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Feline Behaviour Mini Series

Session Three: Medical Influences on Feline Behaviour

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Delegate Notes for Medical Issues Session 3

Medical Problems that are Interlinked with Behavioural change

In many medical conditions there is considerable overlap between behavioural changes and other clinical signs and it can sometimes be difficult to distinguish between the two. Often, particularly in older animals, the first signs noticed by owners may be changes in behaviour rather than overt clinical signs. On initial presentation it may therefore be difficult to decide whether it is a medical problem, a behavioural problem or a combination of the two. Ensuring a good working relationship with your local behaviourist is crucial in such cases for making a correct diagnosis and providing appropriate management and treatment. A sudden onset of behavioural change would more commonly be associated with a medical condition than a condition that has begun more gradually. However with cats being particularly sensitive to change, a sudden change in the environment or the social setting that a cat lives in could also result in a relatively sudden onset behaviour change. Identifying potential triggers can help to distinguish the cause in this case. Changes related to old age such as osteoarthritis or cognitive dysfunction may result in more gradual changes in behaviour over time. In medical conditions presenting with behavioural signs there may be associated loss of condition such as muscle wastage or poor coat condition such as might be noted in hyperthyroidism or in dental disease. However this may not be present early on in the course of the disease. Lack of normal maintenance behaviours for example poor appetite, poor self-care or an abnormal toileting pattern may be a result of environmental stress or due to medical issues such as pain. Perhaps the most important consideration is whether the behaviour being shown is out of the normal range of expected behaviour for that individual animal and if this is the case then medical involvement is more likely. Learned components due to associations made when the pain has been experienced may be on-going even if the pain is no longer current. Stress may be brought on via the environment, both social and physical but it may also be exacerbated by medical issues particularly those resulting in pain so it is a complex interplay between the two.

Feline Idiopathic Cystitis

There are very often clear behavioural reasons why cats urinate inappropriately in the home setting. However in some cases there is a genuine medical condition underlying this behaviour. Feline idiopathic cystitis is a very complex situation where stress brought on by environmental and social factors interacts with pathophysiological changes. Cats diagnosed with this condition will benefit from seeing a veterinary behaviourist. In milder cases where recurrence rates are relatively low and clinical signs are mild, general practitioners may be able to provide sufficient advice to owners to reduce the frequency and severity of flare-ups. Although FIC is a medical condition, the primary focus of treatment should be behavioural and environmental management to reduce stress. Current medical treatments are very limited in their efficacy in this disease process.

Potential Medical Causes of Urinating in the House

In some cases there may be entirely a medical issue and once that is treated the cat will toilet appropriately again. However this is quite unusual due to various factors such as the habitual component of toileting preferences, where cats tend to urinate where they have been before, and due to potential learned aversion responses to litter trays during painful urination. Feline Lower Urinary Tract Disease (FLUTD) is a broad term that includes any disease of lower urinary tract including the bladder and the urethra. The urinary tract has limited ways to respond, so very different disease processes may result in very similar clinical signs. Osborne et al1996 listed about 36 different causes of lower urinary tract signs. Potential responses of the urinary tract include alterations in frequency of urination, volume produced, presence of blood, the location of toileting or difficulty urinating. Examples of disease that might cause these signs include bacterial infection (which is often secondary to underlying medical conditions), neoplasia, inflammation, trauma, urolithiasis, incontinence, urethral plugs and anatomical abnormalities.

Clinical Signs of FLUTD

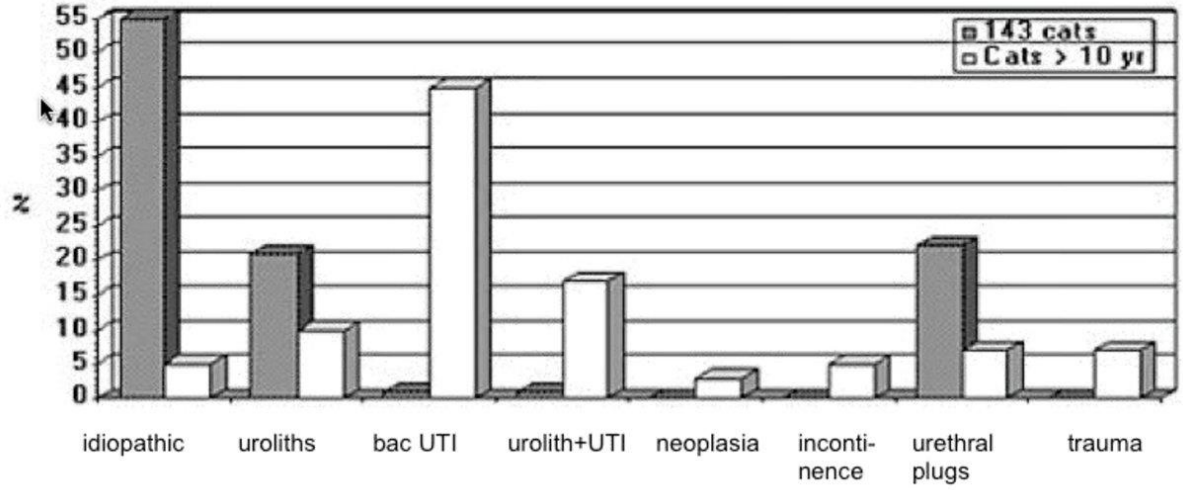
Any of the following may be observed:

- Abnormal urination:
    - Dysuria (difficulty urinating)
    - Pollakiuria (increased frequency which may or may not result in smaller volumes of urine depending on concurrent polydipsia due to other disease processes)
    - Haematuria
    - Urethral obstruction
    - Periuria (toileting around the litter tray rather than in it)
    - Multiple locations of urination (rather than the normal pattern of returning to the same location)
    - Spraying rather than squatting
    - Agitation/anxiety/vocalisation when urinating
- Aggression
- Inappetance
- Over-grooming of lower abdomen or perineum

Blood is a common finding but only indicates damage to the urinary tract with no indication as to the cause of that damage. Difficulty urinating indicates a partial or complete blockage which may be due to inflammation, causing narrowing of the urethra, a tumour may cause partial obstruction, urethral plugs or calculi may cause blockage. Urethral plugs are a common finding secondary to inflammation so this may be an indication of FIC.

This is a graph below, taken from European College of Veterinary Internal Medicine Proceedings 2002, shows the causes of feline lower urinary tract disease. The vast majority of FLUTD clinical signs in cats under the age of 10 years are caused by idiopathic cystitis.

In these cases medical treatments such as analgesia or nutraceuticals may be warranted but it is also crucial to address behavioural components. In the light of concerns over antibiotic resistance and over-usage of these precious drugs please note that the most cases presenting with FLUTD clinical signs do not require antibiotic treatment.



Diagnosis of FIC

Although FIC is the most common cause of lower urinary tract signs in cats under 10 years old, there is no diagnostic test for this condition. FIC is diagnosed based on the clinical presentation and by ruling out other conditions.

Hoet et al 2013 used infrared microspectroscopy to examine blood samples and found a significant difference between tryptophan metabolites in cats affected by FIC compared to healthy cats. Further research is being carried out on this technique with the hope that a commercial diagnostic test may become available in the future.

Predisposing Factors for FIC

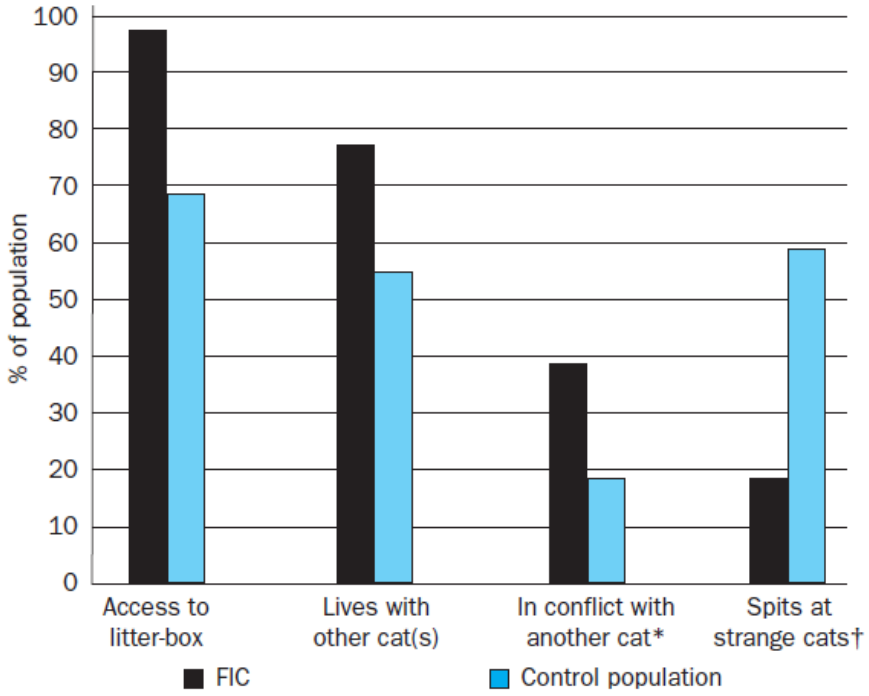
As with any diagnostic process, but particularly one for which there is no diagnostic test, considering predisposing factors plays a role. The following have been identified by various researchers as risk factors for development of FIC:

- Neutered cats are more at risk than entire cats
- Fed exclusively on dry food
- Reluctant drinkers (not linked to diet)
- Multi-cat households
- High cat density neighbourhoods
- Age under 10 years old.
- Inactive
- Obese
- Cats confined indoors. Unpredictable access to outdoors (e.g. dependent on owner opening door) may prove more stressful than cats who are either confined constantly or have free access via a cat flap.

Identifying a stress inducing trigger for the episode of FIC also aids diagnosis. Owners may need to be carefully questioned to help find such triggers.

Evidence for Risk Factors

Cameron et al 2014 identified various risk factors in their questionnaire based study involving comparisons of FIC affected cats with their unaffected housemates and healthy control cats. They identified being male, being pedigree and being overweight as risk factors in developing FIC although other studies have suggested equal risk for males and females. Inter-cat conflict within the household was the most significant risk factor which is not surprising given the inappropriate way in which many multi-cat households are created and managed. This study also supports the hypothesis that stress plays a crucial role in FIC and that individual cats show varied ability to cope with their environment.



Investigations Required

If a young cat is presented for the first time with clinical signs of cystitis, he or she fits the risk profile and a likely trigger factor is identified this may be sufficient to make a presumptive diagnosis of FIC. If it is straight forward and involves minimal stress to the patient then a fresh urine sample to test with a dipstick and refractometer would be ideal. Collecting a urine sample may in itself cause the cat additional stress and exacerbate the clinical signs, for example if the cat usually toilets outdoors and is not used to a litter tray.

If a cat is suffering from recurrent episodes or the clinical picture is unusual then further work-up is warranted to rule out other medical conditions and if a diagnosis of FIC is made behavioural referral would be advisable.

Older cats are more likely to be diagnosed with diseases other than FIC, such as a primary bacterial infection, diabetes mellitus, hyperthyroidism, renal disease or neoplasia. In hyperthyroidism the rest of the clinical picture is usually quite clear but in terms of behavioural signs, such as excessive vocalisation, increased activity and irritability, there is some overlap with cognitive dysfunction syndrome. There would also usually be associated weight loss. Renal disease also often has concurrent weight loss so keeping regular records of weights when cats visit the surgery is a useful early warning sign of a problem. If the cat concerned is not relaxed about being handled it can be beneficial to check urine specific gravity to check renal function before considering taking blood samples because if it is FIC again we need to avoid causing further stress.

Accurate results in urine tests rely on rapid testing of fresh samples. Delays result in cell lysis, changes in pH and precipitation of crystals, all of which affect your results. Dipsticks used in veterinary practice are usually designed for human use, therefore results should be taken in that light but are a good starting point. Specific gravity should always be accurately measured using a refractometer. Monitoring specific gravity is useful in cats with FIC because part of the treatment plan should be to increase water intake and dilute the urine. Culture and sensitivity testing of a cystocentesis sample is essential if bacterial infection is suspected or needs to be ruled out. Cats often tolerate cystocentesis under minimal restraint and this is often the least stressful manner of obtaining a sample. If measuring water intake is used as part of the diagnostic process, the implications of potentially increasing stress when confining a cat to avoid him gaining access to other water sources should not be forgotten as this may well exacerbate clinical signs of FIC and may also inhibit drinking and therefore give an inaccurate result. If there is concern about medical causes such as renal disease, diabetes or hyperthyroidism then clearly the appropriate blood tests should be performed.

Pathophysiology of FIC

This is not yet fully understood but some good hypotheses have been put forward and it is an area of on-going research. Abnormal stress responses in FIC cats have been identified and an abnormal bladder lining may also play a role. Understanding the effects of stress in this condition if the main focus because trying to reduce the chances of activation of the stress response system is key to effective management.

FIC is a condition that waxes and wanes and usually flare-ups last for 3-7 days and resolve spontaneously. The interplay between stress and general health and welfare are well known. In FIC stress plays a significant role in relapse rates and the likely underlying pathophysiology. Every individual is unique in their response to potential stressors and this is an important aspect for understanding the management of this disease. In multi-cat households owners may be less aware of environmental inadequacies if some of the cats are more confident and relaxed. They need to understand that what one cat can cope, another individual cat may struggle with. These differences are a result of socialisation, genetics and so on as discussed in the first session.

The effects of neonatal stress and intrauterine stress on the priming of the HPA axis are also likely to be relevant. Severe acute stress or lower level chronic stress can cause abnormal development of this stress response system.

Stress Response Differences

Westropp et al 2006 assessed bladder permeability and urine cortisol:creatinine ratios in cats with FIC and in normal cats who were experiencing stress. FIC cats had higher levels of circulating catecholamines but there were no differences between the urine cortisol:creatinine ratios. The authors suggests that in FIC cats there is an uncoupling between the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis stress response.

In healthy cats stress causes sympathetic activation resulting in the release of corticotrophin releasing hormone (CRH) from hypothalamus. This acts on the pituitary to release adrenocorticotropic hormone (ACTH) which causes the adrenal glands to release cortisol. This is the normal HPA axis response which results in the flight/fight response. However the FIC cats had a reduced or failed release of ACTH and cortisol. Their resulting behavioural response involved displacement behaviours such as grooming, drinking, eating and urinating. Displacement behaviours are behaviours that are seen within the normal repertoire but out of context.

Acoustic Startle Response

Buffington 2002 studied differences in the responses of FIC cats compared to healthy cats to sudden loud sounds. This response is increased if an animal is fearful or anxious. Further evidence that there is an abnormal stress response system in cats affected by FIC comes from this study where they found an increased acoustic startle response in FIC cats compared to normal cats even when they were in an appropriate enriched environment. FIC cats placed under stressful conditions showed an even more marked difference in this response.

Avoiding Stress

Ensuring that cats with FIC live in a low stress environment is crucial to managing this condition so individual factors for each patient that might activate the stress response system should be identified. One of the key aspects for cats is to feel in control of their environment and resources. Predictability is crucial as is immediate access to resources. During sessions one and two we have examined potential stressors for cats such as encounters with unfamiliar cats or cats that are not within the same social group, meeting unfamiliar people, sound sensitivity, concerns within the household such as the presence of children or other pets and so on. Each patient will have their own individual issues that need addressing.

Effects of Stress on the Bladder

Stress causes release of corticotrophin releasing factor (CRF) from hypothalamus and this affects two areas of brain. In addition to the release of ACTH from the anterior pituitary, CRF also affects the locus coerulus to increase tone in the sympathetic nervous system.

This may result in neurogenic inflammation in bladder lining and the histology of the submuscoa in FIC cats is does fit with this hypothesis. Bladder distension stimulates activity in the locus coerulus, which is also involved in global functions such as vigilance and arousal, mediated via the release of noradrenaline. Given the symptoms of FIC waxing and waning in response to stress it is likely that this link between bladder pathology and activity in the locus coerulus plays an important role in this disease.

More than just the Bladder

Research over the last few years has suggested that chronic idiopathic cystitis in cats and the parallel disease in humans may be a manifestation of an underlying systemic disease rather than isolated to the bladder itself. Buffington 2011 refers to this as 'Pandora' syndrome. This syndrome involves idiopathic cystitis plus clinical signs related to other organ systems with the signs waxing and waning associated with stress. Resolution of these signs is associated with effective environmental enrichment and reduction in stress. These FIC cats may therefore present with other concurrent diseases affecting other systems of the body which also wax and wane over time. This might involve for example recurrent gastrointestinal problems, cardiovascular disease, dental disease such as severe gingivitis or stomatitis, recurrent respiratory disease. Chronic stress in this patients and the underlying abnormal stress response system may be resulting in a general deterioration in health. Such patients may be even more in need of behavioural referral to address environmental stress in an attempt to reduce recurrence of a multitude of clinical signs.

Bladder Changes in FIC

There are many areas of anatomy and physiology that could be affected by the disease process of FIC including the epithelium, the neurovascular supporting tissue, the smooth and striated muscle, the complex neuroendocrine communication involving many neural connections and neurotransmitters and the adrenocortical and sex hormones. Westropp 2006 used fluorescein to test bladder permeability. FIC cats showed a higher permeability than normal cats and therefore alterations in the bladder lining have been hypothesised as part of the disease process. The bladder lining is composed of the urothelium and tight junctions covered in a layer of glycosaminoglycans peptides (GAG). GAG works as a protective layer against the irritant effects of urine, crystal adherence and microbe infection. Alterations in this protective layer may exist in FIC cats such as the bladder permeability differences identified, changes in GAG layer effectiveness and GAG concentration in urine.

Management of FIC

As this condition is closely related to stress and assuming that FIC cats have abnormal stress response systems the focus of long term management is to reduce the likelihood of flare-ups via environmental modification. Treatment for flare-ups should focus on identifying and reducing the trigger factors and providing pain relief. Buffington's 2006 demonstrated the importance of multimodal environmental modification to reduce likelihood of stress response activation.

In this study 46 indoor cats with FIC were followed for 10 months following advice such as improving the three dimensional environment, avoiding punishment, changing to wet food, increasing water intake and advice about litter trays.

Environmental enrichment was been found to:

- Reduce clinical signs of FIC
- Less fearful and nervous
- Reduced respiratory signs
- Reduced aggression
- Normalise
    - Circulating catecholamines
    - Bladder permeability
    - Cardiac function
- Decrease acoustic startle response

Factors to Reduce FIC Signs

1. Increasing fluid intake to dilute urine and reduce irritation in the bladder.
    a. Feed at least some wet food
        i. Do not change diet suddenly as this will cause stress – novel foods must be introduced gradually
        ii. For cats who are not keen on wet food try adding a small amount of water to the dry food and gradually increase that as they get used to it
        iii. Ensure free and immediate access to food to reduce stress.
    b. Increase volume of water drunk
        i. Water fountains – many cats prefer drinking from running water sources
        ii. Wide-brimmed bowls to avoid whiskers being bent
        iii. Water dishes away from feeding area
        iv. Multiple sites for water around the house and garden
        v. Provide flavoured water e.g. from cooking meat or fish
        vi. Experiment with different materials for water vessels as this can affect taste e.g. water, plastic, glass, ceramic.
    c. Encourage frequent urination
        i. Cats with outdoor access may still prefer to use a litter tray indoors or a purpose built outdoor latrine
        ii. Consider all aspects of the litter tray such as design (depth, height, hooded or not), type of litter used, depth of litter, frequency of cleaning, location of tray etc.
    d. Pheromone diffusers used appropriately.
    e. Address interactions between other members of the household (cats, humans, other pets).

f. Environmental modification to ensure plenty of hiding and perching opportunities both inside the house and in the garden (see session 2 for more detail on this).

Roles for Medical Treatment

Although stress reduction is the major factor in managing this disease there is also a role for medical treatment. Analgesia is essential during bouts of clinical signs of cystitis. Meloxicam may be sufficient but for cats whose pain is severe the use of buprenorphine should be considered. This is effective when used transmucosally in cats so can be administered by owners at home. Cats that are not keen on being handled may require counter-conditioning training to teach them to cope with regular medication so that the process of medicating does not inadvertently increase stress. Nutritional anxiolytics or nutraceuticals that help repair the bladder lining may be beneficial in some cases. Cystophan, an L-tryptophan supplement, may increases serotonin and alpha-casozepine is thought to work via GABA receptors and shows benzodiazepine like properties. GAG supplements have been reported anecdotally to show some success in a proportion of cases but there is little evidence of clinical efficacy. It is always important to bear in mind that these nutritional supplements do not undergo the level of peer-reviewed double-blinded control trials that are essential for licensing of drugs and therefore evidence of their efficacy is often lacking.

Anxiolytic Medication

This may be warranted in some cats who continue to show relapses and an inability to cope despite environmental assistance. This is only recommended if the cat has undergone a full home visit by an appropriately qualified and registered feline behaviourist.

Cognitive Dysfunction Syndrome in cats

This is a key disease that veterinary staff should be actively searching for in order to be able to offer support to owners and their aging pets. This table below is taken Landsberg 2012 showing medical causes which have potential behavioural signs.

Table 1
Medical causes of behavioral signs

Medical Condition/Medical Presentation	Examples of Behavioral Signs
Neurologic: central (intracranial/ extracranial), particularly if affecting forebrain, limbic/temporal, and hypothalamic; REM sleep disorders	Altered awareness, response to stimuli, loss of learned behaviors, house soiling, disorientation, confusion, altered activity levels, temporal disorientation, vocalization, soiling, change in temperament (fear, anxiety), altered appetite, altered sleep cycles, interrupted sleep
Partial seizures: temporal lobe epilepsy	Repetitive behaviors, self-traumatic disorders, chomping, staring, alterations in temperament (eg, intermittent states of fear or aggression), tremors, shaking, interrupted sleep
Sensory dysfunction	Altered response to stimuli, confusion, disorientation, irritability/aggression, vocalization, house soiling, altered sleep cycles
Endocrine: hyperthyroid or hypothyroid, hyperadrenocorticism or hypoadrenocorticism, insulinoma, diabetes, testicular or adrenal tumors	Altered emotional state, irritability/aggression, lethargy, decreased response to stimuli, anxiety, house soiling/marking, night waking, decreased or increased activity, altered appetite, mounting
Metabolic disorders: hepatic/renal	Signs associated with organ affected: may be anxiety, irritability, aggression, altered sleep, house soiling, mental dullness, decreased activity, restlessness, increase sleep, confusion
Pain	Altered response to stimuli, decreased activity, restless/unsettled, vocalization, house soiling, aggression/irritability, self-trauma, waking at night
Peripheral neuropathy	Self-mutilation, irritability/aggression, circling, hyperesthesia
Gastrointestinal	Licking, polyphagia, pica, coprophagia, fecal house soiling, wind sucking, tongue rolling, unsettled sleep, restlessness
Urogenital	House soiling (urine), polydypsia, waking at night
Dermatologic	Psychogenic alopecia (cats), acral lick dermatitis (dogs), nail biting, hyperesthesia, other self-trauma (chewing/biting/sucking/scratching)

Several behavioural signs come up repeatedly, anxiety, irritability, aggression, housesoiling. Owners may present their pet to you with these vague signs that something is amiss and there may not yet be specific clinical signs like vomiting or weight loss to aid diagnosis. As with FIC, there is no diagnostic test for cognitive dysfunction syndrome and we are reliant on ruling out differentials and identifying a pattern of clinical signs that are consistent with impaired cognition. In these elderly cats concurrent disease may also be present which can make the diagnosis more complicated.

What is Cognitive Dysfunction Syndrome (CDS)?

Some decline in cognitive ability during the normal ageing process is expected but CDS refers to a pathological process of neurobehavioural degenerative disease. The pathology is similar to that of Alzheimer's disease in humans. It can be seen from the age of seven years but is generally not diagnosed until around 11 years of age. Some clinicians recommend precautionary supplements to protect against the development of this pathology in senior diets which would usually start at around 7 years of age. Owners who train their cats, for example if they do agility training or trick training, may see a decline in their cat's ability to learn new behaviours or a loss of previously learned behaviours.

A high prevalence of CDS exists in elderly animals and this not only affect the quality of life of animals themselves but can also have a significant impact on owner welfare. In cats the most common clinical signs is overnight vocalisation which can be very disruptive for clients with respect to sleep disturbance. Cats may also show anxious and fearful behaviours which may have been pre-existing but show an increase in severity or they may appear for the first time as the disease progresses. Cats are living longer lives due to improvements in healthcare and are therefore more at risk of developing this age related disease. Euthanasia is complex due to the difficulties of assessing quality of life in an animal who is not cognitively normal. Euthanasia may often be considered for the owner's benefit due to disruption or distress but the cat may be physically healthy in all other ways. If owners do need to make a decision to euthanase their pet we must support them and help them in their decision making process.

Early Diagnosis

Early diagnosis is crucial because this is a progressive disease and therefore gets worse over time. Once clinical signs are severe and the pathological changes have occurred there is generally a poor response to treatment. The aims of treatment and management are to try and slow down progression of the disease because it cannot be cured. There can be a good response if treatment is started early so as to reduce the rate of deterioration. Giving owners an early diagnosis gives us the opportunity to explain the disease to them so that they have expectations about how their pet is likely to deteriorate over time. This makes the future more predictable for them so they are better able to cope with the difficulties that their pet is experiencing.

Pathology of CDS

Understanding the pathology allows us to know where to target preventative treatments and gives us an explanation for the clinical signs observed. Considerable research has been done on dogs and humans but there is less known about felines. Changes that occur in humans and dogs include decreased brain volume, oxidative damage, cellular apoptosis, neuronal loss in the hippocampus, beta-amyloid deposits and cerebrovascular compromise. The hippocampus is an area of the brain primarily involved with memory formation and therefore neuronal loss in this region explains the cognitive changes we see associated with memory and learning in these species. In cats neuronal loss and a reduction in synapse density occurs in the caudate nucleus and the locus coeruleus.

The caudate nucleus plays an important role in memory and learning, voluntary motor control and goal-directed actions. Pathology in this area may be responsible for motor function impairments such as aimless pacing. As mentioned above in relation to FIC, the locus coeruleus is the main source of noradrenaline and plays a role in arousal states. Alterations in this area of the brain may be responsible for changes in the sleep-wake cycle and reduced activity levels see in CDS. Acetylcholine, a neutrotransmitter vital for learning and memory is produced in the locus coeruleus in cats. Impaired memory and cognitive function are correlated with reduction in acetylcholine and with the presence of beta-amyloid plaques in humans and dogs so it is likely this is similar in cats. The reduction in acetylcholine is particularly significant because patients should not be given medications that affect the cholinergic system adversely and inadvertently exacerbate the clinical signs. Beta-amyloid accumulates between nerve cells, interfering with communication between cells. In cats beta-amyloid plaques differ in their structure and are more diffuse than in dogs and humans. In cats there is not a significant correlation between the amount of beta-amyloid and the clinical signs of cognitive dysfunction unlike the situation that we see in humans and dogs. Changes in the neurotransmitter levels in the brain are significant with reductions in acetylcholine, dopamine, noradrenaline and serotonin. Alterations in dopamine and serotonin levels are likely responsible for the increase in anxiety and fear related behaviours in these patients. Phosphorylation of tau proteins in neurons causes cells death and in cats this change appears to be related to the development of seizures.

Prevalence

These figures on prevalence of CDS follow some unpublished research by Moffat.

- Cats over the age of 11 years:
    - 67% showed signs of cognitive dysfunction
    - Medical causes of these behavioural changes were identified in large proportion
    - 35% were diagnosed with cognitive dysfunction once medical issues excluded
- Cats 11-14 years old
    - 30% had 1.8 signs of CD with altered interactions being the most common presenting sign
- Cats over 15 years old
    - 48% had 2.5 signs with alterations in the sleep/wake cycle being the most common presenting sign.

Landberg 2011 published the table below which shows housesoiling to be the most prevalent presenting behavioural sign in cats over 10 years old. Excessive vocalisation, housesoiling, disorientation, aimless wandering and restlessness were commonly presented in cats over the age of 12 years.

TABLE 1 Behavioural problems reported by owners of senior cats

Behaviour referral practices (83 cats, aged >10 years)*	VIN boards (100 cats, aged 12–22 years)
House soiling (elimination and marking) 73%	Excessive vocalization 61% (night vocal 31%)
Intercat aggression 10%	House soiling (elimination and marking) 27%
Aggression to humans 6%	Disorientation 22%
Excessive vocalization 6%	Aimless wandering 19%
Restlessness 6%	Restlessness 18%
Overgrooming 4%	Irritability/aggression 6%
	Fear/hiding 4%
	Clingy attachment 3%

*Cases derived from Chapman and Voith (n=25),[2] Dr Gary M Landsberg (n=25) and Dr Debra Horwitz (n=33) and discussed in Landsberg et al (2003)[1]

Under-Diagnosis

Despite high prevalence rates cats are likely to go undiagnosed. Many people generally accept these types of change as 'normal' aging rather than recognising it as a pathological process that can be supported with medical and behavioural interventions. Initially signs may be subtle and owners may not be concerned if they are unaware of the link between these signs and disease. It is therefore really important that we pro-actively look for this disease by questioning owners about their cat's behaviour, rather than waiting for owners to report a problem to us.

Clinical Signs

As discussed above there is no definitive test for CDS and it is a matter of ruling out other potential causes of the presenting clinical signs.

DISHA – disorientation**, i**nteraction**, s**leep/wake cycle**, h**ousesoiling**, a**ctivity

Disorientation may be manifested by excessive and/or out of context vocalisation or aimless wandering and reduced spatial awareness so for example they may become stuck in corners or behind furniture. They may also stand and stare at no apparent stimulus.

Social interactions often change although this will vary from cat to cat depending on the relationship owners normally have with their pet and to what degree their individual cat is sociable. The cat may show altered greeting behaviour or altered interest in interacting at other times. There may be issues within multi-cat households as relationships with other cats alter.

It is more common to see reduced social interaction but in some cases a higher dependence on the owner due to anxiety issues could be manifested as an increase in attention seeking behaviours.

Disturbances in the sleep/wake cycle are the most commonly reported sign in cat owners with overnight vocalisation being a really significant factor. Again it is important to interpret this based on what used to be normal for that individual cat. Cats are naturally crepuscular so we need to be asking about *changes* in behaviour and also vocalisation, pacing and an inability to settle. Increased sleep during the day time may be difficult to assess if owners are out the house and also cats sleep for a high proportion of the day anyway.

Housesoiling problems may be related to disorientation, loss of previously learned behaviour and their general state of confusion. It is also common to see a decrease in self-hygiene particularly a lack of grooming. Activity patterns alter and there can be an increase in non-goal directed activity such as the random pacing about and excessive vocalisation that are often associated with disorientation. In contrast, goal-directed activities such as play and interaction with the environment may well be decreased.

Due to the effects on learning and memory they might also show reduced ability to cope in novel situations such as a visit to the cattery or a change in the house layout. Cats may of course struggle with this anyway due to their natural behaviour patterns so owners should be asked about *changes* in their ability to cope. We may also see changes in emotionality and anxiety and fear related disorders are the most common change to see.

Differentials for CDS

This table below is taken from an excellent review article by Danielle Gunn-Moore 2011which provides a thorough list of differentials to consider when presented with a cat showing signs consistent with cognitive dysfunction. In conjunction with the table above from Landsberg 2011 this provides a comprehensive check list.

Box 1. Potential Causes of Behavioral Changes in Geriatric Cats

- Cognitive dysfunction syndrome
- Osteoarthritis*
- 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
- Diabetes mellitus
- Urinary tract infection
- Gastrointestinal disease
- Liver disease (hepatic encephalopathy)
- Reduced vision or hearing
- Brain tumors (e.g., meningioma, lymphoma)
- Infectious disease (e.g., feline immunodeficiency virus, feline leukemia virus, toxoplasmosis, feline infectious peritonitis)
- Pain and/or inflammation in general (e.g., dental or periodontal disease)
- True behavioral problems, stress

The role of pain is often the most difficult to rule out because this can cause housesoiling, lack of interest in interacting with social stimuli and the environment, increased resting or sleeping, lack of grooming and so on. The most significant cause of pain in the elderly cat is likely to be osteoarthritis and sadly this is very underdiagnosed and under-treated in our feline patients, not only by owners but also by veterinarians. The only true measure of pain effects is a trial of analgesic medication and an observation for improvement in behavioural signs in addition to environmental modification to make daily life easier for the cat to manage. Remember that given the age of these patients they are at risk of suffering from both osteoarthritis and cognitive dysfunction!

What Wuestions should We Ask?

Salvin et al 2011 designed a Canine Cognitive Dysfunction rating scale which is pictured below. This showed 98.9% diagnostic accuracy in dogs but sadly at this point in time we do not have a validated feline equivalent that I am aware of. However this study can form a basis of what types of questions we should be asking owners of elderly feline patients.

Table 2
Canine cognitive dysfunction rating scale with example data for a dog over the threshold (⩾50) for query diagnosis.

	(1) Never	(2) Once a month	(3) Once a week	(4) Once a day	(5) >Once a day		Score
How often does your dog pace up and down, walk in circles and/or wander with no direction or purpose?				X			4
How often does your dog stare blankly at the walls or floor?			X				3
How often does your dog get stuck behind objects and is unable to get around?	X						1
How often does your dog fail to recognise familiar people or pets?				X			4
How often does your dog walk into walls or doors?		X					2
How often does your dog walk away while, or avoid, being patted?			X				3
	Never	1–30% of times	31–60% of times	61–99% of times	Always		
How often does your dog have difficulty finding food dropped on the floor?				X			4
	Much less	Slightly less	The same	Slightly more	Much more		
Compared with 6 months ago, does your dog now pace up and down, walk in circles and/or wander with no direction or purpose					X		5
Compared with 6 months ago, does your dog now stare blankly at the walls or floor			X				3
Compared with 6 months ago, does your dog urinate or defecate in an area it has previously kept clean (if your dog has never house-soiled, tick 'the same')				X			4
Compared with 6 months ago, does your dog have difficulty finding food dropped on the floor				X		x2	8
Compare with 6 months ago, does your dog fail to recognise familiar people or pets					X	x3	15
	Much more	Slightly more	The same	Slightly less	Much less		
Compared with 6 months ago, is the amount of time your dog spends active				X			4
					Total		60

Gunn-Moore's questionnaire (below) was published in the American Association of Feline Practitioners (AAFP) Senior Care Guidelines and can be used to aid diagnosis of painful conditions and cognitive dysfunction.

TABLE 3 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			
shows signs of being stiff at times			
is less agile than previously			
cries when lifted			
shows signs of lameness or limping			
has difficulty getting in or out of the cat flap/cat door			
has difficulty going up or down stairs			
has more accidents outside the litter box			
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			
has become more fearful and/or more aggressive			
appears forgetful			

*Ensure there have been no environmental reasons for the change.
Table provided courtesy of Danièlle Gunn-Moore

These could be posted out in advance with booster reminders, giving owner the opportunity to think, observe their cat at home and perhaps also take video footage in the home environment to show you when they attend their appointment. In cats who are inhibited in the surgery environment it can be difficult to assess their mobility so owners providing information from home can be invaluable.

Management

Educating owners that cognitive dysfunction is a degenerative condition that cannot be cured is a vital aspect of making a diagnosis. Treatment strategies aim to reduce the rate of deterioration and hopefully improve existing clinical signs. Using the term management rather than treatment with clients avoids the risk of them having false expectations of what can be achieved. Treatment infer a resolution whereas management makes it clear that we are aiming to cope with a situation that cannot be resolved.

Environmental enrichment that results in mental and physical stimulation can maintain and enhance cognitive function. However, remembering their natural ethology, care must be taken in feline patients in case they struggle to cope with change in routine or the introduction of novel objects.

In addition if they are suffering from anxiety as a symptom of their CDS their inability to cope with change may be heightened. Predictability of routine and of interactions can aid cats who are showing signs of disorientation and/or anxiety. Discriminative cues can help with predictability although severely affected individuals will struggle to learn these cues. For example if affected cats need supervised access to the garden due to impaired cognitive ability, giving them a clear signal on the cat flap so they know when it is accessible can improve their ability to cope with this restriction. This might involve placing a piece of coloured card over the flap when they do not have access. Owners must be supported making any changes because if done inappropriately they may exacerbate anxiety and unpredictability for the cat. Tailoring enrichment to what the individual cat enjoys and can cope with might involve active social interaction, activity feeders, training sessions, regular introduction of novel toys and provision of outdoor access.

Nutrition

Changes in nutrition can improve clinical signs in mildly affected cats and slow the rate of deterioration. Given the pathological processes involved in this disease, diets and supplements aimed at reducing oxidative damage, improving mitochondrial function and neuron health would theoretically be beneficial.

Hills diet J/D is supplemented various anti-oxidants, essential fatty acids, chondroprotectants, L-carnitine and lysine. In a two month questionnaire based study using this diet owners reported that more than 70% of the cats showed improved cognitive function. Tests with Purina Proplan 7+, another diet supplemented with anti-oxidants have not looked specifically at cognitive function, however cats who were fed this diet lived significantly longer and healthier lives. In 2013 Purina published a study on dietary supplements showing beneficial results of including fish oil, B vitamins, antioxidants and arginine.

As mentioned when discussing treatments for FIC diets and nutritional supplements do not undergo the same rigorous testing for licensing purposes that medication must. Theoretically nutritional supplements such as Aktivait cat and Senilife should show beneficial effects in cats but so far we are lacking evidence for their efficacy. There is some evidence in dogs but we really need to see research on cats to back up their usage in this species, particularly given the slight differences in the pathology observed between these two species.

S-adenosyl-L-methionine (SAMe)

This compound is an endogenous metabolite acting as a methyl donor in various transmethylation reactions involving neurotransmitters as well as other molecules. Treatment with SAMe is suggested to maintain cell membrane fluidity and receptor function, regulate neurotransmitter levels and increase glutathione production. Glutathione reduces oxidative stress which is one of the processes heavily implicated in the pathology of CDS.

Araujo et al 2012 tested SAMe using the preparation marketed as Novifit. With a small sample size of only 16 cats further work is required but initial findings are promising. Supplemented cats showing mild signs of cognitive dysfunction showed an improved performance of learning. Severely affected cats did not gain any benefit from the supplement. This reconfirms our current understanding that treatment of severe cases is unrewarding and emphasises the need for pro-active searching of cases for early diagnosis.

Combining Environmental Enrichment and Nutritional Supplements

Work published in dogs and humans may perhaps be extrapolated to our feline patients. Brain derived neurotrophic factor (BDNF) promotes the survival of cell types that are affected by Alzheimer's. It is also an activity-dependent modulator of long-term potentiation and therefore a key molecule for learning and memory. BDNF is at lower levels in older cognitively impaired animals compared to younger animals. Research in dogs has shown that a combination of environmental enrichment and nutritional supplements was required to increase BDNF levels. It has been suggested that the two interventions are working synergistically with anti-oxidants possibly making the brain more receptive to effects of environmental enrichment. Increasing BDNF levels correlated with lower brain beta amyloid and improved spatial memory performance. However preservation of neurons in hippocampus was only affected by environmental enrichment and not by the nutritional supplementation. In the future hopefully we will see research along these same lines in our feline patients but in the meantime ensuring that a combination of nutrition and environmental enrichment are used is likely to give the best outcome. In addition to mental enrichment, physical exercise promotes neurogenesis and synaptic plasticity and modulates BNDF mRNA and protein levels. It has been shown to decreases beta amyloid in transgenic mice and also improves cognitive function. So encouraging cats to be active should also be of benefit.

Medication

At the current time there are no drugs licensed for feline CDS in the UK. Selegiline hydrochloride (Selgian) is licensed for canine CDS in Canada and USA. It is licensed in the UK for 'behavioural problems of emotional origin' in dogs but it does not have any license for cats. Improvement in clinical signs of cognitive dysfunction in cats has been reported and its use is supported by the American Association of Feline Practitioners. At lower doses this drug increases dopamine and phenylanine levels whilst at higher doses it also affects serotonin and noradrenaline levels. It also shows neuroprotective effects which is perhaps as a result of reducing free radical production, increasing free radical scavenging enzymes or a combination of both of these. The dose rate in cats is 0.25-1mg/kg once daily in the morning and this should be given for a minimum of 2 weeks to see if there is a beneficial effect. In cats an improvement has been observed in the clinical signs of excessive vocalisation, disorientation and of stereotypic behaviour such as the pacing or circling. The use of this drug is most likely to be successful if started early on in the course of the disease and if a beneficial response is seen then treatment should continue long term.

Drugs that increase cerebral blood flow such as propentofylline (Vivitonin) and Nicergoline (Fitergol) have shown no efficacy in improving signs of CDS in cats. Anxiolytics may be warranted in some cases and do remember to avoid drugs with anticholinergic effects.

Summary

- Be proactive about finding these cases because early diagnosis is crucial for the success of the interventions currently available to us.
- Client education regarding the expectations is vital in terms of explaining to them that we are looking at management rather than treatment.
- Client support is essential because this is a difficult condition for them to cope with and due to the on-going progression of the disease their needs will change over time so progress should be monitored regularly and interventions adapted as required.
- Interventions to consider:
    - Exercising the brain with mental enrichment,
    - Physical exercise
    - Addressing nutrition
    - Medication with selegiline hydrochloride

Pain in Cats

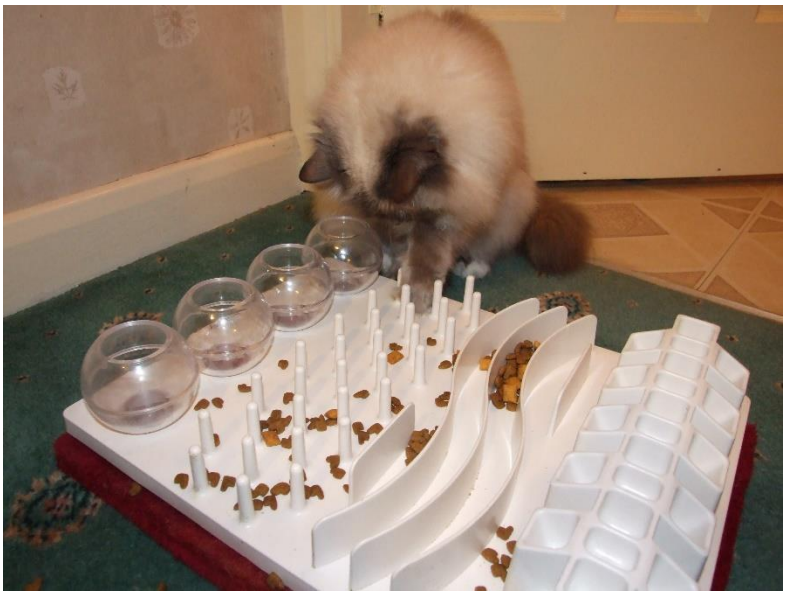
Unfortunately there was not the time during this mini-series to discuss pain in detail but please look at these suggested resources for further information. There are also aspects of pain covered in references on the general reference list for this series.

- Handling the cat that is in pain, in Feline Behavioural Health and Welfare, Roden and Heath 2015, pages 287-305
- Acute pain and behaviour, in Feline Behavioural Health and Welfare, Roden and Heath 2015, pages 162-183
- Chronic pain and behaviour, Feline Behavioural Health and Welfare, Roden and Heath 2015, pages 184-212
- Pain-related aggression in Chapter 9 of Manual of Clinical Behavioural Medicine for Dogs and Cats by Karen Overall 2013, pages 401-406.
- Protocol for assessing pain in cats in Manual of Clinical Behavioural Medicine for Dogs and Cats by Karen Overall 2013, page 764.

Obesity – Behavioural Influences

This was another topic that we unfortunately did not have time to discuss so again please find some further reading below and also some simple bullet points to bear in mind when aiming to reduce weight in cats.

- Feeding cats on a meal basis encourages over-eating due to their natural feeding patterns of eating small meals frequently. If larger meals are provided infrequently cats are liable to gorge and eat more over time than if allowed to graze.
- Competition in multi-cat households is a common underlying cause of over-eating. Addressing resource distribution and identifying social groups is an essential foundation to achieving successful weight loss in this context. Referral to an appropriately qualified and registered feline behaviourist in this context may be warranted.
- The use of activity feeders that slow the rate of eating can be useful aid to introducing ad libitum feeding as well as providing a means of environmental enrichment. Cats seem to respond better to activity feeders where they can visualise the food. The Trixie activity board is an excellent means of encouraging frequent small meals rather than gorging and can really aid success of a weight loss programme.



- Remember to take into account the psychological effects on compliance for the owners as well.
    - It is important for cats to lose weight slowly for health reasons and owners must be given realistic targets so they do not feel disheartened by lack of progress.
    - Do not weigh cats as frequently as you weigh dogs in weight loss programmes – weighing every few months is sufficient to see observable beneficial results.
    - It is also important to look at percentage weight loss rather than actual figures given that cats are small anyway. A 6kg cat that has a target weight of 5kg may only lose 200g (which to an owner will feel a small amount) in a few months but that is a significant percentage of the target.
- Feline Obesity, Jon Bowen, Proceedings of the APBC October 2012 Feline Conference.

Behaviour Referrals

This was another topic that we did not have time to discuss in detail and is so vital. At the current time there is no legal regulation of the behaviour profession and any person of any experience or qualifications may call themselves a behaviourist. As per the RCVS code of conduct when referring patients the vet must feel confident that they are referring appropriately and they retain responsibility for that patient's welfare and health. Over the last few years there has been considerable progress in developing a regulatory body for the behaviour profession, The Animal Behaviour Training Council. This is now widely recognised as the source for vets and vet nurses to go to when searching for trainers and behaviourists. When referring a behaviour case a member of the Clinical Animal Behaviourist or Veterinary Behaviourist category should be used. The referral procedure for behaviour cases should be as for any other type of referral with the referring vet making contact with the behaviourist with details about the case and a request for the behaviourist to take on that patient. At the current time the only individuals who are appropriately qualified to be registered as Clinical Animal Behaviourist or Veterinary Behaviourist are RCVS Specialists in Veterinary Behavioural Medicine, Diplomats of the European College of Behavioural Medicine, ASAB Certificated Clinical Animal Behaviourists and Full Members of the Association of Pet Behaviour Counsellors (APBC).

Members of the above organisations can be found via the following links:

https://www.rcvs.org.uk/education/specialist-status/rcvs-list-of-specialists/

http://www.asab.org/ccab-register Given the limited number of RCVS specialists in veterinary behavioural medicine, the CCAB register should be treated as the gold-standard qualification for behaviourists.

http://www.apbc.org.uk/apbc/memberlist

http://www.ecawbm.com/diplomates-2/ (note this lists Animal Welfare diplomats as well as Behavioural Medicine diplomats)

http://www.abtcouncil.org.uk/clinical-animal-behaviourists.html

http://www.abtcouncil.org.uk/veterinary-behaviourists.html

References and Recommended Further Reading for Feline Behaviour Mini Series

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    - Ellis et al, 2013. Feline Environmental needs Guidelines, Journal of Feline Medicine and Surgery, 15, pp219-230.
    - Carney et al. 2012. Feline-Friendly Nursing Care Guidelines, JFMS, 14, pp337-349
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- Van Hoek et al, A Diagnostic Test for Feline Idiopathic Cystitis Based on Infrared Microspectroscopy, 2013 ACVIM Forum Research Abstract Program, Seattle, Washington, June 12–15, 2013
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APBC cat box training video
https://www.youtube.com/watch?v=tSp8nl9xK3g&feature=youtu.be

International Cat Care
http://icatcare.org/

Behaviour referrals:
http://www.asab.org/ccab-register
http://www.apbc.org.uk/apbc/memberlist
http://www.abtcouncil.org.uk/

Owner resource for pain identification:
http://www.pledgeagainstcatpain.co.uk/