuring that she had easy access to all her key resources (food, water, litter box, resting places, hiding places/escapes routes, and company). Her food and water bowls were moved to lower surfaces, ramps were added to allow easier access to favored sleeping areas, a deep comfortable heated bed was added, and a large low-sided litter box was placed within easy reach. These changes were made gradually. It was hoped that they would help Sally's CDS and OA, and the newly added litter box meant any polyuria caused by the early CKD had less chance of resulting in peruria. Sally's

food was slowly changed to a feline OA diet containing a mixture of antioxidants (e.g., vitamins C and E, and beta carotene), essential fatty acids, chondroprotectants (e.g., methionine, glycosaminoglycans, glucosamine and chondroitin sulphate), and L-carnitine (as its formulation was considered beneficial to both her OA and CDS). Together these changes resulted in a significant improvement that was noted within a month of instigating the changes. Sally cried less at night, had no further episodes of periuria, and ate better.

Six months after the initial investigation Sally was reported to be doing well, but still crying at night, which her owner felt was due to progression of the OA as the vocalization appeared to occur when Sally was changing position during sleep or when she was leaving her bed. Full reassessment, including repeated assessment of serum biochemistry, urine specific gravity and systemic blood pressure revealed little change. Sally was started on a two-week trial of low-dose meloxicam® (0.01 mg/kg PO q24 hours). At Sally's reassessment two weeks later, her owner reported that the night crying had almost completely resolved. Repeat serum biochemistry and urine analysis showed no worsening of kidney function. It was recommended that Sally's owner should monitor Sally's behavior and appetite closely and only give the meloxicam if Sally was first willing to eat her food. To date, Sally has been on this regimen for nearly six months and continues to do well, with regular full checkups scheduled every three to four months.

Further information for owners of cats with geriatric diseases can be found on the FAB Website (*www.fabcats.org*). Books written to help owners of cats with CKD, FLUTD, hyperthyroidism or blind cats are available at *www.catprofessional.com*.

Plough), buspirone and benzodiazepines (e.g., diazepam, although hepatotoxicity is a particular risk with this drug), or antidepressants (that lack anticholinergic effects) such as fluoxetine.

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## **Q&A** Discussion

Q: Dr. Esther Plantinga, Utrecht University: I saw your advice to use NSAIDs in this particular case, but this cat had moderate renal insufficiency. Normally, veterinarians are reluctant to use NSAIDs with moderate renal insufficiency. What is your opinion about that? When is it an advantage to use them, and when do you try not to?

A: Dr. Gunn-Moore: I use a lot of them in elderly cats despite the fact that some of the elderly cats will have apparent reasons for never going anywhere near them with a non-steroidal. But it's about weighing the risks, using the safest non-steroidal you can, and making sure that the owners understand the risks. And I tend to do a pain trial first using buprenorphine, but getting buprenorphine into some of these older cats on a daily basis isn't easy. We've also used tramadol, etc., but I really like meloxicam, providing their kidneys are stable. And, as we heard yesterday, there's a much bigger risk of GI ulceration, etc., in old cats. This particular cat was only an IRIS stage 2 and stable with a sensible owner. And so, I said, "Let's try the meloxicam; let's see how it works." But she's not allowed any meloxicam unless she eats all her breakfast. So the moment she won't eat, she doesn't get dosed because she could be hydrated, her stomach's hurting her, etc. And also, we're using tiny drops, so literally a drop per cat per day. So, it's tiny doses, and that's often enough. If some days she's much worse perhaps buprenorphine or tramadol is added on those days, so it's balanced. Other people are using other analgesics; people are using things like gabapentin, things as well. But I'm very comfortable with non-steroidals, particularly meloxicam, if the owners understand the potential risk,s and we keep a very good assessment. We regularly recheck ureas, creatinines, that sort of thing. Thank you for that question because it's always so important to the whole health of the older cat.

Q: Dr. Steve Ettinger, California Animal Hospital: I think we all understand the need to give things to clients to give their pets, but I'm a little bit bothered about the lack of evidence-based medicine on many of the medications that you're suggesting. The fact that those medications are apparently only legal in a very narrow area of countries and have never been taken anyplace else because I think it's pretty clear that they would never be approved anyplace else. And I guess I'm just a little bit bothered by that because, you know, it goes back to the whole holistic approach. "Give this, give that, give a little bit of this." It's just bothersome to me when we start doing that and passing it around at meetings to veterinarians as if these products really are effective.

A: Dr. Gunn-Moore: As I said, we have no good data. I com-

pletely agree with you, and I have been campaigning to try and get some of these studies done. We desperately need them, and then we can make more educated comments. Yes, there is often a feeling that you need to do something, but it's also getting the owner to look at the whole picture. And so much can be done by helping these animals, by making a good investigation and finding out what other things may be wrong. There maybe is a bit more science base but also all the environmental stuff. So, that's why I said we have no data on any of those drugs. I mean it really is frustrating. I quite agree.

Dr. Gary Landsberg, Moderator: If I could make a comment. That doesn't dismiss the need for welfare and treatment of these animals. Dr. Ettinger was talking in part about safety. We're not talking about safety of these products that are licensed for cats anyway, such as the diet. And I have a partner who's a dermatologist and know quite a bit about the dermatology that they practice, and I'll defer to any dermatologist in the room. But they'll feed something like JD occasionally for skin problems to get the extra fatty acids into that skin in a way that's in the diet. So these things are being done if there's logic and science to them and as long as they're not, as Dr. Ettinger suggested, harmful for the pet.

**Q: Dr. Gary Pan, Nestlé Purina Research:** Are you aware of any risk factors that increase risk of cognitive disorder syndrome in cats?

A: Dr. Gunn-Moore: Again, data is so limited because we still don't have a way to diagnose it premortem. Following on post-mortems, we can look back retrospectively and try and find some of the factors, for example, the slide of tau phosphorylation I showed you. We found that in aged cats, but they were also cats that had had seizures. And in humans, we know you get tau phosphorylation as a response to seizure activity. So we are just at the start of the discipline in cats. There's a little bit more on dogs, which my eminent colleague commented on, but at the moment it certainly is purely the anecdotal stuff like uncontrolled high blood pressure, kidney disease, that sort of thing. Interestingly, in Britain, we still see cats with dysautonomia, and some of the cats that we got through the dysautonomia, they've then gone on to develop dementia at quite young ages. And when they had their postmortems done there was quite a lot of vacuolization in those brains. I think there are so many different insults that can lead to a damaged brain so cognitive dysfunction will probably end up being a dump diagnosis just the same way inflammatory bowel disease is. We can't properly diagnose that either. But we need a lot more work on cognitive dysfunction.