Reference Point

External and internal influences on disease risk in cats

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Owners surrender millions of cats to animal shelters each year for euthanasia.[1] Inappropriate elimination, most commonly associated with urologic signs, was the most common reason given for abandoning the cat. Oral disease recently was reported to be the most common health problem of cats, with a prevalence ranging from 23 to 67% of cats examined.[2] Obesity is also a common problem of cats; the prevalence ranges from 1.8 to 40% and appears to be increasing. Hyperthyroidism, first reported in 1979, also appears to be diagnosed with increasing frequency. The causes of these problems have not yet been clearly elucidated and may be influenced by both internal and external factors. Internal factors include the cat's genetic and experiential background as well as its temperament. External factors include such variables as the complexity of the environment, resource quality and availability, and presence of sources of threat and conflict. Of course, these factors are not mutually exclusive and vary over a continuum that includes elements of each.[3]

The external environment has long been recognized to influence the risk of infectious diseases in animals. Indoor housing has become increasingly common veterinary advice to owners of pet cats to avoid exposure to infectious diseases, as well as injury from vehicles or other animals. Although studies of comparative mortality between indoor housed cats and those permitted access to the outdoors are not available in the North American veterinary literature, indoor housed cats are thought by many to be at reduced risk. Recently, the AVMA stated that it "strongly encourages owners of domestic cats in urban and suburban areas to keep them indoors."[4]

As early as 1925, Kirk[5] suggested that "too close confinement to the house" (an external factor) and Persian breed (an internal factor) may increase the risk of signs of lower urinary tract disease. Results of subsequent epidemiologic studies have confirmed this suspicion.[6,7] Other studies suggest that indoor-housed cats and some breeds also may be at increased risk for odontoclastic resorptive lesions, obesity, and hyperthyroidism.

The question of the merits of indoor housing to promote the welfare of cats (and the different opinions on what constitutes animal welfare in general) is a subject of controversy among experts.[8,9] The purposes of this report are to briefly review some of the epidemiologic data concerning the role of environment on disease risk, to describe some physiologic factors that may mediate the effects on susceptible cats, and to suggest some interventions that may reduce the disease-related risk of the environment on indoor cats.

Epidemiologic Factors

External—Available epidemiologic studies of **feline urologic syndrome (FUS)** suggest an overall incidence rate of somewhat less than 1% and a prevalence rate from 1 to 6%; a recent study[10] reported a prevalence rate of approximately 1.5%. Many environmental risk factors for FUS have been investigated, using case-controlled studies.[6,11,12] Case-controlled studies often report results as **odds ratios (OR)**. The OR is calculated by dividing the odds of exposure of cats in the diseased group to a factor by the odds of exposure of cats in the control group to the same factor. An OR of 1 indicates no association between the factor and the disease. The higher the OR, the greater the association between the presence of the factor and the presence of the disease; the lower the OR, the greater the association between the presence of the factor and the absence of the disease. It is important to state that such studies can identify associations, but they are powerless to determine causality. Odds ratios often are reported as a mean and its 95% **confidence interval (CI)**. The larger the CI, the lower the precision of the estimate; if the CI includes 1, no inference of difference in risk can be inferred.[13]

Excessive body weight and decreased activity were associated with increased risk for FUS in some studies, and cats that only had access to indoor litter pans had an increased risk of FUS, compared with cats that were allowed to eliminate outdoors. Living with other cats also may increase the risk,[7,14] suggesting that social interactions or a horizontally transmitted infectious agent may play a role in the development of FUS. The lack of difference between cases and controls in viral disease rates[7,15] and the increase in risk associated with increasing amounts of time spent indoors (**Table 1**) seems to argue against an infectious agent as a common cause in multiple-cat households. A case-controlled study of cats with FUS in New Zealand during

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Supported by NIH grant-NIDDK DK 47538.

Table 1—Risk (odds ratio [OR]) of indoor housing for development of feline urologic syndrome (FUS), calcium oxalate urolithiasis, odontoclastic resorptive lesions (ORL), obesity, and hyperthyroidism. An attempt was made to extract the most pertinent results from the cited studies, but readers are encouraged to consult the original study for further details

				OR	95% CI[a]
Study	**Cases**	**Controls**	**Measured variable**	**Indoor housing**	
FUS					
Jones et al[7]	193	378	Uses litter tray (sleeps inside)	11.25	1.89–66.69
			Sleeps inside (uses litter tray)	16.03	2.28–113
Reif et al[11]					
	2	11	51–99% outdoors	0.16	0.04–0.77
	8	27	50% outdoors	0.24	0.10–0.55
	37	28	1–49% outdoors	1.51	0.83–2.73
	54	35	0% outdoors	2.17	1.23–3.82
Walker et al[14]					
	32	115	12–24 hours outdoors	0.37	0.22–0.51
	181	312	3–12 hours outdoors	0.66	0.52–0.85
	82	98	0.5–2 hours outdoors	1.19	0.86–1.65
	33	10	< 0.5 hour outdoors	4.85	2.36–9.96
	51	27	None	2.82	1.74–4.58
	51	37	Variable	2.02	1.30–3.15
	7	5	Don't know	1.95	0.61–6.19
Willeberg[6]					
Winter	0	7	12–24 hours outdoors	NR	NR
	22	52	0.5–12 hours outdoors	0.56	0.30–1.06
	45	53	< 0.5 hour outdoors	2.28	1.21–4.28
Summer	5	18	12–24 hours outdoors	0.42	0.15–1.19
	24	56	0.5–12 hours outdoors	0.56	0.30–1.04
	38	38	< 0.5 hour outdoors	2.55	1.37–4.75
Calcium oxalate urolithiasis[24]	84	258	Indoors only vs all other outdoors	3.25	NR ($P < 0.005$)
ORL[17]					
	7	12	≥ 7 hours outdoors	1.00	NA
	10	5	1–6 hours outdoors	4.3	1.1–15.9
	16	10	Not out	4.5	1.3–15.2
Obesity[b]					
Scarlett et al[18]	2,023*		Apartment (yes/no)	1.6	1.2–2.1
			Very active	1.00	NA
			Active	1.9	1.2–3.0
			Inactive	5.2	3.1–8.6
			Very inactive	15.8	4.6–54.1
Robertson[19]	644*		Predominantly inside	1.4	1.0–2.2
Allan et al[20]	202*		Being inactive	3.95	1.56–9.97
Hyperthyroidism					
Scarlett et al[21]					
	7	29	≥ 75% of time outdoors	0.43	0.18–1.06
	34	71	Occasionally outdoor	1.00	0.52–1.92
	15	17	Strictly indoor	2.15	1.00–4.71
			Strictly indoors/mostly outdoors[c]	4.0	1.3–12.1
			Predominantly indoors/mostly outdoors[c]	11.2	2.6–48.0
Kass et al[22]					
	16	20	75–100% outdoors	0.38	0.39–1.71
	33	30	50–74% outdoors	1.13	0.63–2.01
	47	46	25–49% outdoors	0.94	0.57–1.54
	71	65	1–24% outdoors	0.97	0.64–1.48
	207	187	0% outdoors	1.00	NA
Martin et al[23]					
	6	6	Mostly outdoors	3.3	0.9–12.5
	40	59	Sometimes outdoors	1.8	0.8–3.8
	18	17	Rarely outdoors	1.9	0.7–5.1
	14	36	Indoors only	1.00	NA

*Cases and controls were combined.
NR = Not reported. NA = Not applicable.
[a]For studies reporting number of cases and controls but not 95% confidence interval (CI), the CI were calculated from the data.[119] [b]Not case-control studies. [c]Logistic regression model in which all cats were used.

1991 to 1993 was recently reported. In addition to the aforementioned factors, an increased incidence also appeared to occur after moving a cat to a new house within the previous 3 months and during winter months; further analysis revealed a highly substantial association with rainy days during the previous month rather than with season. Access to outdoor prey was found to be protective against FUS.

Dental disease is reported to be the most common disease of pet cats. The 2 most common problems are periodontal disease and **odontoclastic resorptive lesions (ORL)**. In 1992, Van Wessum et al[16] reported that ORL were present in 62% of cats examined in Holland and 67% of cats examined in the United States. Two case-controlled studies[2,17] were performed to evaluate potential risk factors for ORL in feline

teeth. In the first study,[2] cats with ORL were more likely to be older, female, taking medications, and drinking city versus well water. They were less likely to play with toys, have owners who cleaned their teeth, or be fed diets with higher magnesium, calcium, phosphorus, and potassium contents. Without food intake information, the significance of the differing mineral content of the diets is unclear, although it may suggest that diets designed to influence recurrence of FUS were fed. Indoor housing was not identified as a significant risk factor in this study. In a subsequent study,[17] an OR of 4.5 was associated with a history of dental disease (gingivitis, calculus, or periodontal disease), and OR of 4.4 and 4.5 were found for city residence and indoor housing, respectively. Consumption of commercial treats appeared to be protective (OR = 0.3).

Obesity is also a common problem in cats. In a study[18] of the body condition score of more than 2,000 cats evaluated at veterinary hospitals in the northeastern United States, veterinarians reported that 25% of cats were overweight, and owners estimated that 29% of their pets were overweight. Factors associated with obesity included apartment dwelling, inactivity, sex (male), neutered, mixed breeding, and certain dietary factors. The OR for indoor housing ranged from 1.6 to 15.8, depending on the variable measured. The investigators suggested that the increased risk of obesity in apartment-dwelling cats may have been attributable to inactivity and boredom. A recent study[19] of obesity in cats living in metropolitan Perth, Western Australia, in which cats were categorized as underweight, correct-weight, or overweight by their owners, revealed an OR of 1.4 for indoor housing and 1.8 for living in houses with 1 or 2 other cats. The OR for neutered cats was 2.8. In a recently reported study[20] of obesity in an urban cat population in New Zealand, inactivity was identified as significant following univariate analysis but not in the combined logistic-regression analysis.

Prior to 1979, hyperthyroidism in cats was a rare condition. A study performed in 1988[21] identified an OR of 4 to 11.2 for indoor housing, 1 of the strongest risk factors evident in the study. In a subsequent study,[22] no increased risk for indoor housing was identified, whereas the OR for litter use was 3.10 (1.13 to 8.55). The authors commented that these findings complemented those of Scarlett et al.[21] A third study[23] did not identify a difference between cases and controls in housing status.

Internal—Just as environments can range from benign to challenging to threatening, animals also vary in their sensitivity to environmental stimuli. The identification of differences in breed susceptibilities suggests that internal as well as environmental factors can influence disease risk in cats. Internal factors include breed, temperament, and experiential variables. The most commonly assessed internal factors in the aforementioned epidemiologic studies investigating disease risk factors were purebred status and length of coat. In his 1984 review,[6] Willeberg concluded that Siamese cats had a low risk of FUS (OR, between 0.5 and 0.8), whereas Persians were at an increased risk (OR, between 1.4 and 4.3) for FUS. He also pointed out that studies that had not found a difference in risk between purebred and nonpurebred status may have grouped breeds of reduced risk with those of increased risk. More recently, Jones et al[7] reported there was an increased risk of FUS among long-haired, but not purebred, cats in his final stepwise conditional logistic regression model, on the basis of cases and matched controls. For cats with calcium oxalate urolithiasis, an increased risk among Persian and a decreased risk among Siamese cats has been reported.[24]

For dental disease and obesity, no clear breed predilection has been reported. For cats with ORL, neither study[2,17] included sufficient numbers of purebred cats to evaluate breed as a risk factor, although van Wessum et al[25] reported that Asian Shorthairs, Siamese, and Abyssinians were at increased risk. For obesity, both purebred[18] and crossbred[19] cats have been reported to be at increased risk. For hyperthyroidism, a reduced risk has been reported for Siamese[21,22] and Himalayans.[22]

As in other species, individual differences in temperament have been reported in cats.[26-28] Variations in response to the environment occur both among species and within individuals,[29,30] and the range of variation is large. Despite application of an identical stressor, Dumas et al[29] found as much as a 12-fold range in stress response among different strains of rats. Individual variation in experience also influences responses to the environment.[31-33] Some of this variation may be attributable to differences in early experience.[34] For example, it has been shown that short (3-hour) periods of maternal deprivation in rodent pups can result in permanent changes in the CNS, which can predispose the adult animals to visceral hyperalgesia.[35]

Some individual cats also may be unusually sensitive to features of indoor housing environments because of the differences between the behavioral heritage of cats and that of more social animals, including humans and many other domestic species. Cats appear to live as a relatively solitary species, often choosing population densities of < 50 cats/km^2.[36] Although free-ranging male and female cats occupy overlapping home ranges of approximately 100 m in diameter, they avoid meeting each other by keeping to a time schedule.[37]

Most of the epidemiologic studies of disease risk factors, conducted for more than a quarter century, have identified indoor housing as a consistent external risk factor for a variety of diseases in cats. Differences among the studies, particularly those that did not find increased risk, may have occurred for a variety of reasons. The first, of course, is that indoor housing really is not a risk factor. However, the fact that it has been identified in different diseases studied at different times and different places seems to argue against this interpretation. Variation in sample sizes and the questions asked undoubtedly also contributed to the differences. Additionally, the studies that did not identify increased risk for indoor housing were the most recently conducted. If the majority of cats in both case and control groups were housed indoors, it would be difficult to isolate this as a risk factor. Similar arguments may be made for breed as an internal risk factor,

Table 2—Risk (OR) of breed status for FUS, calcium oxalate urolithiasis, obesity, and hyperthyroidism. An attempt was made to extract the most pertinent results from the cited studies, but readers are encouraged to consult the original study for further details

Study	Cases	Controls	Breed	OR	95% CI
FUS					
Jones et al[7]	193	378	Domestic longhair	2.68	1.24–5.81
Walker et al[14]	437	604	Purebred	1.35	0.86–2.11
	32	115	Domestic longhair	1.01	0.76–.34
Calcium oxalate[24]	8	13	Persian	8.0	NR ($P < 0.025$)
	4	31	Siamese	0.57	NR[a]
Obesity					
Scarlett et al[18]	2,023*		Purebred (yes/no)	2.0	1.2–3.3
Robertson[19]	644		Crossbred	2.1	1.1–4.2
Hyperthyroidism					
Scarlett et al[21]	56	117	Non-Siamese	9.6	1.9–48.6
Kass et al[22]	5	13	Himalayan	0.29	0.09–0.89
	29	55	Siamese	0.44	0.26–0.74
	2	2	Burmese	0.79	0.11–5.88
	73	55	Domestic longhair	0.94	0.61–1.44
	8	7	Persian	0.94	0.33–2.69
	268	216	Domestic shorthair	1.00	NA
	4	3	Manx	1.18	0.26–5.35
Martin et al[23]	10	22	Siamese	0.4	0.2–1.1

[a]Not significant.
See Table 1 for key.

particularly small sample size (**Table 2**). Individual variation in experience also influences responses to the environment.[31-33] Thus, in any given environment, the response of any particular animal cannot be predicted. Moreover, both the animal and the environment are constantly changing.

Although the available epidemiologic studies permit one to formulate the hypothesis that indoor housing and breed status may increase disease risk, they cannot be used to test the hypothesis. They also do not permit identification of what features of indoor housing or breed status increase or decrease disease risk. For example, Jones et al[7] found no apparent interaction between breed and long hair, suggesting that long-haired cats may be at increased risk of FUS, because their owners may be reluctant to let them out during wet weather. Similarly, Scarlett et al[21] suggested that if some breeds were at increased risk for ORL, it may reflect owner reluctance to permitting valuable animals access to the outdoors (although it seems that all purebreds would be at increased risk if this were the case).

Physiologic Factors

The sensitivity of cats to their surroundings and their responses to threatening stimuli have been studied for decades[38,39]; indeed, Cannon's description of the fight or flight response resulted from studies of cats. Masserman[40] investigated cats' responses to environmental threats during the 1940s. He reported[41] that cats deprived of food for 24 hours that were exposed to an innocuous puff of air while they were eating (that elicited no response when administered at other times) became fearful and easily startled by minor stimuli. Later studies suggested that housing the cats in individual cages also may have increased susceptibility to the stressor.[42] Ethological studies in zoos,[43] research laboratories,[44,45] and boarding facilities[46] demonstrate that cats subjected to impoverished or unpredictable environments have decreased activity levels and increased hiding behaviors. For example, Carlstead et al[44] recently reported effects of caging and stress on the physiologic variables and behavior of healthy domestic cats. They found that unpredictable manipulations, such as unfamiliar caretakers or altered feeding schedules, resulted in increased urine cortisol concentrations, enhanced adrenal sensitivity to adrenocorticotropic hormone, and reduced pituitary sensitivity to luteinizing hormone-releasing hormone. Active exploratory and play behaviors were suppressed, and stressed cats spent more time hiding. The investigators concluded that the unpredictable environment had induced a stress response in the cats. Similar problems have been reported in carnivores housed in zoos.[47]

The indoor environment of some house cats also may be monotonous and predictable. This unchanging and nonstimulating predictability also is considered by some researchers to be stressful.[48] The success of adaptation of cats to indoor environments may thus depend on the quality of the environment and the adaptive capacity of the cat.[49]

The stress response involves immune, neurologic, and vascular alterations that underlie the behavioral response.[50,51] In response to epithelial injury or exposure to a noxious stimulus, such as an invading microorganism, a variety of local cells become activated and generate cytokine, lipid, and neuropeptide inflammatory mediators. Epithelial cells slough, taking organisms with them, and local vessels dilate and become more permeable. The vascular response permits blood flow to increase, and the increased permeability may lead to plasma extravasation and accumulation of inflammatory cells from the vascular space into the local tissues. Local sensory nerve fibers also are activated to initiate local responses and signal the CNS of tissue damage.

If the problem is severe, the **hypothalamic-pitu-**

itary-adrenal (HPA) axis and the pontine **locus coeruleus-norepinephrine (LC-NE)** systems may be activated by sensory neurons or by blood-borne inflammatory mediators. Activation of the HPA axis leads to release of cortisol from the adrenal cortex, which may act to increase endothelial permeability[52] or to modulate the local reaction to avoid tissue damage. Activation of the LC-NE system is associated in the periphery with release of epinephrine and NE from the adrenal medulla and NE from sympathetic postganglionic nerve terminals.

The environment also may result in an uncontrolled or inappropriate stress response by reducing the animal's perception of control of the environment[53] or by increasing its perception of threat. Animals have been selected by evolution for reproductive success. Essential criteria for reproductive success include the ability to find mates and to perceive and respond to environmental threats to sustain life long enough to ensure transmission of genetic material.[54] To find mates and reproduce, animals must act in the environment. Their actions result in acquisition of new information from the environment, collected by all the appropriate sensory apparatus of the animal (pheromonal, olfactory, gustatory, auditory, cutaneous, and visual). These signals are integrated by the CNS[55,56] and are perceived by the animal as not threatening or threatening in a constant reiterative cycle with a time constant of milliseconds.[57]

If the animal perceives no threat, the initial course of action may progress. If a threat is perceived, a stress response occurs, resulting in different actions.[58,59] Stress response mechanisms have been selected over millennia and are therefore complex and interactive, with multiple fail-safe backup systems. These may have developed initially as local defense responses to noxious environmental stimuli and have been built on and expanded as the vascular and nervous systems developed increasing complexity.[60]

The responses of the HPA axis recently were the subject of a comprehensive review.[58] In the classical view, secretion of glucocorticoids was thought to help mediate ongoing or pending stress responses[61]; this hypothesis was replaced by the view that they suppressed the stress response, preventing it from injuring the host. In contrast, Sapolsky et al[58] now suggest that glucocorticoids may permit, stimulate, or suppress an ongoing stress response or prepare for a subsequent stressor. Responses of the HPA axis may be activated peripherally by environmental factors or centrally by the perception of threat.

The LC-NE system contains the largest number of noradrenergic neurons in the body and is the most important source of NE in the CNS.[62] The LC plays important roles in orienting behaviors, vigilance, and autonomic activity.[63,64] The association between stress factors and FUS[7,65] suggests the possibility of dysfunction of neural circuits that coordinate elimination behaviors.[64] Barrington's nucleus, a candidate region for integration of forebrain activity with visceral function, is located in the dorsolateral pons.[64,66] Neurons from this nucleus also project to the LC. A substantial increase in tyrosine hydroxylase (the rate-limiting enzyme of catecholamine synthesis) immunoreactivity in the LC of cats with **feline interstitial cystitis (FIC)** has been reported.[67] In healthy cats, acute environmental (noise, restraint) stressors that increase LC activity also increase plasma NE concentrations.[68] Cats with FIC also have increased plasma NE,[69] as well as enhanced stimulus-induced local NE release from the urinary bladder[70] and down regulation of central **α-2 adrenoceptors (α-2 AR)**.[a] In normal feline spinal column, α-2 agonists inhibit transmission of noxious afferent signals to the brain.[71,72] The receptors appear to be located on the central processes of sensory neurons.[73-75] Although spinal α-2 AR activation can inhibit nociceptive input acutely, these receptors seem to become desensitized or down regulated after chronic stimulation.[74,76]

The catecholamines also have complex pro- and anti-inflammatory actions on the immune system, including mediating a shift from cellular to humoral immunity. Although beyond the scope of this review, recent evidence suggests that many important interactions occur between the immune and neuroendocrine systems.[77] Moreover, the responses observed in clinically normal animals may not be identical with those observed in animals with naturally occurring diseases. In cats with FIC, for example, the sympathetic nervous system appears to be chronically activated, whereas the HPA axis responds normally to **corticotropin releasing factor (CRF)** infusion. This could mean that the HPA axis is not involved in this disorder or that CRF receptors have been desensitized by a chronic increase in corticotropin hormone release. The complexities of the interactions between the LC-NE and CRF systems have only recently begun to be understood but may play a role in various disease processes.[56]

Several physical and mental stressors can activate the HPA and LC-NE systems and their subsequent physiologic responses. In rodents, restraint,[78] water avoidance,[79] alterations in environmental temperature[80-82] or lighting,[82,83] and even changing rooms in an animal housing facility[84] can induce the same stress responses as local stimuli at all epithelial surfaces investigated. Recently, evidence has accumulated that indicates that external stressors also can activate the vascular system component of the stress response.[84-86] These studies suggest that endothelial permeability is regulated by a complex interplay between mast cells and nerves. Evolutionarily, increasing endothelial permeability during the stress response may have been conserved, because it permitted circulating defense molecules to gain access to extravascular spaces or circulating neurotransmitters to activate sensory neurons to provide more rapid information updates to the CNS. These observations suggest that acute stress responses occur commonly and are extinguished in most animals without progression to pathologic consequences.

Stress response mechanisms may underlie the increased endothelial and epithelial permeability in response to physical and mental stressors that has been reported to occur in some diseases of the urinary bladder[87] and gingival tissues,[88,89] as well as the skin,[90] lung,[91] and gastrointestinal tract.[92,93] Additionally,

inflammation has been associated with toxic nodular goiter[94] (the common human thyroid disorder most closely resembling hyperthyroidism) and obesity,[95] both of which are exacerbated by stressors.[96-98] What factors result in pathologic changes localized to 1 organ system and why some animals appear to be more susceptible than others are crucial research questions.[99,100]

Provisional Recommendations

Bracke et al[3] recently presented a list of needs formulated to be used for **overall welfare assessment (OWA)** of sows. The list included availability of food, water, and rest areas and the opportunity for social contact, reproduction, kinesis (locomotion, play, and stretching[101]), exploration, body care (grooming, thermoregulation, comfort-seeking, evacuation, and territorialism), and reactivity (predictability and controllability, self protection, ability to avoid danger, and aggression). To the author's knowledge, such an OWA list has not yet been assembled for indoor pet cats, but some recommendations are available.[102-105] The consensus seems to be that cats appear to benefit from appropriate access to resources, control of interactions with owners, and a tolerable intensity of conflict.

The research[40] demonstrating that behavioral abnormalities can result from blowing an innocuous puff of air into a cat's face while it eats suggests that cats should be fed individually in a quiet location where they will not be startled by other animals, sudden movement, or activity of an air duct or appliance that may begin to operate unexpectedly. Cats may prefer dry or canned foods[106]; offering choices in separate, adjacent containers rather than replacing the usual food with a new food permits cats to express their preferences. If experimental studies support the associations between nutrients and ORL or ingredients and hyperthyroidism, specific diet recommendations may be necessary. Feeding behavior also includes predatory activities. These may be simulated by hiding small amounts of food around the house or by putting dry food in a container from which the cat has to extract individual pieces[45] or move to release the food pieces, if such interventions appear to appeal to the cat.[104] Cats also seem to have preferences for water. Consideration may be given to freshness, taste, movement (water fountains, dripping faucets, or an aquarium pump-bubbled air into a bowl), and shape of container (some cats seem to resent having their vibrissae touch the sides of the container when drinking). Food and water bowls should be cleaned regularly unless individual preference suggests otherwise.

Cats interact with both the physical structures and other animals, including humans, in their environment. The physical environment should include opportunities for climbing, scratching, hiding, and resting. Cats seem to prefer to monitor their surroundings from elevated vantage points; provision of climbing frames, hammocks, platforms, raised walkways, shelves, or window seats has been recommended.[104,105] Playing a radio to habituate cats to sudden changes in sound and human voices also has been recommended,[107] and videotapes to provide visual stimulation are available.[104]

Some cats may prefer to be petted and groomed, whereas others may prefer play interactions with owners.[108] The play interactions with cats may include lures, laser pointers, or teaching behaviors.[103,104] Cats also may enjoy playing with toys, particularly those that are small and mobile and that mimic prey characteristics.[109,110] For cats that prefer novelty, a variety of toys should be provided and rotated or replaced regularly.[110]

In multiple-cat houses, cats also interact with each other. Because cats housed in groups do not appear to develop distinct dominance hierarchies or conflict resolution strategies to the extent that some other species do, they may attempt to circumvent agonistic encounters by avoiding others or decreasing their activity.[111] Unrelated cats housed together in groups appear to spend less time interacting with conspecifics than related ones do.[112] These cats may prefer to have their own separate food and water sources, litter box, and resting areas to avoid competition for resources and to permit cats to avoid unwanted interactions.[111] Published guidelines for introducing new cats into a home are available and may be recommended to clients adding cats to their household.[103]

Placing litter boxes in quiet, convenient locations could help improve conditions for eliminative behavior. If different types of litter are provided, it may be preferable to offer them in separate boxes, because individual preferences for litter type have been documented.[113] For cats with a history of lower urinary tract problems, unscented clumping litter should be considered.[114] Litter boxes should be cleaned regularly; some cats seem quite sensitive to dirty litter boxes. Litter box size and whether or not it is open or covered also may be important to some cats.[115,116]

Because of the dearth of controlled trials, it currently is not possible to prioritize the importance of any of these suggestions or to predict which would be most appropriate in any particular situation. Appropriately designed epidemiologic studies[117] may be able to identify particularly important factors, after which intervention trials could be performed to determine their efficacy in circumstances where owners successfully implemented the suggested changes.

The prognosis for diseases affected by environmental factors may depend on the animal, the housing situation, and the client. Animal factors include genetic predisposition and prior individual experience, the duration of the problem, the frequency of occurrences, and for FUS, the number of areas and different types of surfaces soiled. Housing factors include the number of cats in the household, the number of affected cats, the advisability of allowing limited outdoor access, and the feasibility of rearranging the environment. Client factors include the owner's ability to identify modifiable causes, the strength of bond to affected cats, their willingness to pay for treatment, the amount of time available to devote to solving the problem, and the willingness to accept and use adjunctive medications as indicated.

Ethological and behavioral studies demonstrate that captivity may elicit a stress response in some cats. Behaviorists report that indoor cats are disproportionately more often represented among cats with behav-

ioral problems evaluated by pet behavior counselors, most of which are related to improper housing conditions.[118] Moreover, available epidemiologic evidence suggests that indoor housing is a risk factor for some common diseases of cats. Risk factors, however, must be kept in perspective. Indoor housing is likely to interact in complex ways with other factors. These factors may include unidentified microorganisms and predispositions in some cats. What these predispositions may be remains to be determined, but the breed predispositions found in epidemiologic studies of some problems suggest they may be partially genetically determined.

Outdoor living increases the risk of cats for fighting, accidental injury, and exposure to infectious diseases. Although cats appear to have evolved as solitary hunters, evidence suggests that they are capable of living indoors in quite high population densities under appropriate circumstances.[111] The challenge is to develop, validate, and promulgate recommendations to enrich the indoor environment so the advantages of removal from exposure to outdoor risks are sustained.

[a]Buffington CAT. Functional assessment of α-2 adrenoreceptor sensitivity in cats with interstitial cystitis (abstr). *Soc Neurosci* 1998;24:595.

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