

## STRESS STATUS (MILD, MODERATE AND SEVERE) VIZ -A-VIZ LEADING RISK FACTORS AMONG CLIENT-OWNED DOMESTICATED CATS (*Felissilvestris*) AFFECTED WITH THE 'PANDORA' SYNDROME: A RETROSPECTIVE STUDY

A. Naureen<sup>1</sup>, M. S. Khan<sup>1</sup>, M. A. Khan<sup>1</sup>, A. Maqbool<sup>2</sup>, J. A. Khan<sup>1</sup> and M. Avais<sup>1\*</sup>

<sup>1</sup>Department of Clinical Medicine and Surgery, <sup>2</sup>Department of Parasitology, University of Veterinary and Animal Sciences, Lahore 54000, Pakistan

\*Corresponding author email: mavais@uvas.edu.pk

### ABSTRACT

The present study was conducted to analyze association b/w depression status (mild, moderate and severe) and different risk factors (n=14) leading to the 'Pandora' syndrome among cats. To this end, risk factors were divided into 2 groups on the basis of demography (n=5) and general history (n=9). No particular breed predilection was found, however, majority (n=300) of cats attended were Siamese. Male to female ratio was found to be 2.5:1. Depression status was found to be highly associated (P-value = 0.000) with winter season, and all but one (stranguria; P-value = 0.774) clinical signs. Remaining risk factors were not in close association with that of depression. This study debunked previous notions like strong association of commercial diets and canned foods with this syndrome, in Pakistan majority fed with home-cooked food. Moreover, cases in Siamese breed were larger than Persian breed. The proportional morbidity rate (PMR) observed was estimated to be 8.7%. The PMR values show more about interests of clinicians rather than the incidence of disease in that population.

**Keywords:** Depression status, risk factors, 'Pandora' syndrome, client-owned domesticated cats

### INTRODUCTION

The 'Pandora' syndrome (Buffington 2011a) has been known as an important leading veterinary problem till antiquity (Kirk 1925), previously designated with different names viz., Feline Interstitial Cystitis (FIC), Feline Urologic Syndrome (FUS), Feline Lower Urinary Tract (FLUT) etc. (Buffington *et al.* 1997 a, b). It has been classified into obstructive and non-obstructive (Walker 2009). Specific clinical signs seen in approx. 1.5% of the cases (Lund *et al.* 1999) attended. Previously, incidence and proportional morbidity rate (PMR) has been reported many times from developed states (Osborne *et al.* 2000), however not reported from developing country like Pakistan till yet. Many risk factors viz., age, breed, sex, neutering, diets, feeding frequency, excessive weight, decreased water consumption, season, indoor life style, etc. have been identified (Willeberg 1981), however, depression is one of the important factors concurrently triggering other factors (Osborne *et al.* 1984) in the form of predictable biochemical and clinical abnormalities viz., hypercalcemia, hyperphosphatemia, metabolic acidosis etc. Public system in Pakistan is rigid compared to those of developed countries especially *w. r. t.* human-animal bond and majority of domesticated cats taking diet based on table-scraps or home cooked food. This is the first ever report from Pakistan regarding the issue of risk factors and PMR values due to poor cognizance of practicing veterinarians.

### MATERIALS AND METHODS

Present study was undertaken to evaluate association between depression status (viz., mild, moderate and severe) and important risk factors (n=14) directing to the 'Pandora' syndrome along with the proportional morbidity rate (PMR) among 502 client-owned domesticated felines presenting within a period of two years (2008-2010) in different clinics (Veterinary Medical Teaching Hospitals as well as private clinics) at 3 cities (Lahore, Faisalabad and Islamabad) of Pakistan.

**Study animals and settings:** Inclusion criterion was based on important signs linked to this syndrome among felines irrespective of sex, age, breed, etc., as per Buffington (1994). Complete history along with depression status was recorded on a modified predesigned proforma by taking complete structured interview of owner as per Osborne *et al.* (1984).

**Categorization of depression status:** Depression status studied was categorized on the basis of depression severity status as: mild (anxiety and anorexia), moderate (aggression towards owner as well as other cats), and severe (moribund), in order to make measurement in improved form (authors' own categorization for analysis) based on depression severity status.

**Risk factors and control measures:** A total of 14 important risk factors viz., gender, breed, age, weight, season, cohort, litter box usage, litter box type, type of food, drinking water, vaccination status, neutering status,

housing type, and recurrence rate, were included in present study and compared with depression status among feline patients. All above mentioned risk factors (n=14) were further distributed into 2 groups as: Demographic distribution (n=5; gender, breed, age, weight, season) shown in Table (1), and General medical history (n=9; cohort, litter box usage, litter box type, type of food, drinking water, vaccination status, neutering status, housing type, recurrence rate) shown in Table (2).

**Diagnosis:** Primary diagnostics made on basis of complete history, gross clinical signs, complete physical examination and urinalysis profiling, and ancillary diagnostics were compiled based on sero-biochemical profiling, radiography, hyperkalemia and ultrasonography. Diagnostic tests were performed and included in data depending on its availability.

**Proportional morbidity rate (PMR):** It is proportional number of cases of any disease calculated out of total number of cases attended (particular animal species) in practice or private clinic as per Willeberg (1984).

**Statistical analysis:** All data were analyzed through SPSS version 16. Chi-square test and Fisher Exact test, applied to see the association in qualitative attribute. P-value less than 0.05 were taken as significant. The Proportional morbidity rate (PMR) is calculated by applying formula as the ratio of cases divided by total number of cases attended in practice, private clinic, or clinic (Willeberg 1984).

## RESULTS

Total of 502 client-owned domesticated felines (n=502) spontaneously affected with the 'Pandora'

syndrome (PS) were included in study (data collected from 2008 to 2010; from different cities viz., Lahore, Faisalabad and Islamabad of Pakistan). Final data analysis was compiled and presented at the Department of Clinical Medicine and Surgery, University of Veterinary and Animal Sciences, Lahore, Pakistan. Out of total feline patients studied (n = 502), 30, 357, and 97 had mild, moderate and severe depression, respectively. According to first table shown, as such no significant association (P-value = 0.715; P-value = 0.224) was found regarding average weight and age of feline patients. However, body weight found to be significantly associated factor (P-value=0.000) in Persian breed as compared to other breeds. No particular breed predilection was found, however majority (n=300) of cats attended were Siamese. Male to female ratio was found to be 2.5:1 in this study and depression status was statistically same (P-value = 0.469) in all breeds, however it was highly significant (P-value = 0.000) in winters followed by summer, autumn, and spring. According to table (2), out of total (n = 502) cats attended majority (n = 427) were exclusively indoor and depression status was found insignificant (P-value = 0.760) related to that of housing-type, recurrence rate (P-value = 0.847), neutering status (P-value = 0.450), drinking water (P-value = 0.574), type of food (P-value = 0.623), vaccination status (P-value = 0.921), cohorts (P-value = 0.269), and the type of litter box (P-value = 0.246). Contrarily, it showed strong association with the litter box usage (P-value = 0.000). On the whole depression was found strongly associated (P-value = 0.000) with all forms of clinical observations except that of stranguria (P-value = 0.774; not mentioned in data).

**Table 1. Depression status (mild, moderate and severe) viz'-a-viz' demographic distribution of risk factors related to spontaneous Pandora syndrome among client-owned domesticated cats**

Demographic distribution of risk factors (n = 5)	Depression (n = 502)			Total (n = 502)	p-value
	Mild (n=30)	Moderate (n=375)	Severe (n=97)		
<b>1. Gender</b>	Male	22	272	76	0.294
	Female	28	111	20	
	Long hair domestic	3	35	5	
	Non-Descript	6	55	14	
<b>2. Breed</b>	Persian	6	48	18	0.496
	Small hair domestic	0	8	4	
	Siamese	15	229	56	
	Autumn	0	39	11	
<b>3. Season</b>	Spring	1	37	6	0.000
	Summer	9	90	45	
	Winter	20	209	35	
<b>4. Weight</b>	Overall	30	375	97	0.715
<b>5. Age</b>	Overall	28	391	83	0.224

**Table 2. Depression status (mild, moderate and severe) viz'-a-viz' risk factors on the basis of general medical history related to spontaneous Pandora syndrome among client-owned domesticated cats**

Distribution of risk factors (n = 9) on the basis of general medical history		Depression (n = 502)			Total (n = 502)	p-value
		Mild (n=30)	Moderate (n=375)	Severe (n=97)		
<b>1. Housing type</b>	Exclusively Indoor	26	320	81	427	0.760
	Exclusively Outdoor	0	4	0	4	
	In-door + Out-door	4	51	16	71	
<b>2. Recurrence rate</b>	No	18	238	59	315	0.847
	Yes	12	137	38	187	
<b>3. Cohort</b>	No	19	273	64	356	0.269
	Yes	11	102	33	146	
<b>4. Litter box usage</b>	No	17	172	47	236	0.496
	Yes	13	203	50	266	
<b>5. Litter box type</b>	Commercial	5	60	16	30	0.447
	Home made	9	145	170	375	
	No	16	30	46	97	
<b>6. Type of food</b>	Commercial diet	2	11	5	18	0.623
	Extensively Home cooked	22	299	78	399	
	Home cooked + Commercial diet	6	65	14	85	
<b>7. Drinking water</b>	Fixed	8	71	20	99	0.574
	Restricted	22	304	77	403	
<b>8. Vaccination status</b>	No	23	275	71	369	0.921
	Yes	7	100	26	133	
<b>9. Neutering status</b>	Castrated	7	128	32	167	0.450
	Nil	19	213	60	292	
	Spayed	4	34	5	43	

## DISCUSSION

Previously, at different times and ages many scientists reported presence of disease worldwide (Engle 1977; Chew *et al.* 1986; Buffington 1997 a, b). An increase in incidence reported to be attributed to high frequency of indoor keeping of cats (Patronek *et al.* 1996) as compared to outdoor cats (Willeberg 1984). The present study shows a total of 8.7% PMR among feline patients attended, actually indicates the interests of clinicians rather than actual incidence of disease regarding population under study because denominator is highly selected and undetermined fraction of the population (Willeberg 1984). This value (PMR) is mostly misinterpreted with that of incidence of disease in the population at risk. Contrarily, true incidence is not too easy to estimate however, retrospective study is reported with preceding 12 months period (Willeberg 1984). The core segment of our study was based on association between depression status and important risk factors leading the 'Pandora' syndrome (from year 2008-2010). All (n=502) feline patients attended in the present study

showed depression (30 mild, 357 moderate and 97 with severe depression) may be attributed to solitary nature of this species and prefer to live either alone or in pair instead of any social group (Gittleman 1989). To this end, cats are more prone to the sensitivity regarding their surroundings as compared to other domestic animals. The element of depression may increase in cats with the increase of threat either related to any conflict (Moesta and Crowell-Davis 2011) or fetal developmental stress response system (Westropp *et al.* 2006; Buffington 2009) as also previously studied (Cadet *et al.* 1986; Braastad *et al.* 1998) in different species regarding maternal stressors. In cats this syndrome is found similar to that in humans (Buffington 2004). Affected cats (36.4%) also reported with high aggression towards owner and other cats (Bamberger and Houpt 2006). One of the tentative diagnostic criteria may include investigation of factors activating central Stress Response System (SRS) (Westropp *et al.* 2006; Stella *et al.* 2011). The activation of SRS may lead to the rushing of environmental factors affecting the sensory neurons (Birder *et al.* 2011) in the form of loop by central as well as peripheral neural activity (Fields 2004). Moreover, this activation (SRS)

may result in different forms of sickness behaviors (SB) (Carlstead *et al.* 1993; Carlstead and Shepherdson 2000). Depression status is attributed to external (environmental) as well as internal (visceral) stressors (Unusual external environmental events triggering hypothalamic SRS) (McEwen 2008; McEwen and Gianaros 2010) leading to changes in moods (Miller *et al.* 2009) and SB viz., vomiting, diarrhea, anorexia, decreased water intake, decreased social interactions, etc (Dantzer *et al.* 2008) and are directly proportional to increase in urination outside the litter box (Stella *et al.* 2011) rather than disease status.

According to data analyzed in first half (Table 1), average weight/age were insignificant factors which contradict the data on mice and cats as per previous studies (Godbout *et al.* 2008; Walker 2009) however, data was inline regarding age as per Stella *et al.* (2011). In the present study, weight *w.r.t.* species was significantly higher (P-value=0.000) in Persian breed as per Defauw *et al.* (2011) as compared to previous study (Willeberge and Priester 1976) that showed trend of breed predilection. Particular breed predilection is supposed to be linked to genetic and epigenetic factors (Buffington 2011b) and found more among Persian breed (Walker 2009). Male to female ratio was 2.5:1 in this study, much higher in male than female possibly due to trend of keeping male cats as pet to avoid litter problem in Pakistan. However, previously, no particular sex predilection was found (Walker 2009). A case control study showed that a high increase in incidence rate increased during winter may be attributed to less activity and excessive body weight (including indoor litter pans) as per Jones *et al.* (1997) which is similar to our results.

According to second half of data (Table 2), majority (n=427) of cats reported were exclusively indoor as per Buffington (2011b). To cope with depression linked to indoor confinement, a new concept was introduced as the implementation of 'Triple Es' (Effective environmental enrichment) as per Herron and Buffington (2010), and thus helps in providing behaviorally enriched environment free of any kind of stressors. To this end, one must organize environment into 5 basic 'systems' viz., physical resource (proper space alone or among cohorts), nutritional (free access to food and water), elimination (located in quiet area), behavioral (provided with the pillows or cat-safe plants for expression of natural investigatory behaviors like scratching and chewing) and social (close friendly relationship should be developed among cohorts as well as with humans in contact with the feline pet), to identify stressors for enhancement of improved health and behavior of feline pets under domestic housing (Barry and Crowell-Davis 1999; Buffington 2002; Van De Weerd *et al.* 2003; Overall *et al.* 2005; Herron and Buffington 2012). Hiding places within homes may help in improvement of feline health (Kry and Cassey

2007). Recurrence rate was found strongly associated with stress triggered either by genetics or by environment (Buffington 2009) irrespective of present study result and it can be overcome by indoor enrichment. Likewise, no association was found between food-type and depression in the present study. Under enriched environment, contents of food play no significant role regarding this syndrome (Westropp *et al.* 2006; Stella 2011). In contrast, Walker (2009) found this syndrome in increased form among cats mainly fed on dry diets. No significant relation between cohorts and neutering status *w.r.t.* depression was found similar with previous study as per Fennell (1974). Some workers relate cohorts directly towards this syndrome due to high increase in conflicts for life resources that can be handled by neutering all cats (Buffington 2011b) kept under one roof. In this study, depression was directly associated with the litter box usage that will help in reducing this disease if placed in noise-free area (Buffington 2011b) along with its specific type (open/covered; Herron 2010) and number (one for each cat; Walker 2009). According to literature cited, diet and drinking water are main factors leading to this syndrome (Jackson and Tovey 1977; Willeberg 1981; Defauw *et al.* 2011). Here in Pakistan most of the cats were on home-cooked diet (table scrap) than commercial food contrary to the trend seen in developed states (Walker 2009) due to presence of more improved human-animal bond. On the whole depression was found strongly associated (P-value=0.000) with all forms of clinical observations as previously studied (Osborne *et al.* 1984; Kirk *et al.* 1995), however, depression was found to be insignificantly related to stranguria (P-value = 0.774).

In conclusion, depression is the main factor leading to PS among domesticated cats in Pakistan not reported thus far specifically. This study negates previous notions 'strong association of commercial diets and canned foods' with PS, in Pakistan majority affected felines fed with home-cooked (table scrap) food. Moreover, cases in Siamese breed are larger than Persian breed. It has been strongly associated with indoor housing management. Additional work is still needed to further validate results and explore untouched areas of epidemiology. According to Buffington (2011b) repeat check-ins at 3-6 week intervals are needed, however, in developing country like Pakistan most of the owners let their animals to come to see vet in case of severe disease issue. Moreover, owners should be made aware of concept of 'Triple Es' for better environmental enrichment to improve the health status of domesticated cats (Anonymous, 2010) and thus owners' education is imperative for a positive response.

## REFERENCES

Anonymous (2010). The Ohio State University College of Veterinary Medicine website. The indoor pet

- initiative. Available at: [indoorpet.osu.edu/](http://indoorpet.osu.edu/). Accessed Oct 1, 2010.
- Bamberger, M., and K. A. Houpt (2006). Signalment factors, comorbidity and trends in behavior diagnosis in cats: 736 cases (1991-2001). *J. Am. Vet. Med. Assoc.* 229: 1602-1606.
- Barry, K. L., and S. L. Crowell-Davis (1999). Gender differences in the social behavior of the neutered indoor-only domestic cat. *Appl. Anim. Behav. Sci.* 64: 193-211.
- Birder, L. A., A. T. Hanna-Mitchell, E.A. Mayer and C.A.T. Buffington (2011). Cystitis, epithelial dysfunction and co-morbid disorders. *NeuroUrol Urodyn.* 30: 668-672.
- Braastad, B. O., L. V. Osadchuk, G. Lund and M. Bakken (1998). Effects of prenatal handling stress on adrenal weight and function and behavior in novel situations in blue fox cubs (*Alopex lagopus*). *Appl. Anim. Behav. Sci.* 57: 157-169.
- Buffington, C. A. T., D. J. Chew and B. E. Woodworth (1997b). Animal model of human disease—feline interstitial cystitis. *Comp. Path. Bull.* 29:3–6.
- Buffington, C. A. T., D. J. Chew, M. S. Kendall, P. V. Scrivani, S. B. Thompson, J. L. Blaisdell and B. E. Woodworth (1997a). Clinical evaluation of cats with non-obstructive urinary tract diseases. *J. Am. Vet. Med. Assoc.* 210:46-50.
- Buffington, C.A.T. (1994). Lower urinary tract disease in cat: New problems, new paradigms. *J. Nutr.* 124: 2634S-2651S.
- Buffington, C.A.T. (2002). External and internal influences on disease risk in cats. *J. Am. Vet. Med. Assoc.* 220: 994-1002.
- Buffington, C.A.T. (2004). Comorbidity of interstitial cystitis with other unexplained clinical conditions. *J. Urol.* 172: 1242-1248.
- Buffington, C.A.T. (2009). Developmental influences on medically unexplained symptoms. *Psychother. Psychosom.* 78: 139-144.
- Buffington, C.A.T. (2011a). Idiopathic cystitis in domestic cats – beyond the lower urinary tract. *J. Vet. Intern. Med.* 25: 784-796.
- Buffington, C.A.T. (2011b). Pandora syndrome: Rethinking your approach to idiopathic cystitis in cats. *Vet. Med.* 106: 515-522.
- Cadet, R., P. Pradier, M. Dalle, and P. Delost (1986). Effects of prenatal maternal stress on the pituitary adrenocortical reactivity in guinea-pig pups. *J. Dev. Physiol.* 8: 467-475.
- Carlstead, K and D.S. Shepherdson (2000). Alleviating stress in zoos with environmental enrichment. In: Moberg, G.P. and J.A. Mench, (Eds.), *The Biology of Animal Stress: Basic principles and implications of animal welfare*. CCABI Publishing, New York. pp: 337-354.
- Carlstead, K., J.L. Brown, and W. Strawn (1993). Behavioral and physiological correlations of stress in laboratory cats. *Appl. Anim. Behav. Sci.* 38: 143-158.
- Chew, D. J., S. P. Di Bartola and W. R. Fenner (1986). Pharmacologic management of urination. In: *Kirk's Current Veterinary Therapy IX. Small Animal Practice*. Kirk, R. W. (editor). 9th Ed. WB Saunders Co. Philadelphia USA. Pp: 1207.
- Dantzer, R., J.C.O. Conner, G.G. Freund, R.W. Johnson and K.W. Kelley (2008). From inflammation to sickness and depression: when the immune system subjugates the brain. *Nat. Rev. Neurosci.* 9: 46-56.
- Defauw, P.A., I. Van de Maele, L. Duchateau, I.E. Polis, J.H. Saunders and S. Daminet (2011). Risk factors and clinical presentation of cats with feline idiopathic cystitis. *J. Feline Med. Surg.* 13: 967-975.
- Engle, G. C. (1977). A clinical report of 250 cases of feline urological syndrome. *Feline Pract.* 7:24.
- Fennell, C. (1974). Some demographic characteristics of the domestic cat population in Great Britain with particular reference to feeding habits and the incidence of the feline urologic syndrome. *J. Small Ann. Pract.* 16: 775-783.
- Field, H. (2004). State-dependent opioid control of pain. *Nat. Rev. Neurosci.* 5: 565-575.
- Gittleman, J.L. (1989). Carnivore group living: comparative trends. In: *Carnivore behavior, ecology and evolution*. Cornell University Press, Ithaca, NY. pp: 183-207.
- Godbout, J.P., M. Moreau, J. Lestage, J. Chen, N.L. Sparkman, J. O'Connor, N. Castanon, K.W. Kelley, R. Dantzer and R.W. Johnson (2008). Aging exacerbates depressive-like behavior in mice in response to activation of the peripheral innate immune system. *Neuropsychopharmacol.* 33: 2341-2351.
- Herron, M.E. (2010). Advances in understanding and treatment of feline inappropriate elimination. *Trop. Companion Anim. Med.* 25: 195-202.
- Herron, M.E. and C.A.T. Buffington (2010). Environmental enrichment for indoor cats. *Compendium: Cont. Edu. Vet.* E1-E5.
- Herron, M. E. and C. A. T. Buffington (2012). Environmental enrichment for indoor cats: Implementing enrichment. *Compendium: Cont. Edu. Vet.*, E1-E5.
- Jackson, O. F. and J. D. Tovey (1977). Water balance studies in domestic cats. *Feline Pract.* 7: 30-33.
- Jones, B. R., R. L. Sanson and R. S. Morris (1997). Elucidating the risk factors of feline lower urinary tract disease. *N. Z. Vet. J.* 45: 100-108.

- Kirk, C.A., G.V. Ling, C.E. Franti and J.M. Scarlett (1995). Evaluation of factors associated with development of calcium oxalate urolithiasis in cats. *J. Am. Vet. Med. Assoc.* 11:1429-1434.
- Kirk, H. (1925). Retention of urine and urine deposits. In: *The diseases of the cat and its general management*. London. pp: 261-267.
- Kry, K. and R. Casey (2007). The effect of hiding enrichment on stress levels and behavior of domestic cats in a shelter setting and the implications for adoption potential. *Anim. Welf.* 16: 375-384.
- Lund, E. M., P. J. Armstrong, C. A. Kirk, L. M. Kolar and J. S. Klausner (1999). Health status and population characteristics of dogs and cats examined at private veterinary practices in the United States. *J. Am. Vet. Med. Assoc.* 214: 1336-1341.
- McEwen, B.S. (2008). Central effects of stress hormones in health and disease: understanding the protective and damaging effects of stress and stress mediators. *Eur. J. Pharmacol.* 583: 174-185.
- McEwen, B. S. and P. J. Gianaros (2010). Central role of the brain in stress and adaptation: Links to socioeconomic status, health and disease. In: Adler, N.E. and J. Stewart (Eds.), *Biology of disadvantage: socioeconomic status and health*. Blackwell Publishing Oxford, UK. pp: 190-222.
- Miller, A.H., V. Maletic and C.L. Raison (2009). Inflammation and its discontents: the role of cytokines in the pathophysiology of major depression. *Biol. Psych.* 65: 732-741.
- Moesta, A., and S. Crowell-Davis (2011). Intercat aggression - general considerations, prevention and treatment. *Tierärztliche Praxis Kleintiere*. 39: 97-104.
- Osborne, C. A., G. R. Johnston, D. J. Polzin, J. M. Kruger, F. W. Bell, E. M. Poffenbarger, D. A. Feeney, J. B. Stevens and M. F. McMenemy (1984). Feline urologic syndrome: a heterogeneous phenomenon. *J. Am. Anim. Hosp. Assoc.* 20: 17-32.
- Osborne, C. A., J. M. Kruger, J. P. Lulich, J. D. Polzin, and C. Lekcharoensuk (2000). Feline lower urinary tract diseases. In: Ettinger, S.J., and E.C. Feldman (Eds.), *Text Book of Veterinary Internal Medicine – Disease of Dogs and Cats*. (5th Ed.), WB Saunders Co., Philadelphia, USA. pp: 1710-1747.
- Overall, K.L., I. Roden, B. V. Beaver, H. Carney, S. Crowell-Davis, N. Hird, S. Kudrak, and E. Wexler-Mitchel (2005). Feline behavior guidelines from the American Association of Feline Practitioners. *J. Am. Vet. Med. Assoc.* 227: 70-84.
- Patronek, G. J., L.T. Glickman and A. M. Beck (1996). Risk factors for relinquishment of cats to an animal shelter. *J. Am. Vet. Med. Assoc.* 209:582-588.
- Stella, J. L., L. K. Lord and C. A. T. Buffington (2011). Sickness behaviors in response to unusual external events in healthy cats and cats with feline interstitial cystitis. *J. Am. Vet. Med. Assoc.* 238: 67-73.
- Van de Weerd, H. A., C. M. Docking, J. E. L. Day, P. J. Avery and S. A. Edwards (2003). A systematic approach towards developing environmental enrichment for pigs. *App. Anim. Beh. Sci.* 84: 101-118.
- Walker, D. (2009). Feline lower urinary tract disease: a clinical refresher. *Irish Vet. J.* 62: 272-280.
- Westropp, J. L., P. H. Kass and C. A. T. Buffington (2006). Evaluation of the effects of stress in cats with idiopathic cystitis. *Am. J. Vet. Res.* 67: 731-736.
- Willeberg, P. (1981). Epidemiology of naturally occurring feline urologic syndrome. *Vet. Clin. North Am. Small Anim. Pract.* 4: 455-469.
- Willeberg, P. (1984). Epidemiology of naturally-occurring feline urologic syndrome. *Vet. Clin. N. Am. Small Anim. Pract.* 14: 455-469.
- Willeberg, P. and W. A. Priester (1976). Feline Urological Syndrome: Associations with some time, space, and individual patient factors. *Am. J. Vet. Res.* 37: 975-978.