Behavioural Problems in Older Cats

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Key Points

- Increasing numbers of cats are living to old age and behavioural changes are common in these cats.
- The behavioural changes reported most frequently to veterinary surgeons are loss of litter box training (particularly inappropriate urination) and crying out 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 tumours.
- Almost a third of pet cats of 11–14 years of age develop at least one geriatric-onset behaviour problem that appears to relate to CDS; increasing to over 50% for cats of 15 years of age or older.
- These conditions occur frequently in older cats, and many older cats suffer from a number of concurrent interacting conditions.
- Owners and vets often mistake these for 'normal aging changes' so many treatable conditions are neglected and go untreated.

Introduction

With improvements in nutrition and veterinary medicine the life expectancy of pet cats is increasing. In the USA over the last two decades, the percentage of pet cats of over seven years of age has increased to over 40% (Laflamme, et al. 2008), there has been a 15% increase in numbers of cats over 10 years of age (Broussard and others, 1995), and over 10% of pet cats are over 12 years of age (Laflamme, et al. 2008). In the UK it is estimated that there are currently over 2.5 million 'senior' cats (Gunn-Moore 2003), and since this accounts for ~30% of the pet cat population (Venn 1992) the good management of these individuals is becoming an ever more important consideration for small animal veterinary practitioners.

Unfortunately, accompanying this growing geriatric population there are increasing numbers of pets with signs of altered behaviour and apparent senility. These behavioural changes may result from many different disorders (Figure 1) including systemic illness (e.g. hyperthyroidism), organic brain disease (e.g. brain tumours), true behavioural problems (e.g. separation anxiety), or cognitive dysfunction syndrome (CDS). Diagnosis involves a full investigation looking for underlying illness (Figure 2) and assessment for behavioural problems. Once these have been ruled out CDS should be considered, although, ante-mortem, this is a diagnosis of exclusion. The most commonly seen behavioural changes include spatial or temporal disorientation, altered interaction with the family, changes in sleep-wake cycles, house-soiling with inappropriate urination/defecation, changes in activity, and/or inappropriate vocalisation (often displayed as loud crying at night) (Figure 3).

Potential causes of behavioural changes in geriatric cats:

Perhaps the most common causes of behavioural changes in older cats are CDS, osteoarthritis (OA), systemic hypertension (commonly secondary to chronic kidney disease [CKD], hyperthyroidism or, possibly, diabetes mellitus [DM]), hyperthyroidism (even without hypertension), deafness, and brain tumours (most commonly meningioma).

Much has been written elsewhere about the diagnosis and treatment of many of the potential causes of behavioural disorders in old cats. Therefore, this paper will concentrate on perhaps the two most common causes, CDS and OA, with only brief comments on the other conditions.

- **Cognitive dysfunction syndrome**

Cognitive dysfunction syndrome is the term applied to age-related deterioration of cognitive abilities, characterised by behavioural changes (Figure 3), where no medical cause can be found (Chapman and Voith 1990, Rheul and others 1995, Landsberg and Araujo 2005, Gunn-Moore and others 2007). A survey looking at older cats (7-11 years of age) revealed that 36% of owners reported behavioural problems in their cats

(Landsberg 1998), and this increased with age to 88% in cats between 16-19 years of age. A more recent study suggests that 28% of pet cats aged 11–14 years develop at least one geriatric-onset behaviour problem that appears to relate to CDS, and this increases to over 50% for cats of 15 years of age or older: excessive vocalisation and aimless activity are the most common problems in this older age group (Moffat and Landsberg 2003, reviewed in Gunn-Moore and others 2007).

The cause of the syndrome is still unknown, but i) compromised cerebral blood flow and ii) chronic free radical damage are both believed to be important (reviewed in Gunn-Moore and others 2007). i) Numerous vascular changes can occur in the brain of old cats, including a decrease in cerebral blood flow, the presence of small haemorrhages around the blood vessels, and a form of arteriosclerosis (reviewed in Dimakopoulos and Mayer 2002, and Landsberg and Araujo 2005). In addition, the brain of an elderly cat may also be subject to compromised blood flow and hypoxia due to heart disease, anaemia, blood clotting defects, or underlying hypertension. ii) A small amount of the oxygen that is used by cells in normal 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 defences, 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 (reviewed in Landsberg and Araujo 2005, Roudebush and others 2005). 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 β-amyloid protein). In humans and dogs, genetics, diet and life-style choices have all been found to influence the prevalence and pattern of neuropathological changes (particularly β-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.

- **Osteoarthritis**

The importance of OA in cats should not be overlooked (reviewed in Caney 2007). When asked, most owners list the diseases they see in their older cats in a different order to veterinary surgeons. Top of the owner's list are OA and CKD, followed by deafness, blindness, hyperthyroidism, bronchitis, and dental problems (V Halls, personal communication, 2002). The importance of OA in older cats is supported by radiographic evidence of OA affecting the appendicular joints in over 60% of cats over 6 years of age (Clarke and others 2005, Godfrey 2005, Hardie and others 2002, Slingerland and others 2011), with changes being seen most frequently in elbows, hips, stifles, tarsus and shoulders (Hardie and others 2002, Clarke and others 2005, Clarke and Bennett 2006, Lascelles and others 2010a, Slingerland and others 2011).

The presence of OA in cats is often overlooked because the changes typically develop slowly, are usually bilaterally symmetrical and cats are good at modifying their lifestyle rather than showing obvious discomfort. Therefore, the signs of OA in cats are much more subtle than those seen in dogs. Common signs include weight loss, depression (typically seen as becoming withdrawn from owners and other companions), reduced time spent playing or hunting, increased time spent resting or sleeping, abnormal or inappropriate elimination of faeces or urine (i.e. constipation or litter box errors), poor grooming (typically over the lumbar region and hind end), aggressive behaviour (particularly towards other cats, children or when being picked up), a reduced ability or hesitance to jump, a stiff or stilted gait, changes in the wear of their nails (overgrown nails, nails clicking on hard floors when walking and/or nails getting caught in carpets), crying from apparent pain when lifted up, and/or a reluctance to use the cat flap (Clarke and others 2005, Godfrey 2005, Clarke and Bennett 2006, Slingerland and others 2011). Unfortunately, many of these changes are misinterpreted as the result of 'normal aging changes' rather than being indicative of OA.

Most OA in cats is believed to be idiopathic (70-90%) (Godfrey 2005, Clarke and Bennett 2006), although this may still be related to low-grade primary degeneration, low-grade trauma, or slight mal-articulation. Secondary OA may result from trauma, infection, diet (there is a five-fold increase in the risk of OA with obesity (Scarlett and others 1994), lifestyle, genetics, or developmental defects such as patella luxation and/or hip dysplasia (Keller and others 1999). Watching a cat walk around the consultation room and

performing a careful orthopaedic examination is often all that is needed to diagnose the presence of OA in a cat. However, when taking radiographs of an older cat for other reasons it is important to look for signs of OA.

- **Systemic hypertension**

Systemic hypertension is a common cause of behavioural change in older cats, and typically causes night-crying, disorientation, altered consciousness, circling and even seizures. The most common causes of hypertension in cats are CKD and hyperthyroidism, with reported prevalence figures varying from ~25% of cats with CKD seen in first opinion practice up to 60-65% in referral practice, and between 10 and 90% of hyperthyroid cats. Other diseases that have been associated with hypertension in cats include hyperaldosteronism, DM, acromegaly, chronic anaemia, and erythopoietin therapy. Additional causes in other species include hyperadrenocorticism, phaeochromocytoma, glucocorticoid administration and obesity. Since many of these diseases occur in older cats this explains why most hypertension is seen in this age group. This is confirmed in a study looking at apparently healthy cats of at least nine years of age (median 13 years) where 13% were found to be hypertensive (Jepson et al 2009).

Unfortunately, hypertension is usually only suspected very late in the course of disease once end-organ damage has already occurred. This is typically seen as cerebral vascular accidents (causing behavioural changes and/or neurological disorders), exacerbation of kidney disease, intraocular haemorrhage and/or blindness, and/or left ventricular hypertrophy (Elliott et al 2001; Henik 1997). Ocular changes include anterior chamber, vitreal or retinal haemorrhage, retinal oedema or detachment, arterial tortuosity, glaucoma and blindness.

Blood pressure (BP) should be evaluated as a routine part of all check-ups of older cats, as should a detailed ophthalmic examination. Various indirect methods exist for the measurement of BP. However, in cats, the Doppler method is currently considered to be the most appropriate, as oscillometric methods tend to underestimate the BP and fail to produce a reading in a significant number of conscious cats (Bartges et al 1996; Brown et al 2000, Jepson et al 2005 JFMS). The only problem with the Doppler method is that it is not always possible to measure the diastolic BP.

Prompt action is needed to minimise long-term damage, so anti-hypertensive therapy should be prescribed where the mean systolic BP reading, taken with the cat in a calm state, is persistently above 170-180 mmHg or where there is evidence of hypertensive retinopathy (Stepien 2004). IRIS Guidelines (for cats with CKD): systolic BP <150 mmHg [minimal risk], 150-160 mmHg [low risk], 160-180 mmHg [moderate risk], >180 mmHg [high risk]. The diastolic BP of normal cats should be <95 mmHg (Mishna et al 1998).

- **Chronic kidney disease**

CKD can be associated with behavioural problems for many reasons: i) polyuria may lead to periuria (inappropriate urination) (i.e. where the periuria is simply related to the need to urinate more frequently), ii) periuria/dysuria may be associated with secondary bacterial cystitis (see below), iii) associated systemic hypertension may result in cerebral vascular compromise (see above), iv) polyuria without adequate access to water can result in significant cerebral dehydration and associated clinical signs (typically seen as confusion and depression), v) polydipsia may lead to drinking from unusual vessels and places, vi) the development of significant acidosis may result in anorexia, weight loss and lethargy (Polzin et al 2000) and vii) severe uraemia may result in uraemic encephalopathy.

- **Hyperthyroidism**

Hyperthyroidism can result in behavioural signs for many of the same reasons as CKD (i-v). However, it can also result in behavioural changes as a direct effect of thyroxin on the brain (typically seen as agitation, restlessness and aggression), or be associated with polyphagia (seen as stealing food and altered appetite). Poorly controlled cases can sometimes be presented with disorientation and signs of bilateral central vestibular disease (dilated pupils, lack of menace response, and neck ventroflexion), which is believed to result from a secondary thiamine deficiency (similar to thyrotoxicosis-associated Wernicke's encephalopathy in humans [Sechi 2008]).

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- **Diabetes mellitus**

DM can result in behavioural signs for many of the same reasons as CKD (i-vi), while also having associated polyphagia (as seen with hyperthyroidism). In addition, cats with unstable DM may develop sensory and/or motor neuropathies, with the former being seen as irritability, sensitivity to touch, and/or muscle pain.

- **Urinary tract infection**

Urinary tract infections (UTIs) typically result in behavioural changes related to bladder and/or kidney pain; being seen as periuria, dysuria, pollakiuria, withdrawal, aggression, depression, and/or pain on being lifted. However, the author has seen cases of *E. coli* UTIs that have presented with confusion and disorientation. This may be similar to a condition seen in elderly humans with quinolone-resistant *E. coli* UTIs (Colodner and others 2008), where the bacteria appear to have a systemic toxic effect.

Unlike the situation in younger cats, bacterial UTIs are a common cause of lower urinary tract signs in older cats (Figure 4) (Bartges and Blanco 2001, Bartes 2002). Infection is typically associated with underlying CKD, hyperthyroidism or DM, which all result in less concentrated urine (in which bacteria can replicate) and may also have local and/or systemic immunosuppressive effects; e.g. uraemia and hyperglycaemia are both believed to have inhibitory effects on neutrophil function. Studies have found that 12% of cats with DM or hyperthyroidism have a UTI at some point during their illness, and this rises to 22-35% for cats with CKD (Demetriou and others 1997; Mayer-Roenne and others 2006). Since the presence of a UTI does not always result in specific clinical signs of either renal or bladder infection it is essential that old cats are regularly assessed for the presence of a UTI. Unfortunately, pyuria and/or active urine sediment is not always present with these diseases (Mayer-Roenne et al, 2006), so the diagnosis can only be confirmed by performing bacterial culture. Urinary tract infections may also be iatrogenic, or secondary to urolithiasis, neoplasia, or an anatomical defect.

- **Changing appetite, weight loss, gastrointestinal (GI), pancreatic and/or liver disease**

Many older cats experience changes in appetite and body weight. This can result from a number of different, often interacting, factors. These may include physiological ageing changes and/or the presence of pathological disease processes. Weight loss is often associated with inappetence and in older cats this commonly results from reduced senses of smell and taste, and/or oral pain associated with periodontal disease. In addition, older cats tend to be less efficient at digesting their food. This probably results from reduced intestinal function, gastric acid production, gastric and intestinal motility, intestinal blood flow, and pancreatic lipase activity and changes in the composition of bile (Polzin and others 1989, Saltzman and Russell 1995, Harper 1998, Burkholder 1999, Fahey and others 2008). While these factors effect the digestion of all dietary components they particularly effect the digestion and absorption of fats and proteins (Taylor and others 1995, Harper 1998, Fahey and others 2008). This can result in some cats needing to increase their intake by as much as 25% (Taylor and others 1995), so weight loss is likely when more frequent meals are not offered or when eating is painful. The presence of GI, pancreatic and/or liver disease can exacerbate this further. Many older cats have significantly reduced serum concentrations of B_{12} (cobalamin) which can in turn result in anorexia, GI dysfunction and neurological disease.

Significant weight changes should always be investigated because weight loss is often the first sign of disease. However, while many of the diseases seen in older cats are associated with inappetence and a reluctance to eat, some conditions, such as hyperthyroidism, and some of the mal-assimilation syndromes (e.g. inflammatory bowel disease, exocrine pancreatic insufficiency associated with chronic pancreatitis, some cases of chronic lymphocytic cholangitis, and early GI lymphocytic lymphoma) may be accompanied by a good or even increased appetite. Owners therefore need to know that any alteration in appetite is significant; increase or decrease. Other behavioural changes may include depression, hiding and reluctance to be picked up, which can be due to intra-abdominal pain and discomfort, and severe liver disease with hepatic encephalopathy may result in disorientation, hypersalivation, collapse and seizures.

- **Loss of hearing and/or vision**

While many old cats cope remarkably well with progressive blindness, progressive deafness often appears more problematic. Deaf cats typically sleep very soundly, then awake startled when touched. Many also meow more loudly than previously. It is perhaps the lack of calming familiar noise that causes a deaf cat to call out loudly when it awakens at night; it may be trying to attract its owner's attention and seek comfort.

- **Brain tumours**

Brain tumours occur most commonly in older cats (average age 11 years), with primary tumours accounting for 70% of cases. The most commonly seen tumours are meningioma (58%), lymphoma (14%), pituitary tumours (14%) and gliomas (7.5%) (Troxel and others 2003); with the most common neurological signs being altered consciousness, circling, and seizures (Nafe 1979, Troxel and others 2003, Tomek and others 2006).

- **Pain**

Chronic pain can be very debilitating. Chronic pain is probably seen most frequently in old cats related to OA (see above). However, it can also result from inflammation or disease elsewhere in the cat, particularly periodontal disease, or chronic GI disorders (e.g. constipation). Evolutionarily, there would be a clear disadvantage for a species like the cat, which is a small solitary hunter, to show obvious signs of pain: the demonstration of pain or injury could result in the damaged cat drawing attention to itself and then being eaten by a larger predator-species. It is believed to be because of this that cats are able to hide pain so effectively.

- **Infectious disease** (e.g. FIV, FeLV, toxoplasmosis, FIP).

Infectious diseases are typically seen much less commonly in older cats than young cats. However, they can still occur and may cause behavioural/neurological abnormalities. The history and more general clinical signs should help in suggesting the possibility of an underlying infectious disorder.

Diagnosis and management of older cats with behavioural disorders

Gaining a correct diagnosis involves a full investigation (Figure 2). Unfortunately, the diagnosis and management of older cats are often complicated by the concurrent presence of multiple interacting disease processes. In some cases, interacting conditions may worsen clinical signs, for example, OA, CKD (or other causes of polyuria), plus or minus increased faecal urgency (with chronic GI disease), or difficult defecation (with constipation) may each exacerbate apparent loss of litter box training. Concurrent hyperthyroidism and 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 (Graves and Peterson 1990, Crenshaw 1996), 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 (Hoenig and Ferguson 1989, Reusch and Tomsa 1999). In some cases the treatment of one disease may worsen another e.g. treatment of hyperthyroidism can unmask the severity of CKD (Graves and Peterson 1990). Prompt and full investigation is therefore essential if management is to be effective.

Unfortunately, it is not always easy for owners to recognise signs of ill health in their cat - they often do not know what signs to look for. Vets need to educate owners as to what should be monitored 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 very treatable disease. Owners need to monitor their older cats for changes in food and water consumption, body weight, production of urine and faeces, and behaviour. It is because of this that the implementation of Senior Health Care Clinics can be very 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 BP, and retinal examination; and ideally, in-practice mobility assessment plus full orthopaedic 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, thyroid level assessment and haematology, serum cobalamin concentration and, where appropriate, serological testing for FeLV and FIV and, where indicated, toxoplasmosis and/or FIP. A urine sample should undergo routine urine analysis, urine protein to creatinine ratio and, where ever possible, bacterial culture. Initially, most cats will

only need to attend a clinic once or twice a year. However, those cats showing significant ageing changes may need to attend more frequently for repeated reassessment, monitoring and treatment.

Management of cats with CDS

Although CDS cannot be cured, its clinical signs can be reduced with suitable intervention. 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 dogs with CDS and even from humans with Alzheimer's disease. Potential interventions include dietary modification, environmental management, and drug therapies (reviewed in Landsberg 2006).

- *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, so reducing β-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 B_{12} 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 (Ikeda-Douglas 2004, reviewed in Head and Zicker 2004, Landsberg 2006, Roudebush and others 2005). For example, a study of dogs over six 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 UK as Aktivait® from VetPlus) over a two month period resulted in significant improvements in signs of disorientation, social interaction, and house soiling (Heath and others 2007). Unfortunately, a different formula is needed for cats as alpha-lipoic acid is toxic in this species (Hill and others 2004) 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.

A number of other supplements have also been investigated in dogs. For example, placebo-controlled studies have shown significant improvements in dogs with CDS when given a supplement containing ginkgo biloba, vitamins B_6 and E, and resveratrol (Senilife® from CEVA Animal Health) (Araujo and other 2008), and activity and awareness were improved when S-adenosyl-l-methionine (SAMe) was given as a supplement (Bottiglieri and others 2002, Rème and others 2008). While SAMe has not been studied for the treatment of CDS in cats, it is known to be safe in this species and may be worth considering for the management of feline dementia (Landsberg and others 2010). There is now a growing list of compounds that have been suggested to have beneficial effects on the aging feline brain (Landsberg and others 2010), however, no placebo-controlled studies have yet been reported relating to their use in this species, either as single ingredients or in potentially synergistic combinations.

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 four year study on the use of an antioxidant-enriched 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) (Hill's b/d®), plus environmental enrichment (e.g. toys, kennel mate, walks, and cognitive experience testing) revealed rapid (2-8 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 β-amyloid while the environmental enrichment did not (Milgram and others 2004, 2005).

The clinical signs of CDS in dogs have also been reduced by feeding a diet enriched with plant-derived medium-chain triglycerides (MCTs) which provide ketones as a more efficient energy source for the brain (Purina One Vibrant Maturity 7+) (Pan and others 2010). Unfortunately, cats are generally not keen on eating diets enriched with MCTs so it is unclear if this approach will be useful for cats with CDS.

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 (7-17 years old; n=90) a diet (Nestlé Purina Pro Plan Age 7+®) supplemented with antioxidants (vitamin E and β-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 un-supplemented ones (Cupp and others 2006). A preliminary study looking at a diet supplemented with tocopherols, l-carnitine, vitamin C, beta-carotene, docosa-hexaenoic acid, cysteine and methionine, which was fed to 46 elderly cats, showed increased activity compared to control cats (Houpt and others 2007). Other similarly supplemented diets are now on the market (e.g. Hill's Feline j/d® which is actually designed for cats with OA, is supplemented with a mixture of anti-oxidants [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 of 75 cats of 12 years of age or older, that were not selected for signs of CDS or (OA), where owners were asked to complete questionnaires >70% improved in one or more signs of cognitive function (and >50% improved in one or more signs of mobility) (Hill's data, 2008).

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) (Houpt and Beaver 1981). For these cats, where possible, change should be kept to a minimum, and when it cannot be avoided it 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 e.g. to a single room containing everything they need; i.e. the **key resources for cats**: food, water, litter box, resting places, either 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). However, there are currently very few that have actually been approved for the treatment of human dementia. Selegiline (Selgian®; Ceva: Anipryl®; Zoetis), propentofylline (Vivitonin®; MSD Animal Health) and nicergoline (Fitergol®; Merial) are the only drugs that have been approved for the treatment of canine dementia in either the United Kingdom or the United States. Although **there are no drugs licensed for the treatment of CDS in cats,** a number of drugs have been used 'off label' (Landsberg and others 2003, Landsberg and Araujo 2005, Studzinski and others 2005, Landsberg 2006). These include selegiline (Selgian®; Ceva: Anipryl®; Pfizer: suggested dose 0.25-1.0 mg/kg PO q24h), propentofylline (Vivitonin®; MSD Animal Health: suggested dose 12.5 mg/cat PO q24h) and nicergoline (Fitergol®; Merial: suggested dose 0.25 to 0.5 mg/kg), 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 (Landsberg 2006) 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®; MSD Animal Health), buspirone and benzodiazepines (e.g. diazepam - although hepatotoxicity is a particular risk with this drug), or antidepressants (that lack anticholinergic effects) such as fluoxetine.

Management of Osteoarthritis

Despite the recent finding that over 90% of owners are willing to have their cat treated for OA (Boehringer Ingelheim 2007) few vets appear to realise that owners can recognise this condition or that they would wish to have their cat treated. Successfully treated cats will experience a reduction in pain and improvements in mobility, activity and overall quality of life.

Environmental changes: Regardless of any other interventions it is important to recommend that owners adjust their homes to accommodate their arthritic cats. This may include moving food and water bowls to lower surfaces (and raising them up a couple of inches for cats with OA in their front legs and/or neck), adding ramps to allow easier access to favoured sleeping areas, providing deep comfortable bedding that will support and protect the cat's joints (heated beds can be particularly soothing), placing large low-sided litter boxes within easy reach and changing the litter to a sandy-type of litter which is often easier on the cats paws. The cat needs to have easy access to all key resources: food, water, litter box, resting places, and hiding places. It is important to realise that while these changes will help the cat to cope with its physical disability and reduce the strain on its joins, the cat may still be in pain.

Weight change: Reducing obesity will reduce the stress on the cat's joints, so reducing pain. It is important to monitor the cat's weight as an unexpected weight loss may indicate that the cat can no longer gain access to its food, that it is experiencing food bowl competition, or that it may have developed significant systemic disease.

Dietary modification: Pet food companies are developing diets that help in the management of pets with OA (Servet and others 2006). Hill's Pet Nutrition developed Prescription Diet Canine j/d®, which contains ingredients which help to reduce joint pain and inflammation and modify gene expression in the regulation of cartilage metabolism, and has been shown to be beneficial either on its own or when given with non-steroidal anti-inflammatory drugs (NSAIDs) (where a lower dose of NSAID is usually required) (Schoenherr 2005, reviewed in Budsberg and Bartges 2006, Hahn and others 2008a and b). A similar approach has also been made with cats (Hill's Prescription Diet Feline j/d®) using appropriate anti-oxidants (e.g. vitamins C and E, and beta carotene), essential n-3 fatty acids, chondroprotectants (e.g. methionine, glycosaminoglycans, glucosamine, and chondroitin sulphate), and L-carnitine and lysine (to aid obesity management and the build-up of lean muscle) and has already shown benefits (see section on CDS). In addition, in a randomized double blind study of 172 cats with an average age of 12 years and obvious evidence of OA, 61% of the cats with moderate or severe OA improved on the experimental food, compared to only 37% on the control food (Fritsch and others 2008). A test diet supplemented with EPA, DHA, green-lipped muscle, glucosamine and chondroitin sulphate was evaluated in a randomized double blind study involving 40 cats with moderate to severe osteoarthritis that lasted for nine weeks. The cats were assessed by owner questionnaires, veterinary examination and activity monitors, and the cats fed the test diet showed a significant increase in the cats' activity (Lascelles et al 2010b).

Glucosamine, chondroitin supplements, extract of tumeric and green-lipped muscle: While no studies have been published on the use of these individual compounds in cats with OA, findings from other species suggest that while likely to be beneficial, they will probably provide only partial relief in early and mild cases, and have little effect once severe changes have developed (reviewed in Sanderson and others 2009). One currently unpublished randomised double-blinded clinical trial compared the effectiveness of a glucosamine/chondroitin supplement with meloxicam and found that while the cats receiving the nutraceutical did improve, but they did not improve as much as those on meloxicam, and it took longer. However, when the groups were changed to placebo the improvement seen with the nutraceutical group lasted longer than that in the meloxicam group (Bennett et al 2012b).

NSAIDs: Treatment with NSAIDs can be very effective. A prospective open-label study using a low-dose long-term (28 day) course of meloxicam resulted in relief from OA in all cats treated, with the effect being considered moderate or marked in 75%. Significant improvements were seen in willingness to jump, height of jump, reduction in joint pain on palpation, and general improvements in temperament (Clarke and Bennett 2006). In a second study, 40 cats with OA were given meloxicam (0.01-0.03 mg/kg PO q24 hours), and 80% reported good or excellent results (Gunew and others 2008). However, since cats can be particularly sensitive to the side effects of NSAIDs care must be taken when considering whether or not to give these potentially nephrotoxic and gastrotoxic drugs to older cats, especially if there is any degree of CKD. Always use the lowest possible dose, and assess serum biochemistry and urine for evidence of renal dysfunction prior to starting treatment and regularly while treatment is ongoing. NSAIDs should only be used with extreme care (or not at all) in dehydrated animals, those with poor circulatory, liver, kidney, gut, or platelet function, or in those animals receiving glucocorticoids or diuretics.

Glucocorticoids do have anti-inflammatory actions but they also have potentially deleterious effects on cartilage, and can cause serious systemic side effects, and/or exacerbate concomitant diseases, such as CKD and DM.

Other treatment modalities include other drugs (e.g. opiates [e.g. fentanyl patches, tramadol, oral buprenophine], tricyclic antidepressants, or gabapentin), or interventions (e.g. surgery, acupuncture, electro-acupuncture, transcutaneous spinal electro-analgesia, physiotherapy, or massage) and while they may be of benefit in individual cases little data is currently available relating to their use in cats (Lindley 2006, 2007a,b, Caney 2007). Surgery (e.g. tibial crest transposition for patella luxation, femoral head resection for hip dysplasia, or arthrodesis for severe joint instability) it is generally considered a salvage procedure.

Treatment of Hypertension

Hypertension should be treated with calcium channel blockers (CCBs) (e.g. amlodipine besylate; 0.625-1.25 mg/cat po q24h), and/or angiotensin converting enzyme (ACE) inhibitors (e.g. benazepril; 0.25-1.0 mg/kg po q24h) and, where possible, any underlying conditions should be treated (fully reviewed in Stepien 2004). For monotherapy, amlodipine appears to be the most successful agent and is associated with few side effects. Response to therapy should be monitored closely. In successfully treated cases, the BP should fall to within the normal range in 7-10 days of initiating therapy (ideally having a systemic BP between 130-170 mmHg and diastolic BP of <95 mmHg). In some cases, it may be necessary to add in an ACE-inhibitor to achieve an adequate response. Once BP is stable, patients should be assessed every 1-2 months, reducing the frequency to a minimum of once every six months in very stable patients. It is important to monitor blood urea and creatinine in all patients; before starting anti-hypertensive therapy and during the initial treatment period. This is particularly important in patients with pre-existing renal disease.

Other aspects of management of behavioural changes in older cats:

- To reduce the risk of dehydration resulting from concurrent CKD, DM, or hyperthyroidism it is often advisable to feed a diet with high water content. However, if cats are unwilling to eat wet food, then it may be helpful to try to increase their fluid intake using other methods. Drinking can be encouraged by ensuring constant access to fresh water (having an adequate number of water bowls that are within easy reach), using bottled water or pet water-fountains, or by giving fishy water or chicken/meat stock (ensure that no onion or onion powder has been added as cats can develop haemolytic anaemia if fed onion, and ensure that the liquid is not too salty as this may lead to sodium overloading).
- UTIs should be treated according to urine culture and sensitivity and, in the case of CKD may need 4-8 weeks of antibiotics. Ideally, the urine should be re-cultured one week after starting treatment to check that the antibiotics are working, and again one week after completing the course to ensure the infection has resolved.
- To compensate for reduced GI function many older cats may benefit from being fed a highly palatable, highly digestible, energy dense food; and that it is offered in small amounts frequently. Serum concentrations of cobalamin (plus folate) should ideally be assessed prior to supplementation of these vitamins.
- Many recent reviews are available for the treatment of hyperthyroidism and DM (Gunn-Moore 2005, Rand and Marshall 2005, Behrend 2006, Rois and Ward 2008), CKD (Lefebvre and Toutain 2004, Elliott 2006, Roudebush and others 2009), and brain neoplasia (Troxel and others 2003) in cats.

Treat the individual

While veterinary medicine can often offer complex therapeutic options and sophisticated prescription diets it is important to remember that older cats are often poorly tolerant of the stress of hospitalisation or of excessive physical handling. Therefore, it is essential that each cat be assessed and treated as an individual. In some cases investigations and interventions may have to be adapted or even abandoned if the cat is poorly tolerant for either medical or temperamental reasons. Also, once our patient's quality of life can no longer be maintained it is important that euthanasia be discussed, and then performed, as compassionately as possible.

While it is true to say that "old age is not a disease", it is important that we pay particular attention to our older cats, feed and care for them appropriately, and observe them closely so we can keep them well, for as long as possible.

Figure 1: Potential causes of behavioural 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, hyperadrenocorticism, hyperaldosteronism, chronic anaemia)
- Hyperthyroidism
- Chronic kidney disease (CKD)
- Diabetes mellitus (DM)
- Urinary tract infection (UTI)
- Gastrointestinal disease
- Liver disease (hepatic encephalopathy)
- Reduced vision or hearing
- Brain tumours (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 behavioural problems

Figure 2: Investigation of behavioural changes in older cats should include:

- Full history, including the possibility of previous trauma (which may have lead 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 alternations in the cat's behaviour can help in determining how the cat has changed (see **Mobility and Cognitive Dysfunction Questionnaire –** see below).
- Full physical examination (including assessment of body weight, calculation of percentage change in body weight, body condition score, and retinal examination).
- **Assess systemic blood pressure** (this is particularly important as hypertension occurs commonly in older cats and produces many of the same signs as CDS)
- **Mobility assessment, plus neurological and orthopaedic examinations -** which can be challenging in some cats
- **Assess haematology and serum biochemistry**, including thyroid hormone level
- **Urine analysis** (including urine protein to creatinine ratio and bacterial culture [even if the urine sediment appears non-reactive [Mayer-Roenne et al, 2006])

  Further investigation may include:
- Where appropriate, serological testing for FeLV, FIV, Toxoplasmosis, FIP or other infectious diseases
- Thoracic, abdominal or skeletal radiography, abdominal ultrasound examination, ECG, echocardiography, intestinal endoscopy / exploratory laparotomy and biopsy collection, as indicated from initial findings.
- Head CT or MRI

Mobility and 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	☐	☐	☐
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 behavioural/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 behavioural 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 (house-soiling is the most common reason for referral of old cats to behavioural specialists)
- Altered social relationships, either with their owners or other pets in the household e.g. increased attention seeking or aggression
- Altered behavioural responses e.g. increased irritability or anxiety, or decreased response to stimuli
- Changes in sleep/wake patterns
- Inappropriate vocalisation 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 that they have just been fed

References

Araujo JA, Landsberg GM, Milgram NW, Miolo A. Improvement of short-term memory performance in aged beagles by a nutraceutical supplement containing phosphatidylserine, Ginkgo biloba, vitamin E, and pyridoxine. Can Vet J. 49(4):379-85, 2008

Araujo JA, Faubert ML, Brooks ML, et al. NOVIFIT® (NoviSAMe®) tablets improve executive function in aged dogs and cats: implications for treatment of cognitive dysfunction syndrome. Intern J Appl Res Vet Med 10: 90-98, 2012

Bartges JW, Blanco L. (2001) Bacterial urinary tract infection in cats. Comp of Standard of Care, 3: 1-5, 9

Bartges JW, Willis AM, Polzin DJ (1996) Hypertension and renal disease. Vet Clin North Am: Small Anim Prac 26, 1331

Bartges JW (2002) What's new in feline LUTD? Proceedings of the European College of Veterinary Internal Medicine, Munich, Germany, 93-97

Behrend EN. (2006) Update on drugs used to treat endocrine diseases in small animals. Vet Clin North Am Small Anim Pract.;36(5):1087-105
Bennett D, Siti Mariam bt Zainal Ariffin, P Johnston (2012) Osteoarthritis in the cat: How common is it and how easy to recognise? JFMS 14: 65-75
Bennett D, Siti Mariam bt Zainal Ariffin, P Johnston (2012) Osteoarthritis in the cat: How should it be managed and treated? JFMS 14: 76-84
Bottiglieri T. S-Adenosyl-L-methionine (SAMe): from the bench to the bedside--molecular basis of a pleiotrophic molecule. Am J Clin Nutr. 76(5):1151S-7S, 2002
Broussard JD, Peterson ME, Fox PR. (1995) Changes in clinical and laboratory findings in cats with hyperthyroidism from 1983 to 1993. JAVMA, 206(3):302-5
Brown SA, Henik RA, Finco DR (2000) Diagnosis of systemic hypertension in dogs and cats. In: Current Veterinary Therapy XIII, ed Kirk RW, Bonagura JD. Philadelphia: Saunders. p835
Budsberg SC, Bartges JW. (2006) Nutrition and osteoarthritis in dogs: does it help? Vet Clin North Am Small Anim Pract.;36(6):1307-23
Burkholder WJ. (1999) Age-related changes to nutritional requirements and digestive function in adult dogs and cats. J Am Vet Med Assoc;215(5):625-9.
Caney S (2007) Feline arthritis. Veterinary Focus 17(3): 10-16
Chapman, B.L., Voith, V.L. (1990) Behavioral problems in old dogs: 26 cases (1984-1987). JAVMA, 196(6): 944-946
Clarke SP, Bennett D (2006) Feline osteoarthritis: a prospective study of 28 cases. Journal of Small Animal Practice 47(8): 439-445
Clarke SP, Mellor D, Clements DN, Gemmill T, Farrell M, Carmichael S, Bennett D (2005) Prevalence of radiographic signs of degenerative joint disease in a hospital population of cats. Vet Rec 157: 793-799
Colodner R, Kometiani I, Chazan B, Raz R. (2008) Risk factors for community-acquired urinary tract infection due to quinolone-resistant *E. coli.* Infection.;36(1):41-5.
Crenshaw KL, Peterson ME. (1996) Pretreatment clinical and laboratory evaluation of cats with diabetes mellitus: 104 cases (1992-1994). J Am Vet Med Assoc.;209(5):943-9
Cupp CJ, Jean-Philippe C, Kerr WW, Patil AR and Perez-Camargo G (2006) Effect of nutritional interventions on longevity of senior cats. Intern J Appl Res Med 4(1): 34-50
Demetriou J, Barber PJ, Elliott J (1997) Influence of urine concentration on growth of bacteria in feline urine. BSAVA proceedings, Birmingham, p241
Dimakopoulos AC and Mayer RJ. (2002) Aspects of neurodegeneration in the canine brain. J Nutr. 132(6 Suppl 2):1579S-82S
Elliott DA. (2006) Nutritional management of chronic renal disease in dogs and cats. Vet Clin North Am Small Anim Pract.;36(6):1377-84
Elliott J, Barber PJ, Syme HM, Rawlings JM, Markwell PJ (2001) Feline hypertension: clinical findings and response to antihypertensive treatment in 30 cases. J Small Anim Pract 42, 122-129
Fahey GC Jr, Barry KA, Swanson KS (2008) Age-related changes in nutrient utilization by companion animals. Annu Rev Nutr;28:425-45
Fritsch D, Allen T, Sparkes A, Marion C, Hahn K (2008) Improvement of Clinical Signs of Osteoarthritis in Cats by Dietary Intervention. Proceedings of the18th ECVIM-CA Congress, 2008
Graves TK, Peterson ME. (1990) Diagnosis of occult hyperthyroidism in cats. Probl Vet Med;2(4):683-92.
Godfrey DR (2005) Osteoarthritis in cats: a retrospective radiological study. Journal of Small Animal Practice, 46: 425-429
Gunew M, Menrath VH, Marshall RD (2008) Long-term safety, efficacy and palatability of oral meloxicam at 0.01-0.03 mg/kg for treatment of osteoarthritis in cats. JFMS, 10: 235-241
Gunn-Moore, D.A (2003) Considering Older Cats. Compendium on Continuing Education for the Practising Veterinarian. (Supplement), 26, No. 2 (A), 1-4
Gunn-Moore D. (2005) Feline endocrinopathies. Vet Clin North Am Small Anim Pract. 2005 Jan;35(1):171-210
Gunn-Moore, D.A., Moffat, K., Christie, L.-A., Head, E. (2007) Cognitive dysfunction and the neurobiology of aging in cats. *JSAP*, 48: 546-553
Hahn KH, Allen TA, Dodd CD, Fritsch DF, Jewell DJ, Sixby KS, Marion CM, Paetau-Robinson IPR (2008) Dose titration effects of omega-3 fatty acids fed to osteoarthritic dogs. Proceedings of the BSAVA Congress, Birmingham, 2008, pp388
Hahn KH, Allen TA, Fritsch DF, Jewell DJ, Sixby KS, Marion CM, Paetau-Robinson IPR (2008) Feeding an EPA-enriched food reduces the doses of NSAIDs in the management of dogs with chronic osteoarthritis. Proceedings of the BSAVA Congress, Birmingham, 2008, pp392
Hardie E, Roe S, Martin F (2002) Radiographic evidence of degenerative joint disease in geriatric cats (1994-1997). JAVMA, 220(5): 628-632
Harper EJ. (1998) Changing perspectives on ageing and energy requirements: Ageing, bodyweight and body composition in humans, dogs and cats. J of Nut, 128: 2627S-2631S
Head E and Zicker SC (2004) Nutraceuticals, aging and cognitive dysfunction. Vet Clin North Am Small Anim Pract 34: 217-228

Heath S, Barabas S, Craze P (2007) Nutritional supplementation in cases of canine cognitive dysfunction. Journal of Applied Animal Behavioral Science, 105: 284-296
Henik RA (1997) Diagnosis and treatment of feline systemic hypertension. Comp Cont Edu Small Anim Pract 19, 163
Hill AS, Werner JA, Rogers QR, O'Neill SL, Christopher MM. (2004) Lipoic acid is 10 times more toxic in cats than reported in humans, dogs or rats. J Anim Physiol Anim Nutr (Berl).;88(3-4):150-156
Hoenig M, Ferguson DC. (1989) Impairment of glucose tolerance in hyperthyroid cats. J Endocrinol. 1989 May;121(2):249-51
Houpt KA, and Beaver, B. (1981) Behavioral problems of geriatric dogs and cats. Veterinary Clinics of North America: Small Animal Practise 11:643-652
Houpt K, Levine E, Landsberg G, Moffat KS, Zicker SC. Antioxidant fortified food improves owner perceived behaviour in aging the cat. Proceedings of the ESFM Conference; Prague, Czech Republic, 2007
Ikeda-Douglas, C.J., Zicker, S.C., Estrada, J., Jewell, D.E. and Milgram, N.W. (2004) Prior experience, antioxidants, and mitochondrial cofactors improve cognitive function in aged Beagles. Veterinary Therapeutics, 5(1):5-16
Jepson RE, Elliott J, Brodbelt D, Syme HM (2007) Effect of control of systolic blood pressure on survival in cats with systemic hypertension. J Vet Intern Med.;21(3):402-9
Jepson RE, Brodbelt C, Vallance C, Syme HM, Elliott J. (2009) Evaluation of predictors of the development of azotemia in cats. JVIM 23, 806-813
Keller GG, Reed AL, Lattimer JC, Corley EA (1999) Hip dysplasia: A feline population study, Veterinary Radiology & Ultrasound 40, 460-464
Kobayashi DL, Peterson ME, Graves TK, Lesser M, Nichols CE (1990) Hypertension in cats with chronic renal failure or hyperthyroidism. J Vet Int Med 4, 58
Laflamme DP, Abood SK, Fascetti AJ, Fleeman LM, Freeman LM, Michel KE, Bauer C, Kemp BL, Doren JR, Willoughby KN. (2008) Pet feeding practices of dog and cat owners in the United States and Australia. JAVMA 232:687-694.
Lascelles BDX, Henry JB, Brown J, Robinson I, Thomson Sumrell A, Simpson W, Wheeler S, Hansen BD, Zamprogno H, Freire M, Pease A. Cross-sectional study of the prevalence of radiographic degenerative joint disease in domesticated cats. Veterinary Surgery, 2010a, 39: 535-544
Lascelles BDX, DePuy V, Thomson A, Hansen B, Marcellin-Little DJ, Biourge V, Bauer JE. Evaluation of a therapeutic diet for feline degenerative joint disease. JVIM 2010b: 24: 487-495
Landsberg G. (2006) Therapeutic options for cognitive decline in senior pets. J Am Anim Hosp Assoc. 42(6):407-13.
Landsberg G (1998) Behavior problems of older cats. In: Schaumburg I (ed): Proceedings of the 135th Annual Meeting of the American Veterinary Medical Association, San Diego, CA, pp 317-320.
Landsberg GL and Araujo JA. Behavior Problems in Geriatric Pets. (2005) Vet Clin Sm An Pract: 35 675-698.
Landsberg GL, Hunthausen W and Ackerman L. (2003) The Effects of Aging on behavor in Senior Pets In: Handbook of Behavior Problems in the Dog and Cat. 2nd edition. London: WB Saunders; P. 269-304.
Landsberg GM, Denenberg S, Araujo JA. Cognitive dysfunction in cats: a syndrome we used to dismiss as 'old age'. J Feline Med Surg. 12(11):837-48, 2010
Lefebvre HP, Toutain PL. (2004) Angiotensin-converting enzyme inhibitors in the therapy of renal diseases. J Vet Pharmacol Ther.;27(5):265-81.
Lindley S (2006) Spotting the clues to feline chronic pain. Veterinary Times, Dec 25.
Lindley S (2007a) Cats in pain: three case studies. Veterinary Times, May 14.
Lindley S (2007b) Management of chronic feline pain. Veterinary Times, Aug 20.
Littman MP (1994) Spontaneous systemic hypertension in 24 cats. J Vet Int Med 8, 79
Mayer-Ronne B, Goldstein RE, Erb HN (2006) Urinary tract infections in cats with hyperthyroidism, diabetes mellitus and chronic kidney disease. JFMS, 9(2): 124-32
Milgram NW, Head E, Zicker SC, Ikeda-Douglas C, Murphey H, Muggenberg BA, Siwak CT, Tapp PD, Lowry SR, Cotman CW. (2004) Long-term treatment with antioxidants and a program of behavioral enrichment reduces age-dependent impairment in discrimination and reversal learning in beagle dogs. Exp Gerontol.39(5):753-65.
Milgram NW, Head E, Zicher SC, Ikeda-Douglas CJ, Murphey H, Muggenburg B, Siwak C, Tapp D, Cotman CW. (2005) Learning ability in aged Beagle dogs is preserved by behavioural enrichment and dietary fortification: a two year longitudinal study. Neurobiol Aging 26: 77-90
Mishina, M, T Watanabe, K Fujii, H Maeda, Y Wakao, M Takahashi (1998) Non-invasive blood pressure measurements in cats: clinical significance of hypertension associated with chronic renal failure. J Vet Med Sci;60(7):805-8
Moffat, K.S. and Landsberg, G.M. (2003) An investigation of the prevalence of clinical signs of cognitive dysfunction syndrome (CDS) in cats. JAAHA, 39: 512 (abstract).
Morgan D. (2002) Comparative aspects of ageing. Veterinary Times, September, 11-12
Nafe LA. (1979) Meningiomas in cats: a retrospective clinical study of 36 cases. J Am Vet Med Assoc.;174(11):1224-7
Pan Y, Larson B, Araujo JA, Lau W, de Rivera C, Santana R, Gore A, Milgram NW. Dietary supplementation with medium-chain TAG has long-lasting cognition-enhancing effects in aged dogs. Br J Nutr. 103(12):1746-54, 2010

Pan Y, Araujo JA, Burrows J, et al. Cognitive enhancement in middle-aged and old cats with dietary supplementation with a nutrient blend containing fish oil, B vitamins, antioxidants and arginine. Brit J Nutr 110:40-49, 2013
Peterson ME, Gamble DA.(1990) Effect of nonthyroidal illness on serum thyroxine concentrations in cats: 494 cases (1988). J Am Vet Med Assoc;197(9):1203-8
Polzin D, Osborne C, O'Brien (1989) T. Chapter 108. In: Ettinger S.J. ed. Textbook of Veterinary Internal Medicine. Philadelphia: W.B. Saunders: 1962-2046
Polzin DJ, Osborne CA, Ross S, Jacob F (2000) Dietary management of feline chronic renal failure: where are we now? In what direction are we headed? J Fel Med Surg 2, 75-82
Rand JS, Marshall RD.(2005) Diabetes mellitus in cats. Vet Clin North Am Small Anim Pract.;35(1):211-24
Rème CA, Dramard V, Kern L, Hofmans J, Halsberghe C, Mombiela DV. Effect of S-adenosylmethionine tablets on the reduction of age-related mental decline in dogs: a double-blinded, placebo-controlled trial. Vet Ther. 9(2):69-82, 2008
Reusch CE, Tomsa K. (1999) Serum fructosamine concentration in cats with overt hyperthyroidism. J Am Vet Med Assoc.;215(9):1297-300
Rios L, Ward C. (2008) Feline diabetes mellitus: diagnosis, treatment, and monitoring. Compend Contin Educ Vet.;30(12):626-39
Ross LA (1992) Hypertension and chronic renal failure. Seminars in Veterinary Medicine and Surgery (Small Animal) 7, 221
Roudebush P, Zicker SC, Cotman CW, Milgram NW, Muggenburgh BA and Head E (2005) Nutritional management of brain aging in dogs. JAVMA 227(5): 722-728
Roudebush P, Polzin DJ, Ross SJ, Towell TL, Adams LG, Forrester SD (2009) Therapies for feline chronic kidney disease. What is the evidence? J Feline Med Surg.;11(3):195-210.
Ruehl, W.W., Bruyette, D.S., DePaoli, A., Cotman, C.W., Head, E., Milgram, N.W. and Cummings, B.J. (1995) Canine cognitive dysfunction as a model for human age-related cognitive decline, dementia, and Alzheimer's disease: Clinical presentation, cognitive testing, pathology and response to l-deprenyl therapy. Prog Brain Research, 106: 217-225
Saltzman JR, Russell RM. (1995) Gastrointestinal function and ageing. In: Morley JE,Glick Z, Rubenstein LZ (eds) Geriatric nutrition, second edition, New York, Raven Press, pp183-189
Sanderson RO, Beata C, Flipo RM, Genevois JP, Macias C, Tacke S, Vezzoni A, Innes JF. (2009) Systematic review of the management of canine osteoarthritis. Vet Rec.;164(14):418-24.
Scarlett JM, Donoghue S, Saidla J, Wills J. (1994) Overweight cats: perspectives and risk factors. Int J of Obesity, 18: S22-S28
Schoenherr WD (2005) Fatty acids and evidence-based dietary management of canine osteoarthritis. Proceedings of the Hill's European Symposium on Osteoarthritis and Joint Health, Genova, 2005, p54-59
Sechi G. (2008) Thyrotoxicosis-associated Wernicke's encephalopathy. J Gen Intern Med.;23(6):897.
Servet E, Biourge V, Marniquet P. (2006) Dietary intervention can improve clinical signs in osteoarthritic dogs. J Nutr.;136(7 Suppl):1995S-1997S.
Slingerland LI, Hazewinkel HAW, Meij BP, Picavet Ph, Voohout G. (2011) Cross-sectional study of the prevelance and clinical features of osteoarthritis in 100 cats. Vet J; 187: 304-309
Stepien RL (2004) Blood pressure measurement: Equipment, methodology and clinical recommendations. 22nd ACVIM Forum Congress proceedings, 605
Studzinski CM, Araujo JA, Milgram NW. (2005) The canine model of human cognitive aging and dementia: pharmacological validity of the model for assessment of human cognitive-enhancing drugs. Prog Neuropsychopharmacol Biol Psychiatry. 29(3):489-98.
Syme HM, Barber PJ, Markwell PJ, Elliott J. (2002) Prevalence of systemic hypertension in cats with chronic renal failure at initial evaluation JAVMA 220, 1799-1804
Taylor EJ, Adams C, Neville R. (1995) Some nutritional aspects of ageing in dogs and cats. Proceedings of the Nutritional Society, 54: 645-656
Tomek A, Cizinauskas S, Doherr M, Gandini G, Jaggy A (2006). Intracranial neoplasia in 61 cats: localisation, tumour types and seizure patterns. J Feline Med Surg.;8(4):243-53.
Troxel MT, Vite CH, Van Winkle TJ, Newton AL, Tiches D, Dayrell-Hart B, Kapatkin AS, Shofer FS, Steinberg SA. (2003) Feline intracranial neoplasia: retrospective review of 160 cases (1985-2001). J Vet Intern Med.;17(6):850-9.
Venn A. (1992) Diets for geriatric patients. Vet Times, May issue.