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Introduction

We are delighted to present the Proceedings of Hill's 11th European Symposium, **'Moving on with Mobility'**, held in Chester from May 21 to 23, 2007.

For us as veterinarians, there can be few more gladdening sights than that of watching animals as they move. After all, most of them – including ourselves – have evolved to be able to move in an efficient and effective way according to the environment and life pattern for which they were intended in the wild. Musculoskeletal structure and function can become compromised though, to the extent that pathological changes occur and movement becomes painful or impaired.

Our Hill's **'Moving on with Mobility'** Symposium explored different aspects of mobility in canine and feline pets. We even looked at some comparative aspects in people too.

I would like to thank all the speakers who helped ensure the success of this event and hope that you find these Proceedings interesting and informative. When you return to your daily pursuit of veterinary clinical excellence, you may never quite look at animal movement in the same way again.

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Behavioural Changes in Arthritic Pets

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GENERAL

The diagnosis and treatment of osteoarthritis is well established in dogs and there is an expectation of recognizable behavioural changes, such as decreased interest in exercise, vocal manifestation of pain, objection to handling and overt lameness in these patients. Indeed behavioural parameters are often used as an index of improvement when evaluating treatment options for dogs.[6]

Recent publications have highlighted the importance of the condition in cats.[1-3] Perhaps one of the limiting factors in the detection of osteoarthritis in the feline patient has been the lack of obvious clinical signs and, in particular, the fact that overt lameness is not the most common clinical feature in this species.[1] This highlights the importance of species specific differences when considering the likely outward manifestations of osteoarthritis and illustrates the importance of looking for more subtle signs of the disease, especially in the cat. Behavioural changes in this species may not be readily reported by the owner and careful history taking may be needed to identify behavioural changes, such as increased resting and decreased locomotion. This is particularly true since owner's expectation of 'lazy' behaviour in the domestic cat is often high. The fact that cats have a number of passive behavioural strategies in place to disguise pain has made them a particular challenge for the veterinary profession and while behavioural change has been well established as an indicator of pain in dogs[4,8] the use of behavioural indicators to develop a pain score for cats has not proved to be so straight forward.[9] It makes sense that more overt changes such as vocalization on handling or resentment of being handled may not be as prevalent in cats, in view of their natural behaviour and the significant difference in handling approaches between dog and cat owners. Clarke and Bennett (2006) suggest that behavioural changes are not reliable as sole indicators of feline osteoarthritis.[1] Certainly, behavioural change cannot be thought of as the sole or even the primary indicator of arthritis in any species but behavioural presentations are regularly reported and it is well recognized that owners will often notice behavioural change as the first sign that all is not well with their pet.[7] The fact is that there is little scientifically validated and published information on the

behavioural changes in arthritic pets. However, clinical experience in behavioural referral practice suggests that behavioural changes associated with the condition may be noticed well before other clinical signs are seen or in association with mild radiographic changes which may have been considered to be insignificant.

AGGRESSION

Perhaps the most obvious behavioural manifestations of pain are those which are directly associated with handling or interacting with the animal. Cases of overt aggressive behaviour in such contexts might readily lead to investigation of a potential medical cause. However, the role of associative learning should not be underestimated and the potential for more diverse behavioural changes in animals with arthritic changes should be considered.

Dogs

One area of interest in a canine context has been the potential relationship between pain from arthritic changes in dogs suffering from hip dysplasia and the onset of dog to dog aggression. Work at Lincoln University (Mills D.S. 2007 - personal communication) gave some interesting preliminary results suggesting that dogs suffering from hip dysplasia were at risk of developing an anticipation of pain when encountering other dogs. However, because a causal link was difficult to demonstrate, this study has not been published so far. Case based evidence from referral practice certainly supports the development of learned associations between pain from arthritic change and the onset of aggressive behavioural responses toward dogs and people. In many cases, the contexts in which the aggression is displayed can lead to confusion with other potential motivations for the behaviour. During this presentation two cases will be presented which illustrate the need for a full medical and behavioural workup in cases of dog to dog or dog to human aggression.

Aggression is not the only potential behavioural manifestation of arthritic change. In cases where individuals develop behavioural coping strategies in order to deal with the pain, it is possible for these responses to become ritualized and even compulsive in nature. Using a case example the potential for interaction between compulsive behaviour and orthopaedic pain will be explored.

Cats

In a feline context there is also the potential for behavioural manifestations of arthritic change and overt aggressive responses to cats or people are certainly possible. However, owing to the unique nature of feline social behaviour it is important to remember that obvious changes in social interactions may not be readily apparent and less directly obvious behavioural consequences may be encountered. Examples would include onset of inappropriate elimination behaviours and marking responses and case histories will be used to illustrate these potential presentations.

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Depression and Mobility Assessing the Connection

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SUMMARY

To evaluate the association between depression and anxiety disorders and excess disability, the authors searched the recent geriatric literature for studies associating late-life depression or anxiety with physical disability.

Community and clinical studies showed depression in old age to be an independent risk factor for disability; similarly, disability was found to be a risk factor for depression. This association persisted when possible confounds, such as age, gender, education, medical burden, social support, income, and cognitive status, were controlled. The association with increased disability was present whether the disorder was diagnosed as major depression, depressive symptoms assessed by a screening instrument, or even as minor depression in some studies. A significant association between anxiety in late life and disability linked to depression was found as well, but the association of anxiety and disability independent of depression was not assessed by any studies.

The cross-sectional studies in this review support the assertion that depression is disabling, but they are not able to separate the extent of this assertion, as compared with the equally valid assertions that disability is *'depressogenic,'* or that other underlying factors, such as socioeconomic conditions or cerebrovascular disease, are both disabling and depressogenic.

Longitudinal studies are helpful in identifying risk factors and delineating the pathways of causality. A number of longitudinal studies found that depression and physical disability, when present, usually occurred simultaneously, i.e. either both would worsen, both would remain, or both would improve. Comparable studies have not been done for anxiety. This *'synchrony of change'* between depression and disability has also been described in younger-aged populations, and it reinforces the construct of depression as a disabling illness. Most intervention studies showed significant improvements in self-rated physical disability of subjects receiving antidepressant medication, relative to placebo, supporting the hypothesis that depression is a treatable source of excess disability. The author further discusses how these findings inform current concepts of physical disability and discuss the implications for future intervention studies of late-life depression and anxiety disorders.

INTRODUCTION

Disability can be defined as a restriction in or lack of ability to perform an activity because of impairment.[1] These activities can include interpersonal relationships, work or school, or physical activities; impairment the latter is defined as *'physical disability'* and will be the focus of this review. Physical disability typically refers to difficulty, restriction, or dependence on others in performing *Activities of Daily Living* (ADL) or *Instrumental Activities of Daily Living* (IADL).

ADLs are self-care tasks, such as feeding oneself, dressing, bathing, toileting, and mobility.

IADLs are less basic tasks that are necessary for independent living, such as preparing food, cleaning, and paying bills.

Although described as physical, these tasks clearly have a mental component as well. In part, it is this mental component that makes *'physical disability'* a distinct concept from *'impairment in physical performance'*, such as objective measures of strength, speed, or range of motion; the two measures are only moderately correlated.[2] For example, in an arthritic person impairment is the decreased range of motion, whereas disability is the need for assistance to prepare or eat food as a consequence of this decreased range of motion. Similarly, disability is a construct separate from *disease severity*. Even though disease is intuitively disabling and more severe disease pathology is in general correlated with greater disability, the correlation is moderate or even low.[3,5,4] This suggests that *physical disability* is a complicated construct that includes elements of physical and mental functioning. However, physical disability should be distinguished from *quality of life*, an even broader measure that takes into account not only physical, social and role disability, but also life satisfaction and pleasure. Measures of quality of life have a great deal of shared variance with depressive symptoms in elderly persons, and studies showing that depression affects quality of life may simply reflect this variance.[5]

Disability and Psychiatric Disorders as a Public Health Issue

According to the Global Burden of Disease study, unipolar major depression is the leading worldwide cause of disability in adults.[6] Anxiety disorders such as panic disorder and posttraumatic stress disorder were found to be important causes of disability as well.

Although the Global Burden of Disease study represents the most comprehensive existing work about disability caused by depression and anxiety, its results are less applicable to elderly patients because role disability, such as inability to work, accounted for much of the disability in the study. Role disability is a less important issue for elderly patients, in whom physical disability is the most important. Persons age 65 and older account for 54 per cent of all physical disability in the United States [7], a percentage that will increase as this age-group is estimated to increase from 17 per cent to 26 per cent of the total adult population over the next 30 years.[8]

An increase in physical disability is a strong predictor of nursing home placement and increased health care utilization[9]; similarly, late-life depression is linked to greater health care utilization.[10] It is hardly surprising, then, that depressed, disabled elderly patients are high health care utilizers.[10] Evidence of a secular trend for lower disability rates in the oldest age-group[11] gives cause for optimism that appropriate management of common medical conditions in elderly patients will result not only in advances in longevity but in decreased disability as well. Depressive syndromes, including major depressive disorder and minor depression, are common in elderly patients, and similar in prevalence to younger age-groups.[12] Though anxiety disorders may be less prevalent in older age-groups, their prevalence is still high, and they are often co-morbid with depression.[13,14] From these perspectives, excess disability owing to depression and anxiety in elderly patients is an important public health issue in terms of burden of disease and health care costs.

Objective

Although there is a consensus that late-life depression leads to, amplifies, or is a consequence of physical disability[15-18], a review of the literature in 1998 concluded that studies at that time could neither elucidate the pathways between late-life depression and disability nor determine the effectiveness of interventions in relieving disability in the context of late-life depression.[14] Although the literature in young-adult populations shows that anxiety disorders are also associated with increased disability there is no consensus regarding the association of late-life anxiety disorders with disability.[19-21]

This article reviews recent advances in our knowledge of the association of late-life depression

and anxiety with physical disability. We specifically sought to answer two main questions:

1) how do late-life depression and anxiety disorders cause or amplify physical disability?
2) how should the findings be applied to future late-life depression and anxiety intervention studies?

Conversely, we also sought to determine how disability causes or amplifies depression and anxiety. The answers to these questions provide important insights into the nature of physical disability and provide directions for mental health intervention research aimed at reducing or preventing excess disability in late life.

MATERIALS AND METHOD

We used MEDLINE and PsycInfo searches to find articles relating late-life depression or anxiety to disability. Search terms were *depression, depressive disorders, anxiety, anxiety disorders, panic disorder, social phobia, obsessive–compulsive disorder*, and generalized anxiety disorder, in combination with *activities of daily living, disabled persons*, and *disability evaluation*, and in combination with aged, for the time frame 1990 – 2000. Additional articles were identified by the authors' knowledge of the literature and review of citations in retrieved articles. Studies of mixed-age populations were included if the average age of the study population was 61 or more. Case reports and reviews were excluded, as were articles specific to dementia. If the same subject population was analyzed by more than one study, only one study was tabulated. Studies of overall quality of life or physical performance but not physical disability were excluded.

The search yielded 66 studies meeting the above criteria associating depression and disability. These include 16 cross-sectional community studies, nine longitudinal community studies, 18 cross-sectional clinical observational studies, 18 longitudinal clinical observational studies, and five intervention studies. Five of them also assessed either symptoms of anxiety instruments or anxiety disorders.

The instruments used in these studies to measure depression and disability were well recognised and published instruments[22-28] or derived from these instruments.

RESULTS

Depression and Disability

Community studies

Cross-sectional studies

The 16 cross-sectional community studies are shown in TABLE 1.[29-44] All but three studies[31,40,43] found a significant association between depression and disability in ADL and IADL using multivariate analyses, controlling for age, gender, education, income, cognition, physical performance measures, and medical conditions.

Two of the three negative studies were small studies of select populations: the first[31] was a group of 89 retired Catholic sisters and the second[43] was a group of 84 nonagenarians and centenarians in residential settings. The third negative study[40] included self-rated health as a covariate, finding that depression was not associated with IADL disability. Perception of health is a measure with considerable shared variance with both disability and depression.[40-45] However, another study found that depression was significantly associated with ADL disability, controlling for self-rated health.[33]

As a whole, these studies show a significant and independent association between depression and disability. Most studies expressed the strength of the association in terms of a correlation coefficient, which ranged from 0.10 to 0.54, or an odds ratio, which ranged from 1.9 to 4.9.

Longitudinal studies

TABLE 2 summarizes the data from nine longitudinal community studies showing the impact of depression at baseline on increase the risk of disability over time. [46-54]

Three of the studies followed subjects who were initially not disabled (no ADL), but suffered depression or anxiety at baseline. [46,51,53] These three studies found baseline depression to be an independent risk factor for disability during the follow-up period, controlling for baseline medical conditions, social support, education, age, gender, and cognitive impairment. They showed that in populations who were initially not disabled, the existence of depression at baseline was associated with a 60 per cent or higher increase in risk of disability. Baseline characteristics accounted for less than half of this increased risk. Adjustment for incident medical problems during the follow-up

	Reference	n	Age mean (range)	Subjects with depression (type of depression)	Results
1	Barberger-Gateau *et al.*, 1992[29]	2,792	75(65+)	13.6%	Depression was associated with increased ADL and IADL disability, controlling for age, gender, education, urbanicity, sensory impairment, and cognition.
2	Beekman *et al.*, 1997[30]	646	(55-85)	12.9% (Minor) 2.0% (Major)	Both minor and major depression were associated with increased ADL and IADL disability, controlling for age, gender, education, urbanicity, marital status, medical conditions and functional limitations.
3	Black *et al.*, 1998[32]	2,823	73(65+)	26%	Greater ADL disability was associated with depression in men and women, controlling for age, education, financial strain, social support and medical conditions.
4	Dentino *et al.*, 1999[33]	1,681	78(70+)	9%	Greater ADL but not IADL disability was associated with depression, controlling for age, gender, race, education, self-rated health, and life satisfaction.
5	Forsell *et al.*, 1994[34]	1,304	85(75+)	5.9% (Major) 8.3% (Dysthymia)	Increased ADL disability was associated with both mood symptoms (depressed mood, poor sleep and appetite, guilt and suicidality) and motivational symptoms (poor concentrations and energy, psychomotor retardation), controlling for age, gender, and cognition.
6	Ganguli *et al.*, 1999[35]	1,554	67(57-95)	10%	In a rural India sample, depressive symptoms were associated with disability, controlling for age, gender, and literacy.
7	Grigsby *et al.*, 1998[36]	1,158	73(60+)	N/A	Depressive symptoms were associated with increased ADL and IADL disability, controlling for age, ethnicity, gender, education, and cognition. Correlation of depression with self-report disability measures was higher than for observed disability measure.
8	Guccione *et al.*, 1994[37]	1,769	74(64-95)	9.1%	Depression was associated with increase IADL disability, controlling for age, gender, and medical conditions.
9	Laukkanen *et al.*, 1993[38]	800	(65-84)	N/A	Depressive symptoms were associated with increase ADL and IADL disability, controlling for cognition and medical conditions.
10	Laukkanen *et al.*, 1997[39]	706	75	N/A	Depressive symptoms were associated with increased ADL disability in one of four population subgroups, controlling for physical performance measures such as balance and strength, and visual impairment.
11	Ormel *et al.*,1998[41]	5,279	70(57+)	17.4%	Depression was associated with increased ADL and IADL disability, controlling for gender, age, socioeconomic status, and medical conditions. Amount of correlation was greater than or equal to most medical conditions.
12	Prince *et al.*, 1997[42]	654	76(65-98)	17.7%	Increased ADL disability was associated with depression, controlling for age, cognition, and life events.
13	West *et al.*, 1998[44]	1,948	(55+)	9.1%	Greater ADL disability was associated with depression, controlling for age, income, education, medical illness, physical performance, and social support.
14	Bienenfeld *et al.*, 1997[31]	89	(65-92)	N/A	Depression was not associated with increased ADL/IADL disability in bivariate analysis.
15	Mulsant *et al.*, 1997[40]	880	76(65+)	N/A	Depression was not significantly associated with greater IADL disability after controlling for self-rated health, age, gender, education, medical conditions, and health care utilization.
16	Ravaglia *et al.*, 1997[43]	84	98(90-106)	15.5%	Depression was not associated with greater ADL disability in either univariate or multivariate analysis, in this small nonrandom sample.

Table 1. Sixteen cross-sectional community studies
All studies found a significant association between depression and disability in ADL and/or IADL, with exception of three studies: Bienenfeld et al. 1997, Mulsant et al. 1997, and Ravaglia et al. 1997 (As highlighted in the table above).
ADL = activities of daily living; IADL = instrumental activities of daily living

period,[51] health behaviours such as smoking and inactivity,[51] and baseline physical performance measures such as strength[46-53] or sensory impairments 53 did not change the increased risk.

The next three studies did not show depression to predict onset of disability.[47-49] One contained wide confidence intervals that included a two-fold increased risk.[47] A second study found minimal or no significant risk of disability onset associated with poor social support and cognitive status both of which are known risk factors for disability.[48] The third study did not find baseline symptoms of depression to be predictive of change in self-rated disability, but did find that increased depressive symptoms over time were associated with worsening disability as well as worsening performance-rated functioning. [49]

This finding suggests that, whereas stable or improving depressive symptoms are not associated with increased disability, worsening depression is associated not only with increased self-rated disability, but also with more impaired physical performance on objective scales.

The last three studies, which were controlled for age, gender, medical conditions and income, found disability to be a risk factor for the onset of depression.[50,22,54] One of them also showed that the appearance of disability tended to coincide with the emergence of depression. [50]

Overall, these results suggest that depression and disability increase the risk for each other. The risk is partly mediated by differences in baseline medical illness, social support, education, and income.

	Reference	n	Age mean range)	Length of follow up	Subjects with depression (initially)	Results
1	Bruce *et al.*, 1994[46]	1,038	(70-79)	2.5 years	N/A	In this population of subjects with no baseline ADL disability, baseline depression predicted incident ADL disability, controlling for baseline physical and cognitive function, age, medical illness, and body mass index.
2	Penninx *et al.*, 1999[51]	6,244	73(65+)	6 years	7.9%	In this population of subjects with no baseline ADL disability baseline depression predicted incident ADL disability: relative risk 1.67 and 1.73 for incident ADL and mobility disability, respectively. Adjustment for age, gender, education, income, physical activity, social support, baseline medical conditions, and incident medical conditions reduced relative risk to 1.45 and 1.37.
3	Tinetti *et al.*, 1995[53]	927	80(72+)	1 year	22% (Depression) 49% (Anxiety)	Baseline depression and anxiety predict greater ADL disability at follow-up, controlling for baseline physical performance, sensory impairment, cognition, and medical use. In those with no disability at baseline, depression, but mot anxiety, was a significant predictor of disability at follow-up.
4	Gallo *et al.*, 1997[47]	653	66(50+)	13 years	1.8% (Minor) 15.8% (Major)	Baseline depression predicted greater ADL and IADL disability at baseline and incident during follow-up. After controlling for age, cognition, gender, ethnicity, education, and medical conditions, only increased IADL disability was predicted and only in the nondysphoric depression group.
5	Herbert *et al.*, 1999[48]	504	80(75+)	2 years	N/A	Baseline depressive symptoms did not predict greater disability at follow-up, controlling for age, living situation, social support, weight loss, falls, morbidity index, cognition, and baseline disability.
6	Kempen *et al.*, 1999[49]	574	72(57-93)	2 years	N/A	In a highly disabled population, baseline depressive symptoms did not predict greater follow-up disability. However, worsening depressive symptoms during follow-up were associated with greater follow-up disability.
7	Kennedy *et al.*, 1990[50]	1457	(65+)	2 years	11.2%[b] (Incident) 7.7% (Persistent)	Baseline and especially incident ADL disability predicted incident depression, controlling for medical conditions, income, social support, life events, and cognition.
8	Roberts *et al.*, 1997[52]	2219	65(50-05)	1 year	8.7% (Baseline) 9.0% (at 1 year)	Baseline ADL disability predicted incident and persistent depression in univariate analysis.
9	Zeiss *et al.*, 1996[54]	680	63(50+)	2 years	14% (IMDD)	Baseline disability (including sensory impairment) predicted incident depression, controlling for age, gender, and medical conditions.

Table 2. Nine longitudinal community studies

Overall, these results suggest that depression and disability increase the risk for each other. The risk is partly mediated by differences in baseline medical illness, social support, education, and income.

ADL = activities of daily living; IADL = instrumental activities of daily living; IMDD = incident major depressive disorder.

	Reference	n	Age mean (range)	Location / characteristics	Results
1	Bond *et al.*, 1998[56]	642	78(65+)	Community residing outpatients 6 months after hospital admission	Of patients living in the community 6 months after a stroke or hip fracture, those with anxiety or depression (41%) were more likely to have ADL disability than those without anxiety or depression.
2	Ehmann *et al.*, 1990[58]	45	67(51-85)	Outpatients with Parkinson's disease	Depressive symptons were correlated with greater ADL disability in univariate analysis
3	Kurlowicz 1998[60]	73	72(65-83)	Patients 6 weeks after elective hip-replacement surgery	Depression and ADL/IADL disability were associated.
4	Menza and Mark, 1994[63]	104	65	Otpatients with Parkinson's disease	Depression was associated with increased ADL disability in Parkinson's patients, controlling for severity of illness and personality dimensions.
5	Murberg *et al.*, 199864	119	66	Outpatients with CHF	Depression scores correlated with increased ADL/IADL disability, controlling for severity of CHF.
6	Ramasubbu *et al.*, 1998[65]	626	63	Inpatients with stroke	One week after stroke, depression, present in 16%, was associated with increased ADL disability, controlling for lesion volume and degree of neurological impairment.
7	Salaffi *et al.*, 1991[66]	61	64(51-79)	Outpatients with oesteoarthritis of knee	Both depression and anxiety were associated with increased ADL/IADL disability, controlling for radiographic score of extent of knee damage.
8	Shmuely *et al.*, 199568	70	77(65+)	Outpatients of a low-vision clinic	Depression present in 39%, was associated with greater ADL/IADL disability, controlling for visual impairment, medical conditions, medication use, age and gender.
9	Steffens *et al.*, 1999[70]	335	67	Cardiology inpatients with CAD	Depression, present in 8%, was associated with greater ADL and IADL disability, controlling for age and medical severity.
10	Yohannes *et al.*, 1998[71]	96	78(70-93)	Medical outpatients with COPD	Depression, present in 46% of COPD patients, was associated with greater ADL/IADL disability, controlling for age, gender, and performance measures of impairment such as FEV1 or walking test.
11	Egan *et al.*, 1992[57]	61	77(65-92)	Rehab, impatients after hip fracture	Depression was not significantly associated with increased ADL disability at discharge, ,nor was age, mental status, health, or social support.
12	Yu *et al.*, 1993[72]	133	85	Female nursing-home residents	Greater ADL disability was associated with depression, controlling for age and cognition.
13	Alexopoulos *et al.*, 1996[55]	75	73(60+)	Impatient and outpatient psychiatric services; all subjects with major depression	Disability by self-rating was associated with severity of depression, medical burden, social support, and age. Several depressive symptoms (anxiety, depressive ideation, psychomotor retardation, and weight loss) correlated most highly with disability. Disability by interviewer rating as associated with initiation-perseveration problems from dementiaa scale but not with depressive severity.
14	Lyness *et al.*, 1993[61]	71	72(60+)	Psychiatric inpatients with major depression	Depressive severity associated with increased IADL but not ADL disability, controlling for GAF score, age, gender, education, medical conditions, and disability due to medical illness.
15	Steffens *et al.*, 1999[69]	211	70(60+)	Depressed subjects from impatient and outpatient psychiatry	In subjects with major depression, greater IADL disability was associated with the following depressive symptoms: depressive severity, mood, anhedonia, anxiety, psychomotor retardation, weight loss, cognitive impairment. Greater ADL disabilitywas associated with psychomotor retardation only.
16	Katz *et al.*, 1995[59]	1,057	84	Residential and skilled-nursing patients	Those with MDD (12.2%) had more disability than those with minor depression (18.4%), who in turn had more disability than non-depressed patients, controlling for medical conditions.
17	Lyness *et al.*, 1999[62]	224	71(60+)	Primary care outpatients	Depressed subjects were divided into major depression (6.5%), minor depression (5.2%), and subsyndromal depression (9.9%). All three groups had greater ADL/IADL disability than non-depressed subjects, controlling for age, gender, education, site and medical conditions.
18	Schulberg *et al.*, 1998[67]	104	69	Primary care patients with depression	Major and subsyndromal depression were equally associated with ADL/IADL disability.

Table 3. Eighteen cross-sectional clinical observational studies

Taken as a whole, these studies replicate findings from cross-sectional community studies; that is, there is a significant association between depression and disability that cannot be accounted for by greater medical illness in depressed subjects.

ADL = activities of daily living; CAD = coronary artery disease; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; FEV1 = forced expiration volume (1 second); GAF = Global assessment for function; IADL = instrumental activities of daily living; MDD = major depressive disorder.

	Reference	n	Age mean (range)	Location/ characteristics	Length of follow up	Results
1	Andersen *et al*., 1995[73]	259	69(25-80)	Medical inpatients with stroke	1 year	Greater baseline post-stroke ADL disability did not predict incident depression
2	Astrom 1996[74]	80	73(44-100)	Medical inpatients with stroke	3 years	GAD, highly comorbid with depression, was significantly associated with greater ADL dependence at all follow-up periods except at initial hospital discharge
3	Barbisoni *et al*., 1996[75]	123	78(60-93)	Rehabilitation admissions	27 days (mean)	Response to rehabilitation (improvement in ADL disability score) associated with improved depressive symptoms, especially when markedly disabled on admission.
4	Callahan *et al*., 1998[76]	342	66(60+)	Primary care outpatients: 266 with depression 82 without	45 months (mean)	Increased ADL/IADL disability during follow-up was associated with increase in depressive symptoms, controlling for baseline disability.
5	Covinsky *et al*., 1997[77]	467 (ADL) 336 (IADL)	(70+)	Medical inpatients	3 months	Depressive symptoms were associated with increased ADL and IADL disability at follow-up controlling for baseline disability, cognition, gender, age, race, marital status, living arrangement and medical conditions. Greater disability was associated with higher depressive symptom severity.
6	Diamond *et al*., 1995[78]	40	77	Rehabilitation inpatients	26 days (mean)	Depression on discharge was associated with greater ADL/IADL disability on discharge, but not after controlling for admission disability.
7	Dunham and Sager, 1994[79]	197	(70+)	Medical inpatients	1 month post-discharge	Depression (present in 24% on admission) was significantly associated with greater ADL/IADL disability one month after discharge, controlling for disability on admission.
8	Hermann *et al*., 1998[80]	136	75(24-101)	Neurology inpatients with stroke	1 year	Depression on follow-up (at 3 months or at 1 year) was significantly associated with poorer functional outcome on follow-up (at both 3 months and 1 year).
9	Koenig and George, 1998[81]	119	70(60+)	Medical inpatients, depressed and disabled at baseline	1 year (median)	Depression and disability tended to change synchronously: either both remained or both improved synchronously in two-thirds of cases.
10	MacNeill and Lichtenberg, 1998[82]	372	78(60-99)	Rehabilitation admissions	19 days (mean)	Depression correlated with greater ADL disability on admission and greater chance of institutionalization upon discharge. Among those institutionalized, depression predicted greater ADL disability on discharge, controlling for admission function.
11	Magaziner *et al*., 1990[83]	333	78(65+)	Hip fracture patients	1 year	Depressive symptoms predicted lower improvement of ADL but not IADL disability, controlling for baseline disability, cognitive status, age, gender, medical conditions, and social support.
12	Mossey *et al*., 1990[84]	196	78(59+)	Women treated surgically for hip fracture	1 year	Those with persistent high depressive symptoms were three times less likely to walk independently and nine times less likely to return to pre-fracture disability level, compared to persistently low depressive symptoms throughout follow-up period.
13	Nanna *et al*., 1997[85]	423	78(60-99)	Rehabilitation inpatients	18 days (mean)	Depressive symptoms on admit predicted lower improvement in ADL but not mobility disability, controlling for admission ADL, race, gender, age, education, medical conditions, cognition, and length of stay.
14	Oxman and Hull, 1997[86]	147	69(55-91)	Inpatients undergoing cardiac surgery	6 months	Greater ADL/IADL disability 1 month after surgery predicted depression 6 months after surgery, controlling for baseline depression and social support
15	Paolucci *et al*., 1998[87]	440	64	Rehabilitation admissions with stroke	111 days (mean)	Depression present in 28% on admission, predicted lower improvement in ADL disability
16	Starkstein *et al*., 1992[88]	92	66	Neurology outpatients with Parkinson's disease	1 year	Patients with major but not minor depression had a greater increase in ADL disability compared to non-depressed, matched for baseline disability and duration of illness.
17	Sullivan *et al*., 1997[89]	198	63(45-79)	Outpatients with newly-diagnosed CAD	1 year	High levels of anxiety and depression at baseline predicted greater baseline disability, controlling for severity of CAD and overall medical illness, but not lower improvement in disability during treatment.
18.	Van de Weeg *et al*., 1999[90]	85	61(27-81)	Rehabilitation inpatients post-stroke	5 months	Depressed post-stroke patients had greater admission and follow-up ADL/IADL disability, but depressed and nondepressed patients showed similar rates of improvement over the follow-up period.

Table 4. Eighteen longitudinal clinical observational studies, which included a wide variety of inpatient and outpatient settings
Overall, these longitudinal studies found depression to be a predictor of both greater disability in medically ill subjects and less recovery from disability after medical events. Similar to findings in longitudinal community studies, baseline and incident disability were also predictors of depression.
ADL = activities of daily living; CAD = coronary artery disease; GAD = generalized anxiety disorder; IADL = instrumental activities of daily living.

Clinical observational studies

Cross-sectional studies

Table 3 shows 18 cross-sectional clinical observational studies.[55-72] They include medical outpatients[62,66,67], medical[65,70] or rehabilitation[57] inpatients, long-term care residents[59-72], and psychiatric inpatients and outpatients.[55,61,72] All but two studies[57,72] found an association between depression and disability in these clinical populations. Similar to community studies, this association remained significant even after controlling for disease severity relating to heart failure[64] or arthritis[66], in fact disability was more strongly associated with depression than with disease severity.

One of the two negative studies[57] is difficult to interpret because of the small sample size (61 subjects); whereas the other[72] was conducted in highly disabled nursing home patients.

Three studies of elderly depressed patients in psychiatric settings examined correlates of disability.[55,61,69] Two found a significant relationship between disability and the degree of social support and cognitive impairment.[55,69] Specifically cognitive deficits in initiation and perseveration were associated with increased disability in a depressed population.[55] These two studies also found increased disability in more severely depressed subjects, consistent with another study of nursing home residents that found more disability in residents with major depression than with minor depression.[59] In contrast, two primary care studies found that subsyndromal depression was as strongly associated with disability as was major depression.[62,67]

Taken as a whole, these studies replicate findings from cross-sectional community studies; that is, there is a significant association between depression and disability that cannot be accounted for by greater medical illness in depressed subjects.

Longitudinal studies

Table 4 shows 18 longitudinal clinical observational studies, which included a wide variety of inpatient and outpatient settings.[73-90] Some followed progression of disability over time in subjects who were assessed for depression at baseline,[76,80,88] similar to previously mentioned longitudinal community studies. They found depression to be a risk factor for increased incidence of disability, even in one study that controlled for baseline disability.[88] One study also found that patients who became depressed were likely to become disabled at the same time.[76]

Several studies followed patients after an incident event such as a stroke[74,80,] hip fracture[83,84], medical inpatient admission[79], diagnosis of heart disease[89], or admission to a rehabilitation setting.[72,82,85,87,90] These studies evaluated the effects of depression on the recovery process, i.e. whether depression would be associated with less functional improvement. In all studies of post-stroke patients[74,80,87] and post-hip fracture patients[83,84], subjects with depression at baseline were less likely to regain pre-stroke levels of functioning, but this was not true in patients treated for heart disease.[89] Three[82,85,87] of five rehabilitation-setting studies found less improvement in disability in depressed individuals.[78,82,85,87,90] One of the three studies was controlled for length of stay[85,] and two were controlled for initial functional status[85,87,] which are known predictors of improvement during rehabilitation.

Of two prospective studies[73,86] examining predictors of depression, one[86] found that baseline disability predicted onset of depression. In addition, three studies found that change in disability coincided with change in depression: improvement in disability was associated with improvement in depression,[75,81] and worsening disability was associated with worsening depression.[76]

Overall, these longitudinal studies found depression to be a predictor of both greater disability in medically ill subjects and less recovery from disability after medical events. Similar to findings in longitudinal community studies, baseline and incident disability were also predictors of depression.

Intervention studies

TABLE 5 shows five depression intervention studies.[91-95] Four studies[91,92,94,95] were six to 12 week placebo-controlled antidepressant trials, using nortriptyline[91,95], fluoxetine[92], or both.[94] In three of the four studies the active treatment group showed greater improvement in physical functioning than the placebo group.[91,92,95] One study recruited healthy community elderly subjects, finding a four per cent improvement in disability attributable to medication.[92] The other three studies, which recruited only medically ill subjects, showed larger improvements in disability attributable to medication.[91,94,95] The most recent study found nortriptyline to be superior to fluoxetine (but not placebo) in post-stroke rehabilitating patients in improving recovery from ADL, as measured by the FIM.[94] One study assessed objective measures of

disease severity, such as expiratory volume and walking endurance in addition to the self-report measures of disability.[91] Although disability measures improved, disease severity measures did not, suggesting that the improvement in disability was independent of disease severity.

A psychotherapy study recruited medical inpatients with sub-syndromal depression and followed them for one year after 10 sessions of interpersonal counselling.[93] Although the study found a positive treatment effect on depression symptoms and self-rated health, there was no significant effect on physical functioning.

Anxiety and Disability

Of the 66 studies previously reviewed, five also assessed either symptoms of anxiety (with screening instruments)[53,56,66,89] or anxiety disorders (with a psychiatric interview).[74] A longitudinal community study found that symptoms of anxiety were as strong a predictor of increased disability on follow-up as were depressive symptoms.[53] Three clinical observational studies showed that anxiety correlated highly with disability[66,74,89] and predicted greater follow-up disability.[74] All five studies found high co morbidity between depression and anxiety, but no studies controlled for one of the two when examining the impact of the other. Thus, these studies suggest that anxiety, similar to depression, is a risk factor for disability, but they do not establish anxiety as a risk independent of depression. No intervention studies assessed the relationship between anxiety and disability.

DISCUSSION

A significant association between depression and disability was found in community and clinical settings. This association persisted when possible confounds, such as age, gender, education, medical burden, social support, income, and cognitive status, were controlled. The association with increased disability was present whether the disorder was diagnosed as major depression or depressive symptoms assessed by a screening instrument. Some[47,62,67] but not all studies of minor depression found similar associations with disability. A significant association between anxiety and disability was found as well, but the association of anxiety and disability independent of depression was not assessed by any studies.

Thus, the cross-sectional studies in this review support the assertion that depression is disabling, but they are not able to separate the extent of this assertion, as compared with the equally valid assertions that disability is 'depressogenic,' or that other underlying factors (such as poverty or cerebrovascular disease) are both disabling and depressogenic. Longitudinal studies are helpful in

	Reference	n	Age mean (range)	Study description	Results
1	Borson *et al.*, 1992[91]	30	61(42-76)	6-week placebo-controlled study of nortriptyline in ambulatory depressed COPD patients	Subjects taking nortriptyline had improved disability (mean 29% decrease in physical scale), greater than placebo. There was no improvement in objective measures of lung function (FEV1, ABG, or 12 minute walk distance).
2	Heilingenstein *et al.*, 1995[92]	532	68(60+)	6-week placebo-controlled study of fluoxetine in outpatients with major depression	Subjects taking fluoxetine had an improvement in disability (mean 4% increase in physical functioning subscale), significantly greater than placebo.
3	Mossey *et al.*, 1996[93]	76	(60+)	10 sessions of interpersonal counseling vs. usual care in patients recently hospitalized for medical illness, with subsyndromal depression	At 6 months, subjects in the interpersonal counseling group had a significantly greater improvement in depressive symptoms and self-rated health but not physical disability, compared to usual care.
4	Robinson *et al.*, 2000[94]	56	67	12-week placebo-controlled study of nortriptyline vs. fluoxetine in depressed post-stroke patients.	Subjects who received nortriptyline had greater reduction of depressive symptoms and greater improvement in disability, compared to fluoxetine, but not compared to placebo.
5	Sullivan *et al.*, 1993[95]	92	62	12-week placebo-controlled study of nortriptyline in depressed patients with chronic tinnitus	Subjects taking nortriptyline had a significantly greater improvement in disability scales, compared to placebo.

Table 5. Five depression intervention studies
ABG = arterial blood gas; COPD = chronic obstructive pulmonary disease; FEV1 = forced expiration volume (1 second)

identifying risk factors and delineating the pathways of causality.[96] Studies in this review showed both that depression is a risk factor for disability[46,51,53] and that disability is a risk factor for depression.[50,52,54] Other longitudinal studies found that depression and disability, when present, usually occurred simultaneously:[49,50,76,81] either both would worsen, both would remain, or both would improve. This 'synchrony of change' between depression and disability has also been described in younger-aged populations,[97] and it reinforces the construct of depression as a disabling illness. Longitudinal studies found that anxiety was a predictor for disability, independent of the same confounds as for depression, but not necessarily independent of depression.[53,74] Most intervention studies showed significant improvements in self-rated physical disability of subjects receiving antidepressant medication, relative to placebo, supporting the hypothesis that depression is a treatable source of excess disability.

How do Late-Life Depression and Anxiety Disorders Cause or Amplify Physical Disability?

The studies reviewed delineate many mechanisms by which depression could lead to disability (FIGURE 1). These mechanisms can be placed within two major causal categories: The depressed state itself is disabling, and/or depression causes increased disability from other medical conditions, either by increasing the risk for these conditions or by poorer health behaviours in depressed individuals with these medical conditions.

The depressed state is disabling

Executive-type cognitive impairments caused by depression may explain why depressed individuals could be more disabled, especially with IADL. Alexopoulos found that depressed individuals with initiation-perseveration deficits had greater global disability.[55] Poor appetite can lead to low body mass index, associated with disability.[108] Prospective studies controlling for cognition and body mass index found that these accounted for some of the increased disability associated with depression. [46,51,53] Psychomotor retardation is frequently seen in depressed individuals.[109,110] One study found a significant association between depressive psychomotor retardation and increased disability.[69] The observation that psychomotor retardation is closely related to such physical-performance

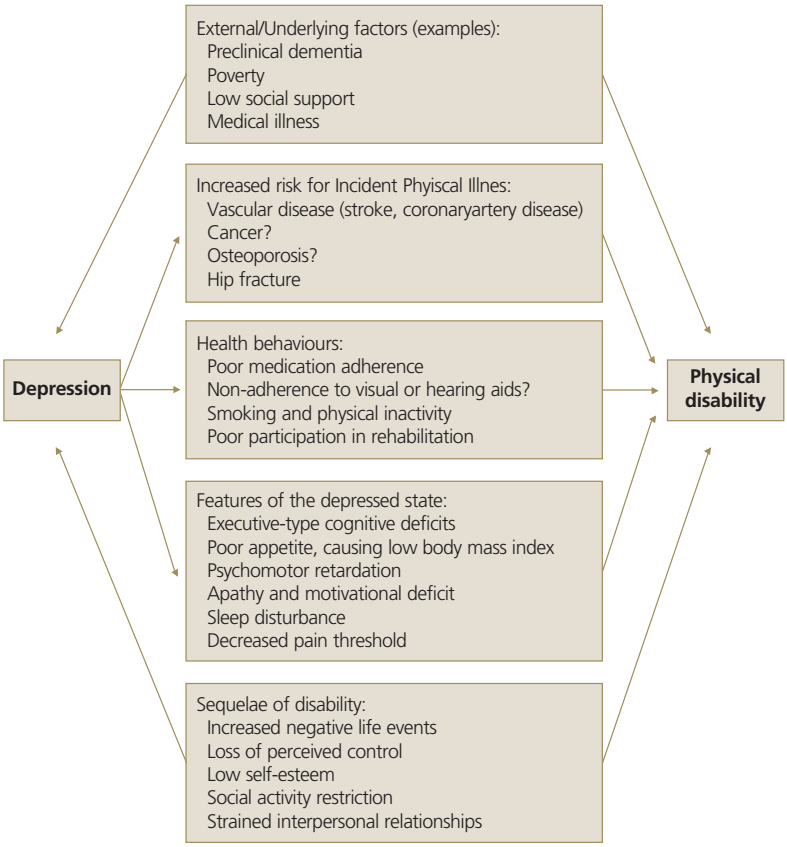

Figure 1. Late-life depression and anxiety disorders cause or amplify physical disability, which in turn can aggravate the state of depression
The many mechanisms, by which depression could lead to disability, can be placed within two major causal categories: the depressed state itself is disabling, and/or depression causes increased disability from other medical conditions, either by increasing the risk for these conditions or by poorer health behaviours in depressed individuals with these medical conditions.

measures as strength and walking speed underscores the interrelationship between depression and physical functioning. Closely related to psychomotor retardation is the apathy and diminished motivation often seen in depression.[111] An hedonia was found in one study to be significantly associated with disability.[69] Sleep disturbances, common in depressed elderly patients, have an independent association with disability.[112] Depression can also confer a lower threshold to pain, which can lead to activity restriction.[113] At present, it is not known to what extent each of these components of depression is responsible for associated physical disability in elderly patients. Future studies should identify not only the extent to which these separable components of depression are disabling, but also the type of disability attributable to the components. This future study will not only reinforce the concept of depression as a disabling illness, but also show us more about the complex nature of physical disability in terms of its cognitive and emotional elements.

Depression and increased risk of medical conditions

Depression increases the risk of several common and disabling medical conditions. Depressed individuals with cardiovascular illness have greater incidence of stroke-related and cardiac-related mortality. [114,115] This may be due to poor health behaviours, such as smoking or physical inactivity, which are risk factors for vascular illness. In addition, depression itself may cause coronary and cerebrovascular events.[116-118] Elevated cortisol levels[119] and other signs of immune dysfunction[33] associated with the depressed state may lead to the increased risk of cancer seen in some but not all studies. [120,121] Depression may increase risk of osteoporosis,[119] which, combined with the increased incidence of falls in depressed elderly patients, leads to an increase in the risk of hip and other fractures.[122] The increased prescription of potentially adverse and sedating medications in depressed individuals also may account for an increase in falls and fractures.[123,124] Thus, depression increases risk for heart attack, stroke, hip fracture, and possibly cancer and osteoporosis, all major sources of disability in elderly patients. An increase in these conditions may not be the main mechanism by which depression leads to disability, however, given that studies controlling for either the occurrence of these medical conditions during the follow-up period [51] or severity of medical conditions [77,80] continued to show greater disability in depressed elderly patients.

Poor health behaviour could amplify disability caused by a medical condition

Poorer health behaviour in depressed individuals could amplify disability caused by a medical condition. Depressed individuals have poorer treatment adherence thereby reducing the benefits of medical treatments.[125,126] Sensory impairments such as poor vision or hearing may be more disabling to depressed elderly persons because of their non-compliance in the use of visual or hearing aids. Similarly, smoking and physical inactivity, associated with late-life depression,[55,120,127] may lead not only to incident medical conditions but to increased disability in those who are already medically ill. The classic example of this would be the patient who does not quit smoking after a coronary artery bypass graft. Finally, rehabilitation from conditions such as hip fracture or stroke is a major way to reduce disability from these conditions; studies show that depressed elderly patients have poorer rehabilitation outcomes.[82,85,87,94] It is believed that depressed individuals may participate more poorly in their rehabilitation,[128-130] although research supporting this idea is minimal.[131] As a result of this belief, however, depressed individuals may be excluded from rehabilitation, as found in one study.[132] So although depressed individuals have greater health care utilization, their adherence to care and to appropriate health behaviours is poorer. One prospective study found that health behaviours such as smoking, alcohol use, and inactivity did not account for the increased risk of disability caused by depression.[51] The extent of increased disability resulting from treatment non-adherence or non-participation has not been assessed.

Anxiety as a risk factor for disability

Anxiety, a risk factor for disability, is common in depressed elderly patients.[14] One study found anxiety and depression to be equal predictors of disability; [53] thus, the pathways by which anxiety and depression lead to disability may be very similar. However, given the absence of prospective studies assessing late-life anxiety disorders in association with disability, it is not known how, or whether, anxiety disorders cause excess disability in elderly patients. Also, it is not known whether co-morbid anxiety confers additional disability beyond that caused by depression. The lack of disability data on anxiety disorders may be a consequence of the perception that anxiety is rare in old age unless secondary to depression.[13] Because co morbid depression and anxiety may be a more severe condition than depression alone,[133] observational studies should identify both conditions, as well as the potential additive or interactive risks of co morbid anxiety and depression on disability.

How Does Disability Cause or Amplify Late-Life Depression and Anxiety?

Several prospective studies within this review found that physical disability is a risk factor for depression.[50,52,54] This finding is not surprising, since the onset of disability is a major stressor that leads to loss of perceived control and lower self-esteem.[148] Physically disabled persons also appear to endure a higher number of negative life events.149 Also, physical disability can lead to restriction of valued social or leisure activities,[113] isolation, and reduced quality of social support,[69] all of which are

psychosocial risk factors for depression. Future studies should consider whether these psychosocial sequelae of disability are modifiable risk factors for depression; that is, the idea that psychosocial interventions for a physically disabled elderly person may prevent or treat depression. Medical rehabilitation itself may successfully treat symptoms of depression, as was found in some studies,[75,150] suggesting that physical disability could be a modifiable risk factor for depression and that depressed individuals should not be excluded from rehabilitation efforts. These studies also remind us of the innate similarities between rehabilitation and psychotherapy: both involve engaging an individual's strengths and support structure to understand and overcome their functional deficits. Studies of the course of psychiatric symptoms during recovery from disability are needed. The bi-directional causality between depression and disability suggests that rehabilitation and medical inpatient settings will be increasingly important settings both to observe and intervene in the course of depression.

CONCLUSION

Recent literature has revealed much about the mechanisms by which late-life depression causes or amplifies physical disability. These mechanisms relate the features of the depressed state itself, such as cognitive impairment and motivation depletion, to physical disability. Understanding these disabling effects of depression helps to better inform our concept of "physical" disability and refine it as a construct with physical, cognitive, and emotional components. Similar studies of anxiety disorders are needed in order to determine whether and by what mechanism anxiety increases risk of disability independently of depression. Depression also appears to increase the long-term risk of disability, possibly mediated by a higher incidence of physical illness and poorer health behaviours. Intervention studies in medically ill subjects, such as those in hospital or rehabilitative settings, may be more likely to show clinically significant effects of psychiatric treatment on disability outcomes. Multi-pronged interventions may target multiple mechanisms of excess disability. Assessing the ability of interventions to prevent as well as reverse disability may enhance studies of treatments for anxiety and subsyndromal depression as well as studies of maintenance treatments for depression. Because disability is a risk factor for depression, the possibility of preventing or treating depression in rehabilitation settings should be explored. Psychiatric interventions may find more favour in medical settings if there is proof that these interventions reverse or prevent disability. Thus, the measurement of physical disability in psychiatric illness may have the most usefulness as a tool for communicating the effectiveness of mental health interventions and in underscoring the inseparability of 'mental' and 'physical' health in later life. [17]

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Feline Osteoarthritis – A Prospective Study of 28 Cases

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SUMMARY

Objectives: This study was designed to identify a cohort of cats with clinical evidence of osteoarthritis, and to report the clinical signs, frequency of joints affected and possible aetiopathogenesis within this population.

Methods: Inclusion criteria for this prospective study were: 1) cats that had historical evidence and/or clinical signs of osteoarthritis together with, 2) radiographic evidence of osteoarthritis and, 3) clinical improvement within four weeks of analgesic administration.

Cats had to be free from other disease processes, which might explain the clinical signs and/or their response to analgesia.

Results: Twenty eight cases were included in the cohort.

The elbow (45 per cent) and hip (38 per cent) were the most frequently affected joints.

Seventy-one per cent of the cases had a primary/idiopathic aetiology.

Alterations in both the ability to jump (71 per cent) and the height (67 per cent) of jump (lifestyle changes) were the most frequent signs of disease.

Sixty-one per cent of owners felt their pet had made a marked improvement following administration of an analgesic/anti-inflammatory.

Comparing data between the start and end of the study, there were statistically significant improvements in the ability to jump ($P < 0.001$), the height of jump ($P < 0.001$), lameness ($P=0.03$), stiff gait ($P=0.04$), and activity level ($P=0.02$) of the cats.

Clinical significance: Osteoarthritis is a clinical problem in cats and overt lameness is not the most common clinical feature.

INTRODUCTION

Osteoarthritis (OA) is an important clinical problem in cats, but the signs of OA in this species appear to be much more subtle than those seen in dogs. The objective of this study was to identify a cohort of cats with clinical OA, and then to report on the clinical signs, frequency of joints affected and possible aetiopathogenesis within this population.

MATERIALS AND METHODS

Establishment of Cohort of Cats with Clinical Osteoarthritis

Two meetings were held with primary care veterinary practitioners who regularly referred cases to the University of Glasgow Veterinary School, Small Animal Hospital. Feline OA and details of a prospective clinical study on feline OA were discussed, and a request for the referral of possible suitable cats. Cases were recruited from January 2003 to December 2004. Because of the study design (which included the fact that owners were not charged) these cases represented a first opinion, rather than a referral population.

Inclusion criteria

Cases for inclusion into the cohort had to meet the following criteria:

1. Historical evidence and/or clinical signs of osteoarthritis together with radiographic evidence of osteoarthritis
2. Clinical improvement within four weeks of the analgesic administration
3. The absence of another disease process, which might explain the clinical signs and/or response to analgesic therapy.

Collection of Owner-assessed Data

All cats were examined by the same veterinary surgeon (DB). During the initial consultation, general information regarding diet and lifestyle was recorded. Subsequently, a questionnaire was completed during discussion with the owner. Information regarding food intake, general demeanour and lameness were recorded using a discontinuous scoring system involving a simple descriptive scale (SDS), with an ordinal score recorded for each parameter (TABLE 1). Behavioural characteristics (seeking seclusion, resentment / vocalisation / aggressiveness on handling, abnormal elimination habits), lifestyle alterations (unwillingness to jump and/or reduced height of jump), and any abnormal gait were recorded as dichotomous variables with a nominal scale.

Investigation of Cats

Each patient was subjected to a full general and orthopaedic examination, followed by blood collection and analysis. Survey appendicular and axial skeletal radiography was performed under general anaesthesia. Additional radiographs were taken as indicated by clinical findings and survey radiographs. Appendicular joint radiographic features consistent with OA were recorded in a manner previously described.[5]

A four-week course of meloxicam oral suspension (Metacam®, Boehringer-Ingelheim Ltd, UK) was dispensed. Each case received the same dose; 0.3mg/kg SID for one day, then 0.1mg/kg SID for four days then 0.05mg/cat for 23 days. Re-examination was performed as close to four weeks after the initial consultation as was possible. Meloxicam administration was continued in all cases until the re-examination had been carried out. At re-examination, the questionnaire, general and orthopaedic examinations and blood analyses were repeated. Owners were asked to give an overall subjective summation as to the degree of improvement their pet had shown during the four weeks. Patient tolerance to and acceptance of meloxicam was also recorded.

Data Analysis

The results of data analysis are presented in the form of descriptive and inferential statistics. Inferential statistical analysis was performed using a McNemar test and a Wilcoxan signed rank test for comparison of dichotomous variables and ordinal data at the beginning and end of the study period. Statistical

	Score	Description
General Demeanour (Activity Level)	1	Normal
	2	Slightly subdued
	3	Moderately subdued
	4	Very subdued
	5	Totally disinterested
Food Intake	1	Unchanged
	2	Slightly decreased
	3	Moderately decreased
	4	Severely decreased
	5	Increased
Lameness (limp)	1	None
	2	Slight lameness
	3	Moderate lameness
	4	Severe lameness
	5	Non-weight-bearing lameness

Table 1. Simple Descriptive Scoring System (SDS) used for assessing food intake, lameness and general demeanour

Joint affected	Elbow	Shoulder	Carpus	Hip	Stifle	Hock
Number of joints with radiographic OA only	3	14	6	11	5	2
Number of joints with equivocal radiographic OA	4	8	0	2	0	4
Number of joints detected as painful on clinical examination	35	3	0	32	10	6
Number of joints assumed painful on orthopaedic examination but with no radiographic OA	2	0	0	5	5	1
Number of joints with clinical OA based on orthopaedic and radiographic examination	33	3	0	27	4	5
Number of clinical cases with bilateral joint involvement	15	1	0	12	1	1
Number of clinical cases with unilateral joint involvement	3	1	0	3	2	3
Per cent of joints with clinical OA that had detectable joint thickening	70	0	0	0	25	80
Per cent of joints with clinical OA that had a reduced range of motion	6	0	0	4	0	20

Table 2. Summary of joint involvement (radiographic and orthopaedic examination data) in the cats studied


a

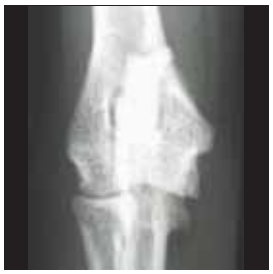
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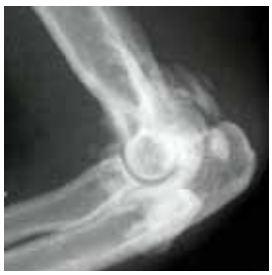
Figure 1. Left elbow joint of a cat with osteoarthritis

Figure 1a: *Mediolateral radiograph of the elbow joint. There is obvious sclerosis beneath the ulnar notch consistent with new bone development.*
Figure 1b: *Craniocaudal radiograph of the same elbow showing osteophyte formation on the medial aspect of both the distal humerus and proximal ulna.*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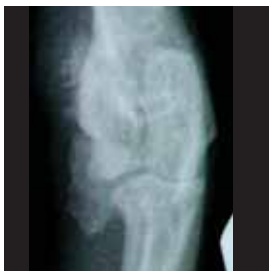
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Figure 2. Right elbow joint of a cat with osteoarthritis

Figure 2a: *Mediolateral radiograph of the elbow joint. There is extensive soft tissue mineralization.*
Figure 2b: *Craniocaudal radiograph of the same elbow showing soft tissue mineralization, osteophyte development and re-modelling of the istal humeral articular surface.*

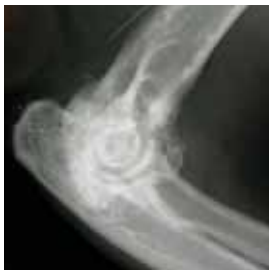

Figure 3. Left elbow of a cat with osteoarthritis

This mediolateral view shows very obvious subchondral sclerosis beneath the ulnar notch, osteophyte development, soft tissue mineralization and possible re-modelling of the supinator sesamoid bone on the cranial aspect of the joint.

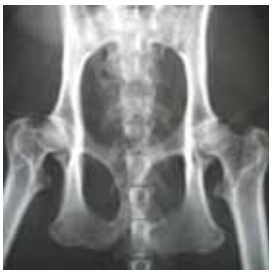

Figure 4. Ventrodorsal radiograph of the pelvis of a cat with osteoarthritis

There is new bone on the femoral necks seen as a sclerotic line. New bone is also seen on the cranial effective acetabular rim especially on the right side. Hip dysplasia is not evident according to the criteria used.

analysis was performed using Simple Interactive Statistical Analysis (http//home.clara.net/sisa/index.htm) and Minitab version 12 (Minitab Inc, USA). Statistical significance was set at $P < 0.05$.

RESULTS

Twenty-eight cats met the inclusion criteria for this study. The mean age of the affected cats was 11 years, and domestic shorthair was the most common breed. Males and females were represented in almost equal numbers (mainly neutered). Three cats were considered obese and 89 per cent had an 'indoor and outdoor' lifestyle whilst only 11 per cent were 'indoor only' cats.

Details of the joints affected and the results of orthopaedic examinations are shown in TABLE 2. The elbow (59 per cent) and hip joints (48 per cent) were the joints most frequently affected with clinical OA (TABLE 2, FIGURES 1 to 5). Spondylosis deformans was not identified in any cats in this study.

In this study 71 per cent of cases had no apparent historical or radiographic explanation for their OA and the authors categorised these cases as potentially primary/idiopathic OA. Secondary OA was identified in 29 per cent which divided into two distinct groups; post-traumatic osteoarthritis (PTOA) and OA secondary to hip dysplasia (HD) (TABLE 3). Hip dysplasia (HD) was diagnosed if less than 50 per cent of the femoral head was contained within the acetabulum or where there was subluxation and/or a misshapen femoral head in combination with incongruity between the femoral head and acetabulum, as assessed on a ventrodorsal pelvic radiograph (FIGURE 5). The mean Norberg Angle (NA) for dysplastic hips with secondary OA in this

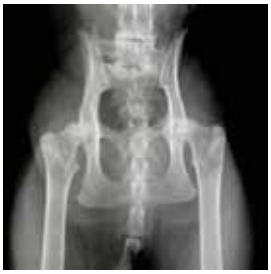
a


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Figure 5. Ventrodorsal pelvic radiographs of two cats with hip dysplasia and osteoarthritis

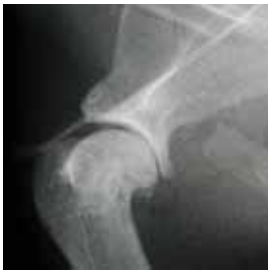
Figure 5a: *Less than 50 per cent of the right femoral head is covered by the dorsal acetabular edge. There is an increased joint space on the right side and sclerosis of both femoral necks, which is consistent with osteophyte development. The radiograph also shows a developmental anomaly of the lumbosacral area.*

Figure 5b: *Both femoral heads are abnormally shaped. Osteophyte formation is present on the cranial effective acetabular rims and caudal acetabular edges of both hip joints.*

Number of cases	Secondary OA (joints affected and aetiology)	Primary OA (joints affected)
1	Left hip: PTOA - previous femoral neck fracture	Bilateral elbows
3	Bilateral hips: hip dysplasia	Bilateral elbows
1	Left hock: PTOA - previous distal tibial fracture Bilateral hips: hip dysplasia	Right elbow
1	Bilateral hips: hip dysplasia	N/A
1	Left hip: hip dysplasia	Bilateral elbow, right hip
1	Right carpus, right stifle, left hip: PTOA - Previous radial and ulnar and femoral fractures	N/A

Table 3. Summary of cats affected by secondary osteoarthritis (OA) with or without primary OA

The joints affected by secondary OA are listed with the primary aetiology, and other joints in the same cat with primary OA are also listed. All other cases were thought to be primary / idiopathic only. PTOA = Post traumatic osteoarthritis; N/A = Not applicable.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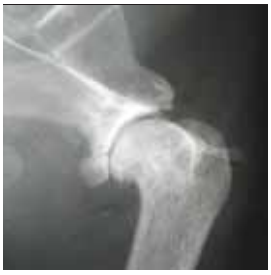
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Figure 6. Radiographs of shoulder arthritis in cats osteoarthritis

Figure 6a: *Mediolateral view of right shoulder - there is osteophyte formation on the caudal edge of the glenoid which has resulted in re-modelling (i.e. an elongation) of the articular surface. Osteophytes are also seen on the caudal edge of the humeral head. The caudal glenohumeral joint space appears reduced.*

Figure 6b: *Mediolateral view of left shoulder - there is osteophyte formation on the caudal edge of the glenoid resulting in an elongation of the joint surface. Osteophyte formation is also seen on the caudal edge of the humeral head and the caudal glenohumeral joint space appears narrowed.*

study was 87.5° compared with 99.2° and 96.6° respectively for normal hips and non-dysplastic hips with OA in this study.

The response of various parameters possibly indicating chronic OA pain during the study are shown in TABLE 4, and the changes in the SDS scoring scheme are shown in TABLE 5. Statistically significant improvements were seen in cats' willingness to jump, the height of their jump, gait stiffness, general demeanour and lameness (limping).

DISCUSSION

This study identified clinical OA in older cats (median age 11 years), in common with other clinical9 and radiographic studies of feline degenerative joint disease.[5,10] The domestic short-hair was the most common breed represented within our study population and most likely reflects the fact that they are the most common breed within the general feline population.

Similar to the results of this study, some previous radiographic studies of feline OA identified the elbow[5,10,14] and hip[5] as the joints being most frequently affected. Hardie[14] also suggested that the shoulder was frequently affected, a finding not substantiated by our study, although cases were seen (TABLE 2; FIGURE 6). The frequency of hip OA, seen in our study, is interesting, since the hip joint was reported as being affected infrequently in some other clinical studies.[8,9]

As in previous reports[8,9,13], periarticular thickening was identified as a common finding on physical examination, although it was generally not marked and is a very subjective feature to assess. Nevertheless its presence was associated with more advanced radiographic OA. An interesting feature of clinically affected joints in this study was that, despite periarticular thickening, only four per cent had a reduction in range of motion. Crepitus was not detected in any joint and synovial effusions were seldom obvious.

Primary and Secondary OA

Hardie *et. al.*[14] postulated that most cases of OA were likely to be secondary to undetermined factors such as elbow dysplasia, chronic low-grade trauma or subtle mal-articulation (as opposed to primary degeneration), despite having no evidence to support this. Examples of secondary OA were identified in our population (TABLE 3), and both

Clinical parameter	Number of cases affected at first presentation	Number of cases showing improvement	McNemar test result
Seeks seclusion	9	2	P = 0.48
Vocalises if handled	10	2	P = 0.48
Resents handling	9	2	P = 0.48
Aggressive if handled	6	2	P = 0.48
Unwilling to jump	20	19	P < 0.001
Reduced height of jump	19	18	P < 0.001
Stiff Gait	9	6	P < 0.04

Table 4. Behavioural and lifestyle alterations in cats at presentation and at the end of the study period
Results of statistical analysis are included.

trauma and HD have been previously recognised as causes of OA in the cat.[5,15,17,19,24]

The radiographic features of feline HD have been previously reported,[17] and OA secondary to HD was diagnosed in six cases in this study; however in only three cases was it of clinical significance. This is not unexpected since there is a poor correlation between HD and clinical signs in the cat.[24] The mean Norberg Angle (NA) for dysplastic hips with secondary OA in our study was 87.5°, only slightly higher than the mean of 84° reported by Langenbach *et. al.*[19] The mean NA for normal hips has been reported to be 92.4°.[19] The mean NA for normal hips and non-dysplastic hips with OA in our study was 99.2° and 96.6° respectively, which would support our opinion that the latter may represent idiopathic/primary OA.

Secondary OA has also been associated with acromegaly in the cat with six of 14 cats affected in one study.[25] These cats have a pituitary tumour which secretes high levels of growth hormone and this is thought to lead to articular cartilage hypertrophy and degeneration. These cats are also diabetic. There is recent evidence that many apparently normal, older cats have increased circulating growth hormone levels and this could be a factor in arthritis development. None of the cats in our study had growth hormone levels measured and this investigation does need to be done.

In man, when there is no obvious aetiology for OA, it is classified as primary/idiopathic.[23] A primary/idiopathic aetiology for feline OA has been previously proposed in radiographic studies of feline OA, [5,10] and this appeared to account for the majority of cases in this study.

Stifle OA

In none of the stifle joints showing pain on manipulation and/or radiographic evidence of OA was there clinical evidence of failure of the cranial cruciate ligament. Rupture of the cruciate ligament in the cat has been associated with severe trauma but also with gradual degeneration similar to that seen in the dog.[12] It is possible that some of our cases could have been cruciate disease without obvious instability being present.

Meloxicam Therapy

Meloxicam is recognised as being an effective analgesic in the cat for single dose pre-emptive analgesia[27,28] and for five-day therapy.[21] The authors have had previous experience of using meloxicam long-term to treat painful locomotor problems in the cat, with apparent success and without complications. Previous reports also suggest successful use of long-term meloxicam therapy.[26] A licence for long-term use of meloxicam in the cat is imminent and the recommended dose is now 0.1mg/kg orally for day one and then 0.05mg/kg orally once daily. However, as with any NSAID, the lowest most effective dose should be used and in some cases the administration can be suspended for a period if clinical response is good. The reason for administering the meloxicam in our study was not primarily to evaluate its efficacy as an analgesic but to assess whether any clinical improvement occurred in the test population, thus giving credence to the diagnosis of clinical OA.

Eighteen per cent of patients in our study developed intermittent gastro-intestinal signs, which may have been associated with meloxicam administration. Two of the three patients who vomited, only did so during the initial five days of therapy. In no case was the severity of gastro-intestinal signs such, that withdrawal of medication was required. Lascelles et. al.[21] reported only a two per cent prevalence of vomiting with meloxicam administration. The palatability of meloxicam was excellent, a finding in common with a previous report.[21] The liquid formulation was easy to administer mixed with food and facilitated accurate dosing by the owners.

Assessment of Pain and Response to Therapy

Assessment of pain in the cat is difficult, since they appear less demonstrative than dogs in indicating that they are in pain, with aggression, resentment to

	SDS scores										Wilcoxan signed rank test
	At first presentation					At re-examination					
SDS Category	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**	
General demeanour (activity level)	11	7	8	2	0	18	6	3	1	0	P = 0.02
Food Intake	22	1	0	0	5	24	1	5	0	0	P = 0.27
Lameness (limp)	15	3	10	0	0	21	4	3	0	0	P = 0.03

Table 5. Results of SDS scores at the beginning and end of the study period
Results of statistical analysis results are included.

handling and lack of responsiveness to human attention being proposed as manifestations of both acute and chronic pain in this species.[20] Resentment to joint palpation and manipulation has been reported as a common finding in feline clinical OA.[9] Our results suggest that, based purely on detection of a patient reaction in response to joint manipulation, there was an overestimation of the number of joints assumed to be clinically affected (TABLE 2). This may be explained merely by the fact that many cats will not tolerate palpation and manipulation of their limbs during a clinical examination. The converse is also likely to be true in that an apparent painful reaction on manipulation of an osteoarthritic joint may not be a true reflection as to whether or not the joint is painful. Three patients demonstrated no pain response to joint manipulation, but had historical and other clinical features felt to be consistent with OA, the presence of which was confirmed radiographically. All three patients showed clinical improvement at the end of the study period.

In our study behavioural variables including seeking seclusion, vocalisation on handling, aggression and/or resentment to handling, were present in only a small number of cats and when present did not show a statistically significant change at the end of the study period, suggesting that these behavioural characteristics may be a 'normal' response in some cats (TABLE 4). We do not dispute that such behavioural characteristics may be a manifestation of acute pain or indeed osteoarthritic pain, but using them in isolation, as indicators of clinical OA may not be reliable.

Although behavioural variables did not show a statistical alteration, importantly we did find statistically significant improvements in lameness scores, lifestyle alterations (willingness and height of jump) and stiff gait between the start and end of the study period (TABLE 4), and of these the willingness to jump and/or the height of the jump showed the most dramatic change.

Although lameness improved significantly in the study, assessment of lameness in feline patients is difficult.[13,21] A stiff gait was present in 32 per cent of patients in our study, a finding similar to that of Godfrey,[8] but limping was identified in only 43 per cent of our patients, compared with the 71 per cent who were unwilling to jump and 67 per cent who had a reduced height of jump (lifestyle alterations). Most studies to date have relied on subjective lameness assessment, which is particularly difficult in the cat. However, if a more objective assessment of limb function is used for example pressure platform analysis,[6] non-observable alterations in limb function may be detectable.

Simple descriptive scales (SDS) consist of four or five expressions, which are used as descriptors of varying degrees of pain, or other variables thought to alter in response to pain.[2,3,16,21,27] Lascelles *et. al.*[21] used SDS to gather data relating to both general clinical and locomotor parameters, when assessing analgesic efficacy in cats with painful musculo-skeletal disorders and their study most likely included some cats with clinical OA. The SDS used in our study differed only slightly from that used by Lascelles et. al.[21] by the addition of another expression, in an attempt to increase the sensitivity of the scale.

An overall change in general demeanour (activity levels) was identified in 46 per cent of our cases (TABLE 5), a clinical feature of feline OA also reported by Godfrey.[9] Further, a statistically significant improvement in general demeanour scores was seen during the study, a finding also demonstrated by Lascelles *et. al.* when assessing analgesic efficacy in cats with painful locomotor disorders.[21] The latter study also demonstrated a statistically significant improvement in patients' food intake over the duration of their therapy although this was not demonstrated in our study (TABLE 5).

Spondylosis Deformans

In an earlier radiographic study we identified approximately eight per cent of cats with spondylosis

Figure 7. Lateral radiograph of the thoracic spine showing vertebral enthesiophytes consistent with spondylosis deformans.

Although these lesions are regularly seen in older cats, none were identified in our study. Their clinical significance is uncertain.

deformans.[5] No cases were identified in this present study. The clinical significance of vertebral enthesiophytes (FIGURE 7), which characterise spondylosis, is difficult to know.

CONCLUSION

OA is an important clinical disease in the cat. Only a small number of primary care practices contributed cases to the study, with one practice contributing 46 per cent of all cases in the final study population. Given this finding, it is very likely that the overall incidence of clinical osteoarthritis in the general cat population is greater than one might believe. Lifestyle alterations (unwilling to jump, reduced height of jump, reduced activity levels) were the most frequently identified signs of disease, as opposed to limping and stiff gait, which were present in less than half of the cases. We prefer to refer to these as lifestyle changes rather than to behavioural alterations. Periarticular thickening is often minimal and affected joints often show a normal range of motion. Synovial effusions are seldom obvious and crepitus on movement is not a feature. A significant improvement in orthopaedic and lifestyle parameters, but not in behavioural parameters was identified at the end of the study period, which might suggest that the latter features are less reliable indicators of clinical OA. This study, in common with previous reports,[5,9,10] provides further evidence that a primary/idiopathic aetiology as currently defined, may explain most cases of feline osteoarthritis.

Therapeutic approaches, other than administrating NSAIDs, are available to manage feline OA and these include nutraceuticals (matrix supplements and essential fatty acid supplementation), anti-oxidants and weight loss where relevant. The provision of comfortable bedding, measures to avoid jumping and the use of shallow litter trays are also important. Altering exercise regimes is difficult in the cat, but less relevant than other species, since the cat is able to decide on its own level of activity to a great extent. These other measures were not considered in this study in order to minimise the number of variables to assess.

Why has OA been missed for so long in the cat? There are several reasons for this. Overt lameness (i.e. limping) is not a common sign and if it is present it is difficult for owners and veterinarians to detect as compared to other species. Stiffness is a subjective feature to define and is often regarded by owners as a 'normal' feature of ageing and not necessarily a sign of pain. Similarly, decreased activity levels are often believed to be a non-specific feature of old-age. Unwillingness to jump or only willing to jump a short distance tends to develop over a long period of time and again is often felt to be a normal feature of ageing. Pain is very difficult to assess in the cat. Many cats do not like having their joints palpated and manipulated. Thickening of joints is often subtle in the cat compared to the dog and again is a subjective feature to assess. Reduced range of motion of and crepitus within arthritic joints are generally not features as is in other species. Synovial effusions are rarely detected with any certainty.

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Canine Hip Dysplasia: Relationship of Phenotype to Genotype

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SUMMARY

The objective of selective breeding is to maximise the pairing of good genes by breeding dogs that are not overtly affected with canine hip dysplasia (CHD). The relationship between phenotype and genotype is embodied in the concept of heritability represented by the symbol h^2. Heritability denotes the reliability of the phenotype in predicting the genotype. The best phenotype for screening is one that is unaffected by environmental (non genetic) factors. Diet restriction (lean body condition) is an environmental factor shown to dramatically suppress the phenotypic expression of CHD including radiographic evidence of osteoarthritis (OA) and subjective hip score. This means that radiographic evidence of OA and subjective hip score are poor predictors of hip genotype and will therefore confuse the selection decision.

Worldwide, the predominant mode of choosing breeding stock is to make selections based on the hip phenotype of individual animals, so-called mass selection. However, this is not the most effective means to select breeding candidates. Rather, the calculation of estimated breeding value (EBV) is far more useful and will result in much faster genetic change. To successfully use such programmes, it is important to know the magnitude of heritability. For a quantitative trait such as CHD, the rate of expected genetic change in the next generation (ΔG) from mating a dog and a bitch is equal to the product of the heritability (h^2) times the selection pressure that is applied. Selection pressure is defined as the deviation of the parental mean of a specific trait from its population mean. The higher the heritability of a specific trait and the greater the selection pressure applied, the more rapid the expected genetic change per generation of breeding.

Research results have shown that the heritability of the PennHIP distraction index to be considerably higher than the heritability of subjective hip scoring for the breeds of dogs studied thus far. Breeders cannot influence the magnitude of the heritability, but they can control the magnitude of applied selection pressure. By utilizing a quantitative phenotype with high heritability (such as PennHIP) and by successfully applying selection pressure, breeders can expect to make rapid and effective genetic improvement in hip integrity.

However, extreme selection, for example by inbreeding and line breeding, may contribute to the loss of some desirable traits or the expression of some undesirable traits. In order to avoid this, a moderate approach has been suggested to go hand in hand with PennHIP testing. One can achieve slower, yet equally effective genetic improvement of hips by selecting breeding candidates from the tighter-hipped half of the breed. Such a practice will result in all positive and no negative selection pressure and will gradually lower the propensity for hip OA and still maintain an acceptable level of genetic diversity.

INTRODUCTION

Genetic control of a complex disease requires: a) a knowledge of the principles of quantitative genetics, b) an accurate screening method keyed to a phenotype with optimal heritability, c) an organized screening program based on a proven screening phenotype, d) a centralized database containing essential phenotypic and pedigree information, and e) trust and cooperation among breeders and the veterinarians who perform the screening procedure.

THE RELATIONSHIP BETWEEN PHENOTYPE AND GENOTYPE

Controlling diseases of complex inheritance (i.e. polygenic diseases) such as CHD requires a concerted and coordinated effort on the part of breeders and veterinarians. As importantly, the integrity of the test used to screen for CHD is central to reducing the frequency of hip disease (FIGURE 1).

The principal objective of selective breeding is to maximize the pairing of good genes by breeding dogs not overtly affected with (and preferably, not susceptible to) CHD.

The purpose of the screening test is to evaluate hip phenotype (that which you can see or measure) as an estimate of the genotype (that which you can't *'yet'* see or measure). The relationship between phenotype and genotype is embodied in the concept of heritability represented by the symbol, h^2. Heritability denotes the reliability of the phenotype in predicting the genotype. A high heritability, say approaching one, means that the phenotype closely reflects the genotype. Or put in other words, all the variation in the phenotype is explained by the genes. Environmental factors, such as diet or exercise, have no influence on the phenotype. In contrast, a heritability of zero means that a disease is not influenced whatsoever by genes and accordingly variation in expression is purely environmental.

Heritability is mathematically defined as the ratio of additive genetic variation to the total phenotypic variation of a given trait (h^2=VG/VP). And the total phenotypic variation, VP, in turn is defined as the sum of the genetic variation, VG, plus the variation owing to environment factors, VE, (sometimes termed variation due to non-genetic factors). Then,

h^2=VG/ (VG + VE)

One can see from this simple relationship that when environmental factors do not influence the trait of interest (i.e. VE is small) then, h^2 approaches one and the trait or disease of interest can be considered purely genetic. Similarly, as environmental factors cause increasingly more variation in the phenotype, h^2 approaches zero.

Examples of environmental factors that contribute to variation in the denominator of the heritability relationship above include diet, exercise, gender, age, and diagnostic error. These factors increase the total phenotypic variance in the denominator of this relationship, VP, and therefore they have the effect of lowering estimates of heritability, the significance of which will be emphasized later. So, complex polygenic traits are influenced by both environmental and genetic effects. For example, a dog's weight is partly influenced by environmental factors in terms of how much it is fed and how much exercise it gets. However, it is known that body weight can also be influenced by genetic factors, i.e. obese parents tend to have obese offspring. Recently, a life span study in Labrador retrievers reported a profound influence of diet restriction, an environmental factor, and associated body condition score on the radiographic evidence of OA of CHD

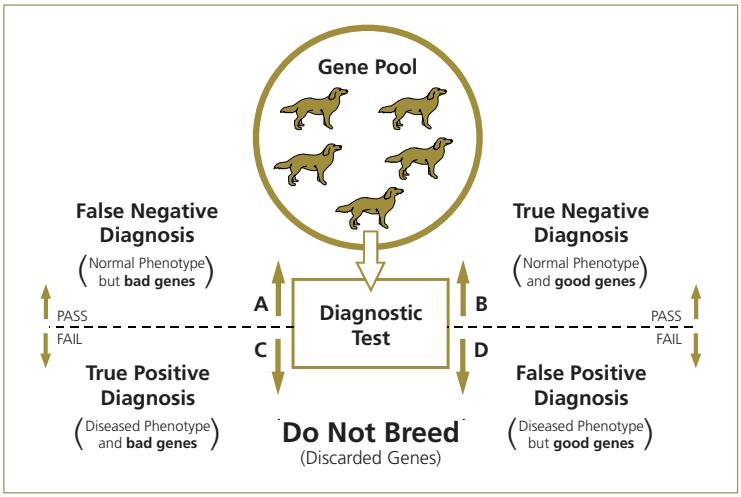

Figure 1. The role of a screening test in improving the gene pool in a Selective Breeding programme

The objective of any screening test for a genetic disease is to lower the frequency of 'bad genes' in the gene pool. This entails using 'what can be seen', as a result of the diagnostic test (the phenotype) to estimate 'what cannot be seen' (the genes). Dogs are permitted to enter the gene pool based on normal results of the test (arrow A or B). A perfect test (arrows B and C only) would be capable of accurately separating 'good genes' from 'bad genes' on the basis of the phenotype alone (i.e. the test result), thereby quickly and effectively ridding the gene pool of bad genes (arrow B: good genes enter the gene pool; arrow C: bad genes are not returned). Unfortunately, no screening test is 100 per cent accurate. For example, a test result may wrongly exclude from breeding a dog that tests positive for a diseased phenotype even though it harbours good genes (arrow D). This would be an unfortunate missed opportunity, as some good genes would not re-enter the gene pool. However, this mistake would not appreciably harm the gene pool. Of much greater potential damage to the gene pool is a test result that indicates a dog has a normal phenotype (negative) but which, in fact, harbours many bad genes (arrow A). Such a mistake would recycle bad genes through the gene pool, resulting in a steady-state level of disease in the offspring derived from that gene pool, despite the best efforts at selection, e.g., breeding excellent to excellent. The frequency of disease coming from the gene pool will depend on the sensitivity of the test to detect bad genes. This sensitivity is directly related to the heritability of the phenotype used for screening, therefore the higher the heritability of the phenotype and the more closely it is associated with the disease of interest, the better the test, and the more rapid the genetic change.

(FIGURE 2).[1] Diet-restricted dogs had a much lower frequency and severity of radiographic hip OA than paired ad lib-fed littermates. Accordingly it is recommended to keep CHD-prone dogs lean thereby delaying or mitigating the expression of a genetic disease. However reliance on a phenotype such as radiographic OA or subjective hip score that is so strongly influenced by environmental factors, such as diet, is not optimal. This environmental influence raises the variance component, VE, in the relationship above, and therefore lowers the estimate of heritability of the phenotype. As shown in FIGURE 2, the leaner restricted-fed dogs had lower expression of radiographic OA despite the close genetic similarity to their paired littermates that were fed ad libitum. In other words diet-restriction can suppress the phenotype thereby masking the genotype for CHD and confusing selection decisions based on that phenotype. The best screening phenotype is one unaffected by environmental factors.

IMPORTANCE OF HERITABILITY

Worldwide, the predominant mode of choosing breeding stock is to make selections based on the *'individual animal's hip phenotype'*, so-called mass selection. It must be stressed, however, that this is not the most effective means to select breeding candidates. More rapid genetic change can be accomplished if the *'hip phenotypes of relatives'* are incorporated into the selection decisions. By incorporating data from relatives, one can calculate so-called *'breeding values'* for each individual dog. Although this method facilitates more accurate selection decisions, it is not widely employed because of the need for extensive record keeping coupled with the availability of accurate pedigree information. The breeder should recognize, however, that there are better tools to help in making selection decisions than just resorting to the individual dog's phenotype such as its hip score.

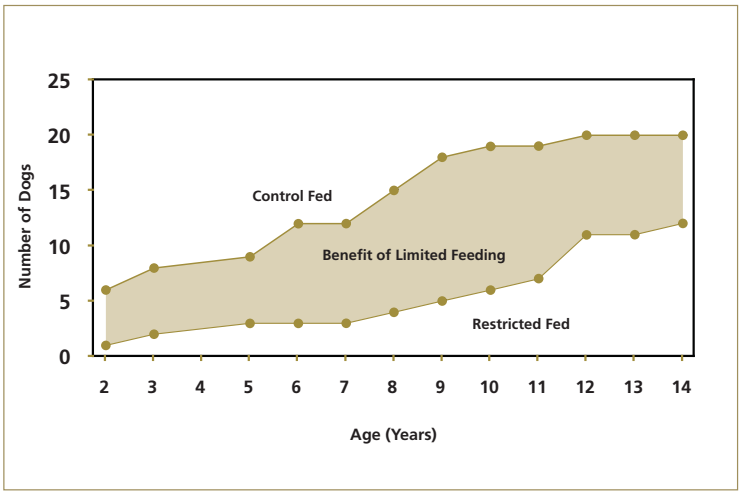

Figure 2. Cumulative prevalence of radiographic OA in 24 control-fed dogs and 24 restricted fed littermates

Compared with control-fed littermates restricted feeding was associated with reduced weight and body condition score of the dogs for life. This environmental factor served to suppress expression of radiographic hip OA in the restricted fed group. Note at two years of age only one of 24 restricted fed dogs showed radiographic evidence of hip OA compared to six of 24 control-fed littermates. The protective effect of lean body condition continued for the life of these dogs. (Reproduced with permission [1])

The common practice of selecting breeders by using only the individual animal's phenotype makes knowledge of the magnitude of heritability of utmost importance. Why is heritability so important in this regard? Because, for a quantitative trait, the rate of expected genetic change in the next generation, (ΔG), from mating a dog and a bitch is equal to the product of the heritability, (h^2), times the selection pressure that is applied (RELATIONSHIP 1 below). Selection pressure is defined as the deviation of the parental mean, e.g. hip laxity, from the population mean.[2]

$$\Delta G = h^2 \times (Avg_{Parents} - Avg_{Population})(1)$$

Where:

ΔG = the expected change in average litter phenotype after one generation

h^2 = heritability of phenotype, eg. DI or subjective hip score

$Avg_{Parents}$ = average hip phenotype of the parents

$Avg_{Population}$ = average hip phenotype of the population from which parents were derived.

Therefore, the higher the heritability of a specific trait and the greater the selection pressure applied, the more rapid the expected genetic change per generation of breeding. Estimates of heritability above 0.4 make feasible selection based on the individual phenotype. These concepts applied to PennHIP data are illustrated in the actual mating of two tight-hipped German shepherd dogs (FIGURE 3). In this example, extreme selection pressure has been applied because the sire and dam are drawn from the tightest fifth percentile of the breed. One can see that the mean hip laxity of the litter derived from these two parents is 0.27. From FORMULA 1, it is possible to calculate the *'realized heritability'* of any metric, for example, DI. The GSD population average DI is 0.39 and the parental average DI is 0.2, therefore the selection pressure applied was 0.19 DI units. Again, the average DI for the nine puppies was

0.27. Therefore the realized heritability from this single mating can be found by rearranging terms in RELATIONSHIP 1:

$h^2 = \Delta G/(Avg_{Parents} - Avg_{Population})$

Plugging in data from the mating in Figure 2

$h^2 = (0.39\text{-}0.27)/(0.39\text{-}0.20) = 0.63$

Currently there are no published estimates of heritability for subjective (OFA) hip scores for the most popular breeds of dogs. A retrospective analysis from the OFA showed heritability in 4 less common dog breeds to average 0.26.[3] Phenotypes with heritability of this magnitude would be considered to be lowly heritable 2 meaning that genetic change will be slow (only 25 per cent of the applied selection pressure will be passed on in each generation of breeding- see RELATIONSHIP 1). These figures are corroborated by 2 well-executed studies of subjective hip score (OFA-type scoring), which yielded similar estimates of heritability of 0.22[4] and 0.43[5] for German shepherd dogs.

The magnitude of selection pressure applied is the other important factor in RELATIONSHIP 1 above. With successful application of selection pressure, offspring within generation will begin to look similar, e.g. more dogs will be normal, meaning that the phenotypic and genotypic variance will get smaller. However, with decreasing variation in the hip phenotype (for example, in subjective score), there may come a point, a steady state, at which little additional incremental selection pressure can be applied by using the subjective score as a selection criterion. That is, if the application of maximum selection pressure, e.g. breeding *'excellent'* to *'excellent'* (FIGURE 1 arrow A), still produces affected progeny, no more genetic progress can be expected (short of incorporating estimated breeding values in making selection decisions, mentioned above, or by bringing new genes into the breed for example by out-crossing). Such has been the experience of The Seeing Eye, Inc. after 17 years of selection against hip dysplasia using a subjective scoring scheme similar to, but more strict than, that of the OFA.[6]

Heritability of a given phenotypic trait is a property of the population under study. Therefore heritability of each trait or diagnostic phenotype must be calculated for each breed and each population of dogs. An example of a calculation of realized heritability was illustrated in FIGURE 3.

The most valid estimates of heritability of DI or subjective hip score are derived by incorporating

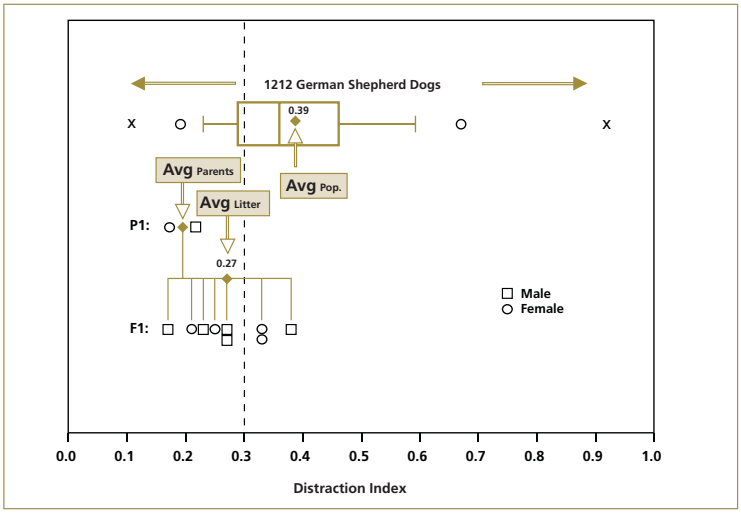

Figure 3. Calculation of 'Realized Heritability' from a single mating
This illustration shows the relative relationships of passive hip laxity of: 1) the German shepherd dog breed at large (DI = 0.39), 2) the dog and bitch (P1) and 3) the litter (F1). Note that the mean litter DI moved approximately 60 per cent of the distance from the mean of the GSD population toward the mean of the parents. Plugging these averages in hip laxity into Relationship 1 yields a realised heritability of approximately 0.6. It is notable that all nine puppies showed hip laxity below the average for the breed and that hip laxity in six of the nine puppies fell below a DI of 0.3, indicating little to no susceptibility to DJD. (See text for full description)

knowledge of relevant phenotypes in the context of the full pedigree. The Seeing Eye, Inc. has maintained a closed colony of dogs intended for use as dog guides for the blind. Leighton, et al. invoked rigorous mathematical methods that incorporated the full pedigree structure, and found the heritability of DI to be 0.46 for German shepherd dogs and 0.46 for Labrador retrievers.[7] More recent analyses (unpublished) put the estimate of heritability of DI over 0.5. The corresponding heritability estimates for subjective hip score (determined by a board-certified veterinary radiologist) were lower at 0.34 for German shepherd dogs and 0.34 for Labrador retrievers. This low heritability of subjective hip score in German shepherd dogs is supported by a recent study from Finland by Leppanen *et al.*[8] Applying Best Linear Unbiased Prediction (BLUP) procedures to analyze 10,335 German shepherd dogs from 1985 to 1997 these investigators found that using subjective hip score as a selection criterion over this 12-year time interval failed to produce genetic improvement.

Heritability analyses using these newer, more sophisticated statistical methods are needed for all hip screening methods applied to all breeds of dogs. Results thus far are promising that the heritability of the PennHIP DI will be considerably higher than the heritability of subjective hip scoring for all breeds of dogs. These findings have great clinical significance owing to the abundant evidence linking hip laxity as

measured by DI with OA of the hip (FIGURE 4).[9,10] To the author's knowledge there are no published estimates of the heritability of other diagnostic hip phenotypes and no similar close correlations with degenerative joint disease (DJD), including the DLS score[11], the DAR score[12], and the scores of Fluckiger[13], Barlow test, Bardens test, or Ortolani test. Such studies are necessary to determine the relative merits of these diagnostic tests as candidate hip screening methods for selecting breeding stock.

USING SELECTION PRESSURE TO MAKE GENETIC CHANGE IN CHD

Breeders cannot influence the magnitude of the heritability of the phenotype, but they can control the magnitude of applied selection pressure, i.e. the difference between the mean of the parents and the mean of the population at large (see RELATIONSHIP 1). Therefore, to the extent that breeders select breeding candidates, they can control the rate of improvement in hip phenotype in each generation. For the most rapid genetic change, the breeder can decide to mate only the tightest-hipped dogs within the breed (those with the lowest DI) and then continue to inbreed for tight hips. This approach would maximize the difference between the parent average and population average i.e. the selection pressure (the second term on the right side of RELATIONSHIP 1) would be large. There would therefore be a greater expected change in each generation assuming constant heritability. This approach, however, creates concern that founding a breeding program on only a few dogs, and inbreeding on these dogs, would reduce the overall genetic diversity in the gene pool and could contribute to the loss of some desirable traits or the expression of some undesirable traits. This reality affects some breeds more than others. For example less than five per cent of golden retrievers have hip laxity in the *'tight-hipped'* range below a DI of 0.3. If one were to require that breeding candidates conform to this standard and must come from this small pool of dogs, the result would be a serious reduction in genetic diversity, not to mention that the strategy would neither be practical nor acceptable to breeders.

To avoid these potential problems accompanying *'extreme'* selection, a *'moderate'* approach has been suggested to go hand in hand with PennHIP testing, particularly in breeds with few or no members having tight (DJD-unsusceptible) hips. In such breeds

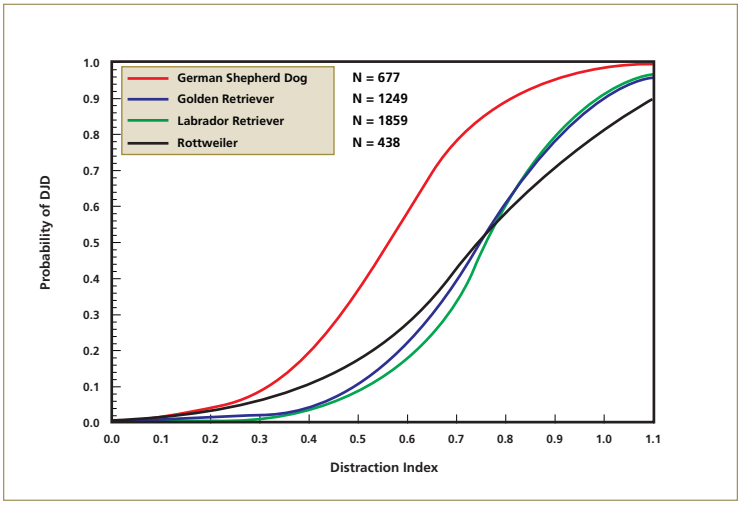

Figure 4. Breed specific DJD probability based on DI for dogs ≥ 24 months of age*Note the Probability of radiographic evidence of degenerative joint disease (DJD) as a function of distraction index (DI) for dogs ≥ 24 months old of 4 common breeds. Note the spatial shift to the left for the German Shepherd Dog breed indicating an increased probability of DJD for any given DI compared to the three other breeds. (Reproduced with permission from Smith, Mayhew, et al. JAVMA 2001[10])*

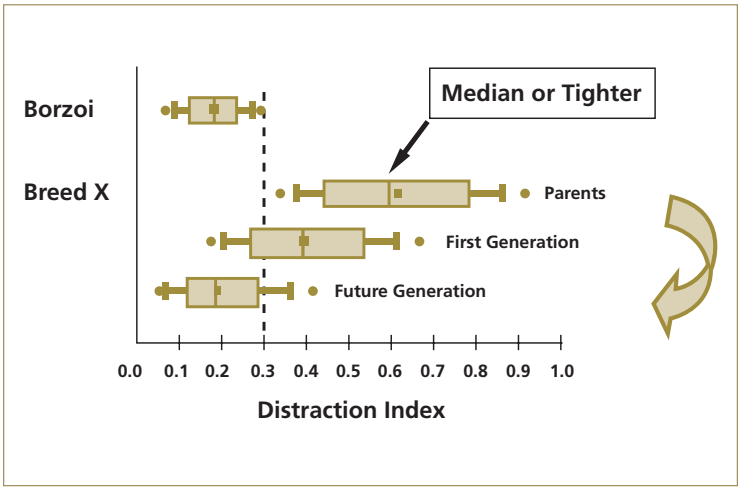

Figure 5. Proposed minimum laxity-based breeding criteria
By using the generational median (or mean) as the minimal criterion for breeding, one can expect genetic change to occur. Breed X displays a range and distribution of hip laxity not unlike the golden retriever breed, for example. Genetic change toward tighter hips can be expected in each subsequent generation by breeding dogs in the tighter half of the distribution (and preferably much tighter). The goal of this strategy is to tighten the hips of Breed X until matching the range and distribution of hip laxity of the Borzoi. Obviously, based on RELATIONSHIP (1), the tighter the parents, the greater the selection pressure will be and the more rapid the expected genetic change toward hip improvement. This logic follows well-established principles of quantitative genetics.

it is recommended that breeders choose breeding stock from the tightest half of the breed, thereby maintaining an acceptable level of genetic diversity while still applying meaningful selection pressure (FIGURE 5). Clearly the more selection pressure applied, the more rapid the genetic change.

The PennHIP database ranks each dog relative to other members of the breed making it possible for the breeder to identify dogs whose DI will apply meaningful selection pressure (FIGURE 6). By

applying at least moderate selection pressure, eventually the average of the population will shift with each generation toward tighter hips, increasingly tightening the minimum standard for breeding. By following these time-tested principles, ultimately fewer dogs will be at risk for developing DJD. Understandably, more rapid genetic change could be achieved by imposing greater selection pressure or by using estimates of breeding value from incorporation of the pedigree. These strategies are recommended for the aggressive breeder wishing to achieve the most rapid hip improvement. Even absent these measures, however, the principle of mass selection if linked to a highly heritable phenotype, such as the PennHIP DI, holds great promise for reducing the frequency and severity of DJD in future generations of dogs.

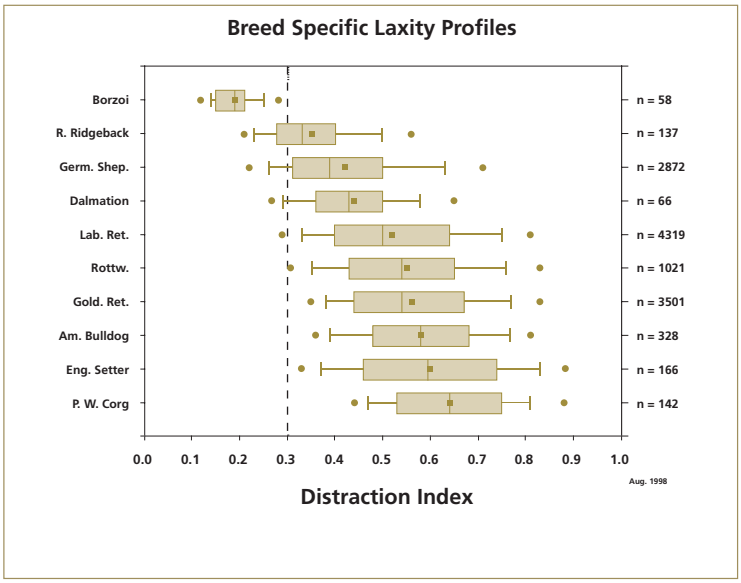

Figure 6. Breed-specific distribution of distraction index
These boxer and whisker plots show passive hip laxity by breed; the data are drawn from the PennHIP database (August 1998). None of the Borzois showed a hip laxity (DI) greater than 0.3. Note also that the golden retriever breed had few members with a DI of less than 0.3. The obvious objective of selective breeding is to move the laxity profiles of the looser CHD-prone breeds, such as golden retrievers, into a hip-laxity range approximating that of the Borzoi, a breed of dog that has negligible incidence of CHD.

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Some Medical Aspects of Premiership Football

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ABSTRACT

This talk briefly outlines the medical services provided to a leading Premiership Football Club in the UK.

Reference is made to the general aspects of the transfer process of professional footballers with special attention for the role of imaging in this. The role of Magnetic Resonance imaging (MRI) in the care of professional footballers will particularly be emphasised, both in the acute and chronic injury setting. Reference is made to the influence of the medical care on this transfer process.

Many of the common football injuries are discussed and illustrated with MR scans. We will emphasise especially on injuries to the knee (FIGURE 1), which is the most commonly injured joint. Ligament (FIGURE 2) and cartilage injuries will also be described in detail, as well as other injuries such as muscle tears (FIGURE 3). Again these will be illustrated with MRI scans.

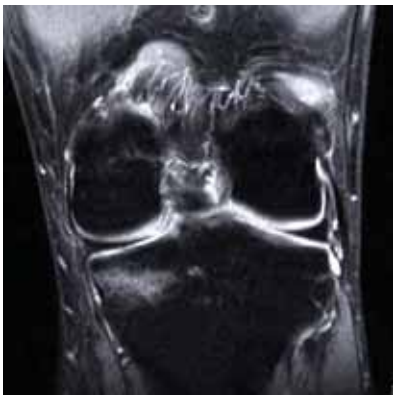

Figure 1. Stress fracture of the left knee

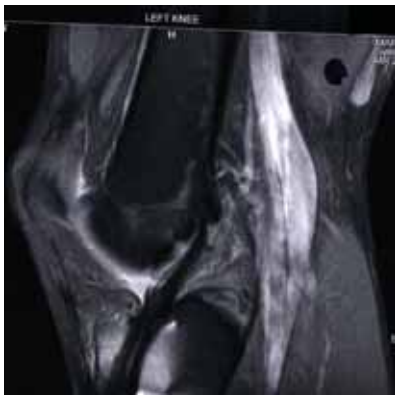

Figure 2. Repair of an acute cruciate ligament injury in the left knee

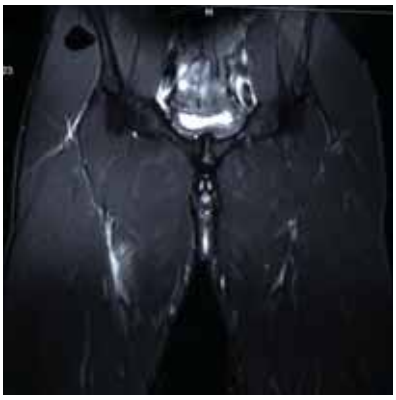

Figure 3. MRI showing an adductor tear


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Vetting Lame Dogs – Objective Assessment of Limb Function in Dogs

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SUMMARY

For many years the veterinarian has relied on a visual assessment of a dog's gait, combined with a history from the owner and a clinical examination, to assess limb function and lameness.

Information from owners has usually been collected in an informal and non-standardised manner. In veterinary medicine, there is a need for standardisation and validation of owner questionnaires to increase accuracy and repeatability of these data.

Improvement in orthopaedic evaluations is also needed. Unpublished studies, evaluating orthopaedic specialist veterinarians, show good intra-observer agreement but poor inter-observer agreement between individuals in their ability to grade hind limb lameness. Therefore, the use of more objective (and reproducible) measures should be encouraged. Recently, force platforms have become the gold-standard for measurement of limb function in dogs, but they have limitations in cats, small dogs and very lame animals. More sophisticated systems are being developed which provide breed specific data.

At the University of Liverpool a Qualisys three-dimensional motion capture system is in use, which is equipped with infrared cameras. In combination with the motion capture system a Kistler force platform then allows the specialists at Liverpool to resolve the forces of movement in to the three orthogonal planes.

INTRODUCTION

Assessing lame dogs is not easy. For many years the veterinarian has relied on a visual assessment of the dog at various gaits (usually walking or trotting), combined with a history from the owner and a clinical examination. The clinical examination may include assessment of pain, swelling, range of joint motion and muscle mass, usually subjectively but sometimes semi-objectively or occasionally objectively. However, as veterinary science progresses perhaps we should consider utilising scientific progress and increased knowledge base to more formally, more reliably and more sensitively assess a lame dog?

OWNER ASSESSMENT

Information from owners has usually been gathered in an informal manner. Whilst there is a huge body of literature in human musculoskeletal medicine on the subject of patient-derived information on musculoskeletal pain and function through patient questionnaires (or metrology instruments), there is minimal literature on the assessment of information form dog owners. Owner questionnaires have been commonly used in clinical trials and follow-up studies from academia and private practice but there are no standardised questionnaires and little validation work has been performed. Validation involves an assessment of the construct validity of the questionnaire, estimation of the reliability of the questionnaire (test-retest scenarios), and estimation of the responsiveness of the instrument to an accepted and proven intervention. To date, we have some studies that suggest owner questionnaires for specific conditions can be reliable and responsive but further studies are required.[9,10,11] At last the veterinary community is taking this seriously and there is a large initiative led by ACVS to develop validated clinical outcomes assessment tools for dogs with musculoskeletal disorders.[17,18]

VETERINARIAN ASSESSMENT

This is what we do as clinicians every day. But how reliable and how sensitive are we? Unpublished studies comparing orthopaedic specialist veterinarians in their ability to grade hind limb lameness showed good intra-observer agreement but poor inter-observer agreement . Earlier work suggested there is a floor effect to visual assessment of lameness.[12] It is also recognised that visual assessment of lameness is insensitive compared to modalities such as force platform measurements.[7]

OBJECTIVE ASSESSMENT OF LAMENESS AND MOBILITY

Kinesiology is the science which involves study of movement. Kinetic gait analysis involves studies of the forces of movement whereas kinematics involves the study of movement of limbs in space with no regard for the forces involved. Kinesiology is the scientific study of movement and has advanced significantly in recent years with the advent of newer technologies. Kinematics is the description of movement without reference to the influences of mass and force, whereas kinetics is the study of the forces involved in movement.

At the University of Liverpool we have a gait analysis laboratory that enables us to undertake studies of normal and abnormal canine and feline movement to enable us to have a better understanding of how disease affects musculoskeletal function. These techniques are also sometimes very helpful in case management because we can measure the response to therapeutic interventions.

At the heart of the gait laboratory are several sophisticated items of equipment. We use a Qualisys three-dimensional motion (QTM) capture system equipped with four infrared cameras. These cameras send out an infrared beam and this is reflected back from small markers placed on the subject's limbs (FIGURE 1). Because the beam is emitted and reflected back to the camera, it is possible to calculate the distance of the marker from the camera and thus generate three-dimensional data on the

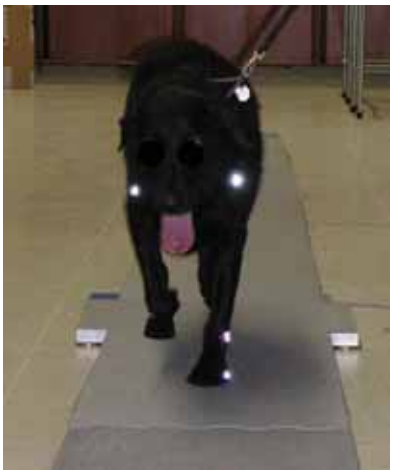

Figure 1. A dog on the walkway with reflective markers placed for motion capture. The force platform is embedded within the runway so that the dog does not know it is there

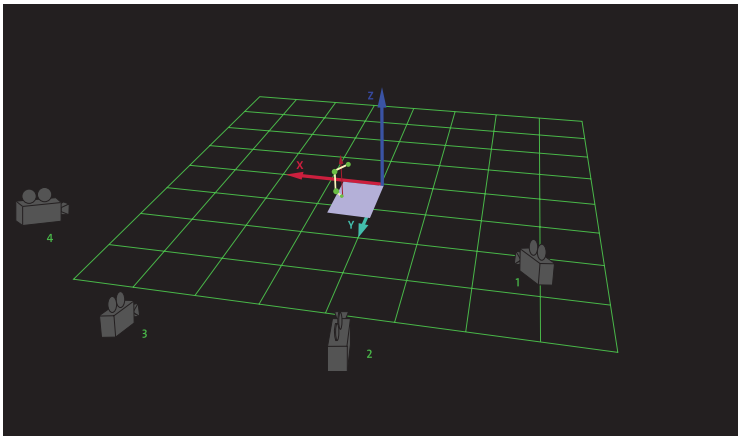

Figure 2. A screen grab from the Qualisys QTM software showing the relative positions of the cameras, the force platform and the reflective markers

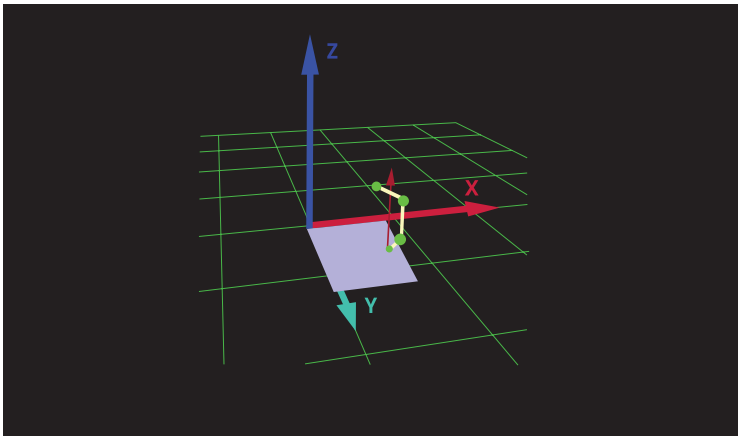

Figure 3. Close-up screen grab showing a dog's forelimb during stance phase on the force platform (grey rectangle). The red arrow emanating from the dog's foot is the centre of pressure vector; the direction and length of this arrow represents the resultant force vector from the action of the limb on the force platform

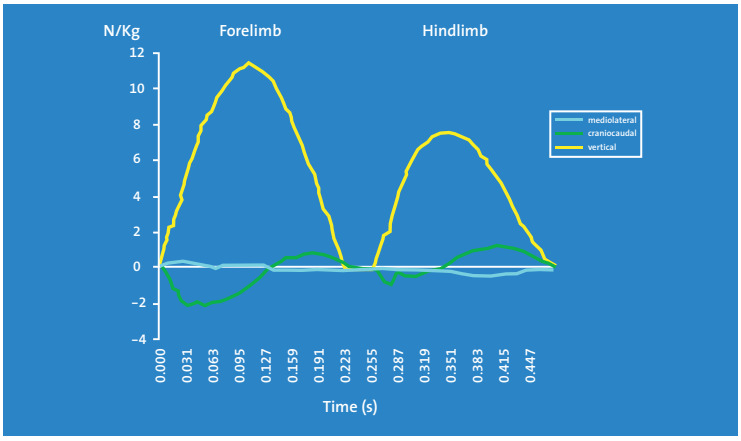

Figure 4. A force-time curve for a normal trotting Labrador. Note that approximately 60 per cent of the dogs weight is taken on the forelimb
N/kg = Newton per kilogram

coordinates of the marker in space (FIGURES 2 & 3). This type of motion capture system is not only used by scientists but is also often used by animators and computer gaming companies to generate realistic movement in their characters!

We combine our motion capture system with a Kistler force platform. The force platform allows us to resolve the forces of movement in to the three orthogonal planes, i.e. craniocaudal force, mediolateral force, and most importantly, vertical force (Fx, Fy, Fz). The force platform measures the forces of movement in N/Kg every millisecond to create the force-time graph. The vertical forces are shown for the forelimb and the hind limb (yellow line in FIGURE 4).

The canine gait laboratory enables us to investigate the fundamentals of locomotion but we are also interested in the link between movement and musculoskeletal diseases, as well as using the measurements to investigate efficacy of medical and surgical treatments.

Force platforms have become the gold standard for measurement of function in dogs.[2,4,5,6,8,15] The peak vertical force (PVF) has become the primary outcome variable in many studies such as those measuring efficacy of NSAIDs and other analgesics.[3,13,16,19] However, whilst there are many advantages to the use of force platforms, there are limitations. Firstly, small dogs and cats may not be suitable because their stride length is too short and they have more than one limb on the force platform at any one time; this can also be a problem with very lame dogs. The vertical impulse (area under the vertical force-time curve) is a useful parameter but may be difficult to measure in very lame dogs. This is because they can have complex force-time curves with overlap between the thoracic and pelvic limbs, making calculation of impulse very difficult.

Pressure platforms such as the Tekscan® and RS Footscan® (FIGURE 5) have started to become popular for use in small dogs and cats. These systems appears to be useful for estimation of PVF and vertical impulse.[1,14]

FUTURE WORK TARGETS

Recent studies have used a combination of morphometric measurements, kinematic data, kinetics and inverse dynamics modelling to estimate the joint movements, as well as powers and forces in canine joints. Studies generating these data do need

to be breed specific, but are starting to shed light on differences between breeds so that we may start to understand breed predilections to acquired musculoskeletal conditions. Further work using telemetric EMG measurements should enable researchers to build muscle forces in to models more accurately. Such techniques are important in assessing normal and abnormal gait but are also very useful in prosthesis design.

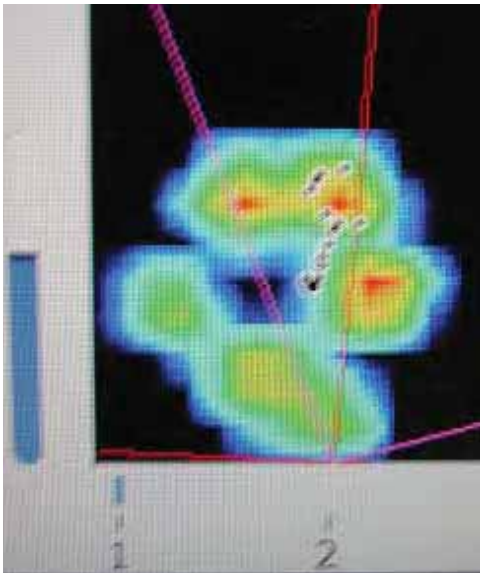

Figure 5. RS Scan image showing pressure distribution in a normal Greyhound

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Rehabilitation Therapy for Pets

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SUMMARY

The interest in veterinary rehabilitation has grown tremendously during the last years. The purpose of rehabilitation in orthopaedic patients is 1) to prevent stiffness and fibrosis in the musculature and soft tissues surrounding the joints; 2) to regain full range of motion and function; 3) to regain muscle mass and strength, and 4) to relieve pain. In neurological patients, early return of neurological function and prevention of muscle atrophy are the main goals.

A rehabilitation plan must always be tailored to the needs of the individual patient. Several techniques are used depending on the condition and the purpose of the treatment. Massage is used to relax soft tissues and improve the circulation in the muscles. Stretching is used to relieve muscular contractures and to facilitate recovery from muscle strain after training, whereas stretching of the soft tissues around a stiff joint is carried out to improve the range of motion. Different techniques of water therapy are widely used in rehabilitation, including swimming and under-water treadmill. The advantage of these techniques is that they can be applied with minimal loading of the joints and that the load on the legs can be adapted to the patient's needs. Weight cuffs on the lower extremities are often used to correct the gait and abnormal movement patterns. Several types of active training exercises are often used and can be executed at home if the owners are well instructed. Transcutaneous electric nerve stimulation (TENS) can be applied to relieve pain and to stimulate muscles that are non-functional, whereas acupuncture mainly serves as a pain treatment.

Rehabilitation should always lead to improvement. Therefore, several parameters should continuously be evaluated and results recorded and compared with previous records. Parameters to check include: maximal flexion and extension of joints, muscle circumference and joint width.

INTRODUCTION

The interest in rehabilitation from the veterinary profession and from animal owners has grown tremendously during the last years. New rehabilitation facilities open in veterinary hospitals and clinics, but also independent physiotherapists with varying background start their own rehab clinics. The positive effects of rehabilitation are obvious, but practicing it without proper education and experience may lead to inferior results and harm patients, thereby discrediting the concept of rehabilitation.

To ensure the quality of treatment it is recommended that rehabilitation be carried out in a veterinary practice or clinic. Physiotherapists should have proper education and experience and work in cooperation with and under direct supervision of a veterinarian. This is also a requirement from animal insurance companies in Sweden.

In Sweden, active rehabilitation started at Stromsholm Referral Animal Hospital around 1990. The first patients were dogs that had undergone surgery for vertebral disc disease or spinal trauma. These patients used to recover slowly, but when rehabilitation immediately after surgery was introduced (including massage, passive range of motion training and swimming several times a day) the speed of neurological recovery and overall prognosis improved dramatically. This success also stimulated further development of rehabilitation techniques for patients after orthopaedic surgery and trauma.

The purpose of rehabilitation in orthopaedic patients is 1) to prevent stiffness and fibrosis in the musculature and soft tissues surrounding the joints caused by inactivity; 2) to regain full range of motion and function; 3) to regain muscle mass and strength, and 4) to relieve pain.

In neurological patients, early return of neurological function and prevention of muscle atrophy are the main goals.

REHABILITATION TECHNIQUES AVAILABLE FOR CATS AND DOGS

Several different techniques can be used in rehabilitation of animals, but it is important that the rehabilitation plan is tailored to the needs of each individual patient.

Massage

Massage is a relaxing soft tissue treatment, improving the circulation in the muscles. Properly applied massage reduces pain by relaxing muscle contractures and releasing endorphins. Simple massage techniques can be taught to the owner. This strengthens the owner's interest and commitment when feeling that they can give the animal comfort and contribute to the rehabilitation of their pet.

Stretching

Stretching is used to relieve muscular contractures and to facilitate recovery from muscle strain after training. It can improve the range of motion of the joints and alleviate pain caused by persistent contraction. The musculature should always be warmed up before treatment. Simple stretching exercises can also be taught to owners.

Mobilization of joints

Mobilization of joints is carried out by stretching of the soft tissues around a stiff joint to improve the range of motion. Joint mobilization is a special technique and must be performed correctly to avoid pain and injury to the joint surfaces. Therefore, it must be carried out without increasing the load on the joint surfaces. The improvement in the range of motion can be maintained by active and passive training, such as sit-and-stand and passive range of motion exercises

Water therapy

Water therapy is very widely used in rehabilitation.

Swimming provides effective muscular and joint-motion training with minimal loading of the joints

Figure 1. Swimming provides effective muscular and joint-motion training with minimal loading of the joints

a

b

Figures 2 A & B. Most dogs accept swimming readily and like it
With swimming many patients are relieved of mental blocks realising that the legs can be used again. It can be made even more attractive by introducing games such as chasing and returning a ball.

Figures 3. Under-water treadmill provides an effective and controlled level of training
By regulating the level of the water and the speed of the treadmill one can adapt the load on the legs and the resistance to moving in the water.

(FIGURE 1). Therefore, swimming can be started early after orthopaedic surgery or neurosurgery. An advantage with swimming is that many patients are relieved of mental blocks realising that the leg(s) can be used again after injury. Swimming also effectively improves the physical condition of the patient. Most dogs, and also some cats, accept swimming readily and like it (FIGURES 2 A & B).

Under-water treadmill provides an effective and controlled level of training (FIGURE 3). By regulating the level of the water and the speed of the treadmill one can adapt the load on the legs and the resistance to moving in the water. After injury, patients often develop bad habits and abnormal patterns of movement. Using the underwater treadmill can normalise the gait, because the resistance caused by the water forces the dog to use its legs properly to maintain balance, and is very effective to improving muscle mass and strength. The under-water treadmill is popular with most patients.

Weight cuffs

Weight cuffs on the lower extremities are often used to correct the gait and to break abnormal movement patterns that persist after injuries have healed.

Active training exercises

Different types of active training exercises can be executed by the owners and are often used as part of the rehabilitation programme. Careful instructions to the owner are necessary.

Active training exercises include:

- hill training (walking uphill or downhill) often used to improve the dog's gait
- walking between obstacles to improve balance, and
- Cavaletti training which also improves balance and is used to restore normal gait in patients that tend to drag their feet.

Transcutaneous electric nerve stimulation (TENS)

TENS is often used to relieve pain and to stimulate muscles that are non-functional as a consequence of neurological injury or immobilisation. By using TENS some of the expected muscle atrophy can be avoided.

Application of temperature therapy

Cooling or warming up tissues from the outside, is often used as a complementary treatment.

Cooling helps to reduce inflammatory responses, swelling and pain. It is used in the acute phase after injury or surgery, and after training when there is a tendency for joint to swell.

Warming may be used from two-to-three days after injury onwards to promote blood flow and healing.

Acupuncture

Acupuncture is used mainly as a treatment for pain.

EVALUATION AND FOLLOW-UP

An extremely important part of every rehabilitation programme is to continuously evaluate and record results. Rehabilitation should always lead to improvement. In order to make sure that there is continuous progress several parameters should be measured, recorded and compared with previous records. These include: maximal flexion and extension of joints, muscle circumference and joint width.

Maximal flexion and extension of joints should always be measured (FIGURES 4 A & B). However, to obtain consistent measurements that can be used to evaluate progression, a minimum of experience is required. Ideally **muscle circumference** is measured using a special measuring tape with a spring-load and should be performed at specified levels of the extremities to give repeatable results (FIGURE 5). **Joint width** is used to evaluate the degree of inflammatory response in a joint. It is measured using a precision electronic measuring device (FIGURE 6).

The animal's weight curve should be followed closely during rehabilitation. The patient may gain or loose weight during the rehabilitation period, and these changes must be monitored and the diet changed accordingly. After extensive trauma and major surgery, the diet should be high in protein to support the healing process and avoid muscle wasting. In addition, the diet must be high in fat to provide sufficient energy to minimise the use of protein to produce energy maximise its availability for recovery and healing. This becomes even more important when the level of training is increased. If the patient is obese a weight loss programme should be started before elective surgery, if time permits. During the rehabilitation period it is difficult to actively reduce body weight, because diets with reduced energy contents may counteract the healing process.

Before and after each session of rehabilitation, the injured tissues are carefully palpated for signs of swelling, increased temperature or pain. Additional information is gained from the use of an infrared thermometer to measure the temperature of injured tissues, and their response to activity and training (FIGURE 7). The pulse frequency is measured with special instruments during training, also in water. We recommend that such equipment be used routinely in rehab clinics to help evaluate the response to training in each patient, and to make sure that the patient is ready to increase the level of activity and exercise.

In case of elective surgery, training is ideally started before the surgical procedure. Water training is especially valuable. Muscle mass, joint motion and pattern of movement may already show some improvement before surgery because such training can take place without loading the joints. An additional benefit is that after surgery the animal will already be used to training.

a

b

Figures 4 A & B. Measuring the level of flexion (A) or extension (B) of a joint using a goniometer is a simple but accurate method to evaluate progression, provided the user has a minimum of experience

Figure 5. Muscle circumference must be measured at a specific level of the leg to give repeatable results

Figure 6. Measuring the joint width using a precision electronic measuring device
It is important to be able to evaluate the degree of inflammatory response over the course of a rehabilitation programme. The best method to obtain objective repeatable data of the degree of swelling of a joint is to measure the joint width using a precision electronic measuring device.

Figure 7. Infrared thermometer measuring the temperature of a joint
The temperature is another measure of the degree of inflammation present in tissues. The infrared thermometer helps to evaluate the response to treatment.

Even if a patient is treated in clinic up to three times a week, most of the rehabilitation period will be spent at home together with the owner. No patient should leave the practice after treatment for an injury or orthopaedic or neurology surgery without a thorough discussion between owner and rehabilitation clinic. The first rehab visit is the most important, because the owner must be made aware of the importance of rehabilitation and strict compliance with all instructions. Most owners are under stress and are less receptive to explanations at that time. Therefore both verbal and detailed written instructions with illustrations of high quality are of great importance.

CONCLUSION

Most owners want to have the best possible treatment for their animals, but some may not be willing to provide optimal rehabilitation, for economic or geographic reasons, or just because they are not committed to achieve the best possible results. Every effort should be made to inform owners of the positive effects of rehabilitation, and the risk for chronic problems if rehabilitation is neglected. Veterinary surgeons and rehabilitation staff must work together to achieve the goal of an optimal treatment.

To avoid having to 'reinvent the wheel' for each patient, a basic plan should be made for rehabilitation after each specific type of injury or surgical procedure. But the plan must always be tailored and adapted to the need of each individual patient. Continuous follow-up of the response and function is an important part of rehabilitation. Even though a plan is made up for the rehab period, at each follow-up visit the patient must be reassessed, the plan re-evaluated and adapted if necessary. A challenge for the rehab staff is to decide whether an unexpected event is a variation of the normal response to the injury or rehabilitation procedure, or indicates a complication, that requires the animal to be referred back to the orthopaedic surgeon. Close contact between the rehab staff and the veterinary surgeons is mandatory.

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The Influence of Diet on Joint Disease – Where Are We Now?

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SUMMARY

Osteoarthritis (OA) is a multi-factorial disease which requires multi-modal management. Nutrition is an integral part of this multi-disciplinary approach to disease management.

Evidence-Based Veterinary Medicine (EBVM) using a grading scale (I – IV) is a more objective tool to determine the optimal treatment strategy for OA, and can be useful when establishing evidence for dietary intervention.

There is good Grade 2 and Grade 3 clinical evidence that feeding diets designed for large breed dogs during growth and maintaining a healthy body weight throughout life will minimize the manifestation of hip dysplasia and osteochondrosis later in life.

Grade 1, 3 and 4 clinical trials also demonstrate that returning dogs to their ideal body weight improves clinical signs of OA. A Grade 4 *in vitro* study, using a canine cartilage model has shown that only EPA is able to abrogate the degrading effect of aggrecanase in canine chondrocytes.

Grade 1, 2 and 3 evidence supports the use of Prescription Diet™ Canine j/d™ for control of pain in dogs diagnosed with OA.

INTRODUCTION

Osteoarthritis (OA) is a pathological condition of diarthrodial synovial articulations, characterized by deterioration of articular cartilage, osteophyte formation, bone remodelling, soft tissue changes and various grades of inflammation. Both dogs and cats are affected. The disease in the dog has been well characterized with regards to aetiologies, diagnostics, treatment and prognosis. In the cat, on the other hand, the disease is less well understood, but is receiving much more attention as awareness and clinical diagnoses increase.

The prevalence of musculoskeletal disorders in dogs seen in canine referral practices has been reported to be 24 per cent, 70 per cent of which involve the appendicular skeleton. Forty-seven per cent of the canine patients diagnosed with an appendicular musculoskeletal disorder were suffering from a joint condition, and 26 per cent had OA as a diagnosis, corresponding to 12 per cent of all dogs with a musculoskeletal disorder. In an identically designed study in cats, with data obtained during the same time period and from the same practices, 70 per cent of all musculoskeletal disorders were localized in the appendicular skeleton. Of the feline patients with an appendicular musculoskeletal disorder, 25 per cent were diagnosed with a joint condition and 13 per cent (three per cent of all cats with a musculoskeletal disorder) had OA as a diagnosis. OA, therefore, does not seem to be as prevalent in cats as in dogs, at least it is not diagnosed as often.

EVIDENCE-BASED MANAGEMENT OF OSTEOARTHRITIS

The rules of Evidence-Based Veterinary Medicine (EBVM) may be used to determine the most optimal treatment strategy for OA. Evidence-based veterinary medicine can be defined as the integration of the best current research evidence with clinical expertise and client / patient values. When applying EBVM to individual interventions, one of the most challenging aspects is evaluating the strength of the evidence. A grading scale may be useful when establishing rules of evidence for recommending therapeutic interventions (FIGURE 1). However, it is important to remember, that the application of evidence-based veterinary medicine does not always lead to a definitive answer, but does provide a framework for making decisions and understanding the risk-benefit relationship of various therapeutic and preventative plans.

Grade I

Well-designed, properly randomized and controlled clinical trial that utilizes patients with naturally occurring disease.

- Prospective studies

Grade II

Well-designed and controlled laboratory studies in the target species with naturally occurring disease.

Grade III

Evidence obtained from one of the following

- Well-designed nonrandomized clinical trial
- Cohort- or case-controlled epidemiologic studies
- Studies using an acceptable disease model
- Case series
- Dramatic results from uncontrolled studies

Grade IV

Evidence obtained from one of the following

- Bench-top *in vivo* laboratory studies
- Opinions based on clinical experience
- Descriptive studies
- Studies conducted in another species
- Pathophysiologic justification
- Reports of expert committees

Figure 1. Study grades* for Evidence-Based Medicine
This grading scale may be useful when establishing rules of evidence for recommending therapeutic interventions.
** Quality of evidence guidelines are adapted from the U.S. Preventative Services Task Force.*

The goals of managing OA include: 1) controlling clinical signs, 2) managing progression of the disease, and 3) prevention or risk factor management. There is a variety of non-surgical options for the management of OA, including activity modification, weight control, medications, supplements, and nutritional management. Combining two or more of these management options tailored to the need of each patient will enhance the quality of life, which is the ultimate goal of therapy. Deciding which options to choose for an individual patient can be challenging. Applying the concepts of evidence-based veterinary medicine to this decision can improve outcomes.

PREVENTION OF FUTURE OSTEOARTHRITIS IN GROWING ANIMALS

In dogs, particularly in large and giant breed dogs, hip dysplasia (HD) and the osteochondrosis (OCD) complex are the major causes of OA during adulthood. In dogs less than one year of age, the prevalence of musculoskeletal problems is about 22 per cent. Approximately 20 per cent of these have a possible nutrition related aetiology, including HD and the OCD complex.

In cats, the diagnosis of HD and OCD is made less frequently, the prevalence of HD and the different types of OCD being five and three per cent respectively of all diagnosed joint diseases. When compared to the dog, environmental influences during development that have long-term effect on the development and prevalence of OA at later age seem less significant in the cat.

The role of nutrition in developmental skeletal disorders of dogs is multi-factorial. Several well-designed and controlled laboratory studies (Grade 2 and 3) have demonstrated that excessive intake of calcium and energy, together with rapid growth, appear to predispose to OCD and HD in large and giant dogs. Consequently, proper nutrition for growing large and giant breed dogs requires specific nutrients to be provided in correct amounts and balances for optimal bone and joint development. Optimal bone and joint development (FIGURE 2) will not only reduce the incidence of HD and OCD early in life, it also may reduce prevalence and severity of OA later in life.

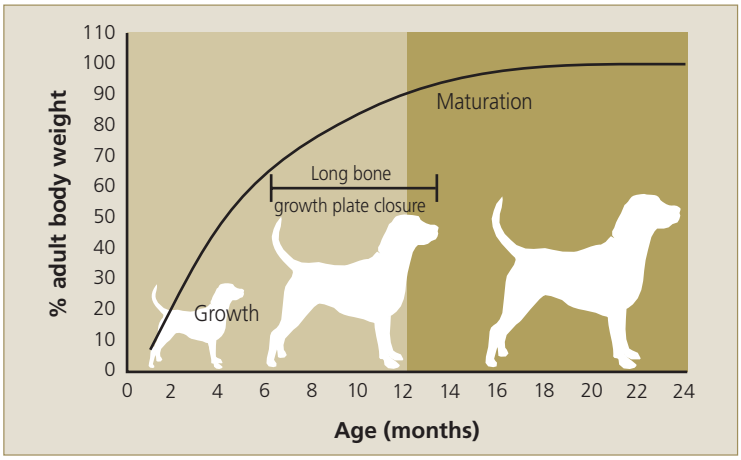

Figure 2. Growth phase vs. long bone physeal closure in dogs
Note that weight gain still occurs under the maturation phase, although growth plate closure is complete. This is attributable to bone remodelling and acquisition of adult body mass (reprinted with permission from Small Animal Clinical Nutrition, 4th Edition Hand, Tatcher, Remillard, Roudebusch edits. 2000)

MANAGEMENT OF OSTEOARTHRITIS

It is generally accepted that obesity is a risk factor for OA. However, the role of obesity in the aetiology of OA is not clear. A conservative estimate of the prevalence of overweight and obesity (BCS >4/5 to 5/5) (FIGURE 3) in dogs and cats is 25 per cent.

Weight reduction alone may result in substantial clinical improvement and should be a fundamental part of the management of OA. In two non-blinded, prospective (Grade 3) clinical trials, dogs with HD and rear limb lameness that were as little as 11 - 29 per cent over ideal body weight had improved clinical scores or force plate measurements once they reached their optimum weight. Weight reduction can help to decrease abnormal forces placed on joints and can help alleviate clinical signs. The improvement in clinical signs has been noted in dogs with only mild to moderate obesity (ten to 20 per cent over ideal weight). This emphasizes that even mildly overweight dogs that have OA should obtain optimal body condition. Weight reduction is best

	Score	Location	Feature	
	1 - Very Thin	Ribs: Bony Prominences: Abdomen:	Visible (on shorthaired cats) & easily palpable with no fat cover Easily palpable with no fat cover Severe abdominal tuck, exaggerated hourglass shape when viewed from above.	
	2 - Underweight	Ribs: Bony Prominences: Abdomen	Easily palpable with minimal fat cover Easily palpable with minimal fat cover Obvious waist, minimal abdominal fat palpable. Abdominal tuck is present, and a marked hourglass shape when viewed from above.	
	3 - Ideal	Ribs: Bony Prominences: Abdomen	Palpable with slight fat cover Palpable with slight fat cover Well proportioned waist, minimal abdominal fat palpable	
	4 - Overweight	Ribs: Bony Prominences: Abdomen	Difficult to palpate, moderate fat cover Difficult to palpate, moderate fat cover Little or no waist, abdominal rounding, moderate abdominal fat pad	
	5 - Obese	Ribs: Bony Prominences: General:	Very difficult to palpate, thick fat cover Distended with extensive fat deposit, Fat deposits over lumbar area, face and limbs, and no waist	

Figure 3. Body Conditioning Score (BCS) system

achieved by initiating an individualized weight management program which includes the use of foods specifically designed for weight loss and monitoring with a body condition scoring system (FIGURE 3). Severely restricting the volume of a maintenance food to reduce calories may alter the intake and balance of other essential nutrients.

Although caloric restriction is important, successful weight loss generally requires participation in an appropriate exercise program. Frequent, mild, weight-bearing exercise over an extended period has been shown to help patients reduce body weight, increase joint mobility, reduce joint pain, and strengthen supporting muscles. The results of a recent non-blinded prospective randomized clinical trial (Grade 1) suggested that caloric restriction in combination with more intense physical therapy may result in more rapid weight loss and improved mobility.

Although weight reduction may abolish clinical sings of degenerative joint disease (DJD), it does not directly deal with the progressive cartilage changes that have been initiated. Without further intervention, the arthritic changes will progress and further joint damage and lameness may ensue.

ENHANCING JOINT HEALTH AND MOBILITY

Food designed for companion animals with OA needs to supply age-adapted nutrition and specific nutrients that help reduce inflammation and pain, enhance cartilage repair, slow the degradation process, compliment the prescribed medications, and provide tangible improvement in clinical signs of OA. Several dietary modifications for OA treatment have been made, including the addition of glucosamine / chondroitin sulphate and anti-oxidants. In general, the glucosamine and chondroitin sulphate concentrations in pet foods are below the recommended therapeutic dosage, and supplements will be needed for treatment of osteoarthritis patients.

A more recent dietary modification is the addition of specific fatty acids (FAs). This modification has had the most significant impact. Recent discoveries in FA nutrition have provided clear evidence that canine OA can be very responsive to dietary additions of specific FAs.

Arachidonic acid (AA; 20:4n-6) and eicosapentaenoic acid (EPA; 20:5n-3) act as precursors for the synthesis of eicosanoids, a significant group of immunoregulatory molecules that function as local hormones and mediators of inflammation (FIGURE 4). The amounts and types of eicosanoids synthesized are determined by the availability of omega-3 (n-3) and omega-6 (n-6) polyunsaturated fatty acids (PUFAs) precursor and by the activities of the enzyme system to synthesize them. In most conditions the principal precursor for these compounds is AA, whereas EPA competes with AA for the same enzyme systems. The eicosanoids produced from AA appear to be more pro-inflammatory than those formed from EPA (FIGURE 4) and when produced in excess amounts may result in pathological conditions. Since n-3 PUFA replace AA in the substrate pool, ingestion of oils containing n-3 PUFAs results in decreased membrane AA levels and an accompanying decrease in the capacity to synthesize eicosanoids from AA.

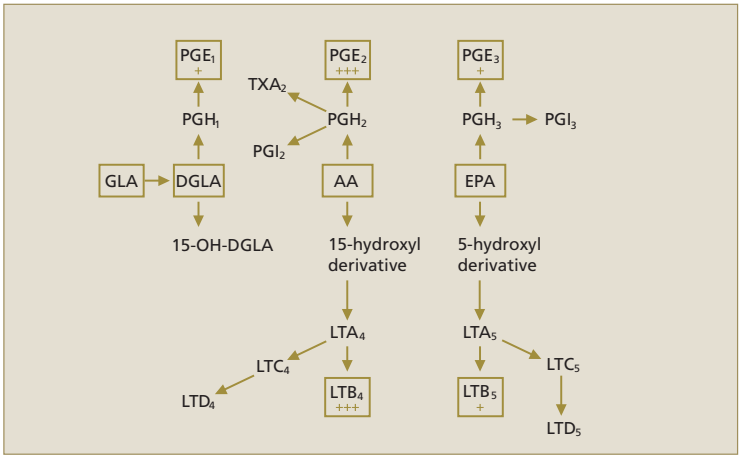

Figure 4. Potential effects of n-3 and n-6 PUFAs on inflammation
+++ strongly pro-inflammatory; + weakly pro-inflammatory

In vitro studies

Mechanisms of cartilage metabolism in canine OA and the potential role of n-3 FAs to ameliorate the early events in the disease process recently were investigated using *in vitro* models (Grade 4). In the canine cartilage metabolism model, aggrecan loss stimulated by oncostatin M (OSM) was associated with increased cleavage by aggrecanases and not matrix metalloproteinases. In this *in vitro* model EPA was the only n-3 FA able to significantly decrease the OSM-stimulated loss of aggrecan. It was concluded that, in addition to replacing AA in membranes, EPA also may alter chondrocyte gene expression and inhibit cartilage degradation.

Clinical studies

Recently, four (Grade 1) clinical studies (randomized, double-blind, controlled studies) have been completed. In these studies, dogs with osteoarthritis were fed either a control food or a food high in n-3 PUFAs (Prescription Diet™ Canine j/d™) designed to manage canine OA. Three of these were prospective studies conducted in veterinary hospitals across the USA, one six-month and two three-month studies. A fourth study was conducted as a three-month prospective study at two University Teaching Hospitals in the USA (Florida State University and Kansas State University).

Inclusion criteria

In all studies, dogs were included after being diagnosed with OA in one or more joints on the clinically affected limb based on compatible history, clinical signs and radiographic evidence. To be eligible for inclusion, dogs also had to be at least one year of age, weigh 12.5kg or more, and be free of systemic disease as determined by history, physical examination, complete blood count, serum biochemistry analysis and urinalysis.

Exclusion criteria

Exclusion criteria included acute traumatic injuries, complicating disease conditions, pre-existing conditions for which corrective surgery was anticipated during the feeding period and recent intra-articular injection or arthrocentesis.

Evaluation

The arthritic condition was assessed at the beginning of the study and at set time intervals after onset of the study, both by owners' observations of clinical signs and veterinary clinical evaluations. Veterinary clinical evaluations consisted of an orthopaedic examination with a specific emphasis on lameness and pain, limitation in weight-bearing ability, range of motion of the affected joint(s) and willingness to bear weight on the most affected limb when the contra-lateral leg was elevated.

In the three studies conducted in veterinary hospitals, veterinarians reported a significant improvement in the range of motion and ability to bear weight in the dogs when fed the EPA supplemented food as compared to their arthritic condition at baseline. In addition, a decrease in pain (upon palpation of the affected joint) and lameness was reported. Pet owners observed improvements in several symptoms associated with OA such as rising from rest, running, walking and playing.

In the fourth clinical study, conducted at two University Teaching Hospitals, variables were assessed at the beginning of the study and after 45 and 90 days. At the same intervals, gait analyses using force plate measurements were also conducted. During each test period, five valid force plate trials were obtained for the most severely affected and ipsi-lateral limb of each dog. Orthogonal ground reaction forces of peak vertical force, vertical impulse, braking and propulsion peak force, and braking and propulsive force were recorded. All forces were normalized with respect to body weight and data from valid trials for each limb were averaged to obtain a mean value at each time period. On orthopaedic examination, a significantly greater percentage of dogs consuming the test food improved compared to those consuming the control food. In addition, at the end of the 90-day trial, more dogs fed the food high in n-3 PUFAs had a reduction in pain when the affected joint was palpated. Vertical peak force was the key parameter measured to determine weight bearing of the affected limbs. There was no significant change in mean peak force over the duration of the 90-day feeding trial for the control group. The mean vertical peak force increased significantly for the test group over the

	Day 0	Day 90	Mean change	% Mean change
Control	72.8	72.6	-0.174	-0.58
Test	9.5	73.2	+3.71	+5.35**

Table 1. Canine force plate gait analysis vertical force* – summary
** % kg BW; ** P=0.04 (Cross et al. Unpublished)*

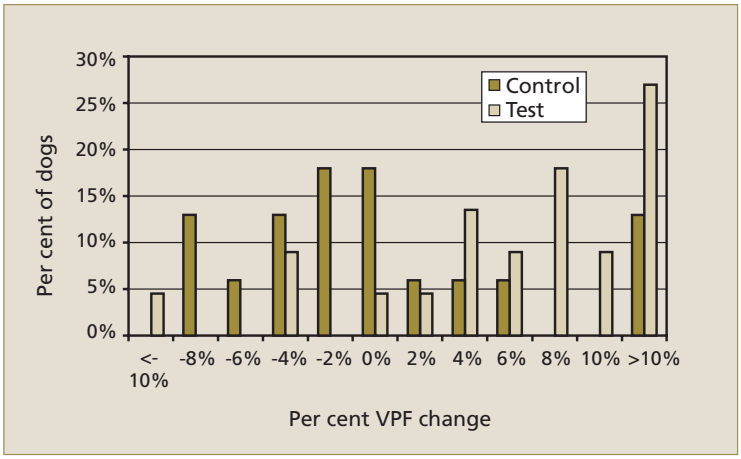

Figure 5. Effects of foods on vertical peak force (VPF) frequency of distribution

same time interval (TABLE 1). The percent mean change in vertical peak force was also significantly different between groups (P=0.04), indicating that the test group increased weight bearing on the affected limb over the course of the study. Additionally, only 31 per cent of dogs in the control group had improved weight bearing after the 90-day feeding trial, whereas 82 per cent of dogs in the test group increased weight bearing (FIGURE 5).

These clinical studies indicate that nutritional management using a therapeutic food with high levels of omega-3 fatty acids, and in particular EPA, helped improve the clinical signs of OA in dogs as measured by orthopaedic examination, gait analysis and pet owners.

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Influence of Diet – What Does the Future Hold?

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ABSTRACT

The completion of the human genome and the mapping of the canine genome in 2004 have led to dramatic changes in the way we think about health and disease. Further, interest in genomic science has spurred technological advances that allow for capturing of biological data at an unprecedented scale. These huge data sets and technological capabilities provide for the ability to develop innovative approaches that are driving business opportunities in agricultural biotechnology, food quality and safety, new food products, biomarker development and personalized nutrition.

Nutrients are considered to be among the most important environmental factors that influence gene expression.[1,2] A better understanding of how these factors govern gene expression will allow nutritionists to individualise dietary recommendations to improve general health and may eventually lead to new methods of managing both inherited and acquired diseases using a nutritional programme.

With around 450 canine genetic diseases identified, which vary according to breed, nutrigenomics has great potential to improve the health of our pets.[3] The role of n-3 fatty acids in ameliorating early events in the disease process of osteoarthritis has already been shown using an in vitro canine cartilage model.[4]

The role of genomic sciences and the growing field of nutrigenomics, as they relate to animal health and pet food industries, will be discussed.

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