Title

Pain and Sickness Behaviors

ISBN

9781119653219

Authors

Stella, JL

Buffington, CA Tony

Publication Date

2022-11-08

DOI

10.1002/9781119653271.ch7

7

Pain and Sickness Behaviors

J. L. Stella and C. A. Tony Buffington

In a nutshell:

What to know before diagnosing and treating pain and sickness behaviors in cats:

- Our understanding of acute and chronic pain in all mammals is rapidly evolving, along with the available treatments.
- Pain, sickness, anxiety, and fear can have similar presentations:
  - Resistance to being touched or moved
  - Increased heart and respiratory rates
  - Dilated pupils
  - Increased licking/grooming of specific body parts
  - Increased vocalization
  - Increased hiding behaviors
  - Toileting outside the litter box
  - Decreased food consumption
  - Decreased socialization with family members.
- Diagnosis of pain is based on history, thorough physical examination, and diagnosis of disease processes with possible pain components.
  - History:
    - Probe for a history of sudden or gradual behavioral or "personality" changes suggesting pain or illness. Each cat is unique, so "changes" are more relevant measures of pain than a list of current abilities or propensities.
    - Ask about previous injuries, and surgeries performed elsewhere, that might inform the current presentation.
  - Physical Exam (if pain or illness is suspected):
    - Observe body language and facial expressions.
    - In cats above middle age, perform a through orthopedic and neurologic examination, remembering that imaging abnormalities may not equal pain.
  - Diseases with known pain components include FIC, osteoarthritis, orofacial pain, inflammatory GI processes (including stomatitis), advanced dental disease, urolithiasis, and others.
- Treating pain can be both important and challenging in cats.
  - Make environmental changes to support painful or sick cat's comfort (see "Behavioral approaches to helping cats…" below).
  - Pharmaceutical pain control options are limited due to the cat's metabolic peculiarities.
  - Use body language and facial grimace scores to assess effectiveness of treatment.

Clinical Handbook of Feline Behavior Medicine, First Edition. Edited by Elizabeth Stelow.

Companion Website: www.wiley.com/go/stelow/behavior

Introduction

This chapter describes behavioral assessment and approaches to management of acute pain, chronic pain, and sickness behaviors. Chapters like this usually begin, appropriately, with definitions. In the case of pain however, a recent discussion of the definition suggested by the International Association for the Study of Pain (IASP)[1] ran to 6700 words,[a] nearly the length allotted to this chapter. For our purposes, the traditional IASP definition of acute pain, *"An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage,"*[b] will serve. We can define "described" as "inferred from the patient's history, behavior[2,3] and the context of the evaluation," since we care for pets "as if" they were in pain based upon our observations even though they cannot self-report their state. Of course, many humans (infants, the obtunded, etc.) also cannot self-report, and even for those who can, their reports can only be believed, not independently validated by any specific "biomarker," so the situation really isn't that different across species. Definitions for the different kinds of chronic pain are presented later.

Acute Pain

A number of recent publications, including a book,[4] have addressed acute pain recognition and management in cats since the early studies of Lascelles et al.[5] Clinicians are encouraged to look for the presence of pain (and fear and anxiety)[6]) as part of every physical examination.[7–9] Robertson[8] has proposed three questions to guide assessment of acute pain in cats after surgery or injury:

1) (To what extent) Is the cat demonstrating normal behaviors?
2) Are any of the cat's normal behaviors lost?
3) Has the cat developed any new behaviors?

These questions should be answerable by anyone who comes into contact with hospitalized cats so that no cats "slip through the cracks" and suffer pain without recognition and appropriate care. For those with less training and experience, alerting a clinician or technician that "something doesn't look right" may be enough until the person can receive training in pain assessment.

Assessing acute pain usually includes determining its location, duration of pertinent signs and behaviors, and intensity.[7] Acute pain behaviors in cats can be evaluated using a range of behavioral (Table 7.1) and physiological variables (Table 7.2).[7,10–12] Changes in physiological parameters are neither consistent nor specific to pain however.[8] They also can occur in the presence of fear and anxiety, which of course also imply implementing appropriate care to resolve these emotional states to normalize the cat's physiology to the extent possible.

Two validated acute pain assessment scales for cats (Table 7.3) are available: the UNESP-Botucatu Multidimensional Composite Pain Scale (UNESP-Botu-catuMCPS),[13–15] and the Glasgow Composite Measures Pain Scale – Feline (CMPS-Feline).[16] One can use these scales to record baseline data for comparison with post-intervention behavior whenever possible; published forms for this process are available.[17]

a Interested readers can find it here.

b Provided by IASP here.

Table 7.1 Behavioral parameters/body postures suggesting acute pain/threat.

Behaviors	Normal	Acute pain/threat
Posture	Relaxed	Immobile – hunched or tense
Attitude/demeanor	At front of cage inquisitive, engaged by surroundings	Withdrawn, indifferent
Facial expression	Relaxed	Narrow palpebral fissure, flattened ear position, bunched and flattened whiskers against the face
Self-care	Eating, drinking grooming, and eliminating normally	Not eating, drinking, grooming, or eliminating
Vocalization	Purring, none	Crying out, groaning, defensive aggression (hissing, growling, spitting, tail twitching, ear flicking, scratching, biting), purring, none
Activity	Stretches on rising, explores cage, purring, kneading, rubbing, etc.	Inactive or hesitant movements, attempts to avoid handlers
Interest in food/water	Yes	No
Eliminations	Yes	No
Attention to the wound	Ignores	Looks at and/or licks wound
Interaction with people	Interested, friendly approach to caregivers	Avoids
Response to touch, pressure, and palpation	Welcomes or at least does not avoid	Avoids, defensively aggressive

Table 7.2 Physiological parameters suggesting acute pain/threat that can be assessed include.

Increase in:	*Presence of*:
• Pupil diameter	• "Sweaty" paws
• Respiratory rate	• Excessive shedding
• Temperature	• Flushing
• Heart rate	• Anxious lip-licking
• Blood pressure	

Limitations to Acute Pain Assessment

Each of the validated tools has limitations. They can be time-consuming to complete, and both have been validated for (presumably) otherwise healthy cats after ovariohysterectomy, so their utility for other pain states is yet to be demonstrated. Behaviors observed in cats with acute pain also overlap with those of cats that perceive the presence of threats, such as presentation to shelters[18] or veterinary practices,[17] and so must be considered in the context of the patient's individual history and presenting complaints. Moreover, differences in age, demeanor,[19] any disease processes present, the nature and extent of necessary interventions (including drug therapy) can occur, so patients need to be evaluated and re-evaluated as individuals. Pain scales also serve as tools to inform, not replace, one's clinical judgment about the cat's state and treatment decisions.

Table 7.3 Assessment categories of validated pain scales.

UNESP-Botucatu Multidimensional Composite Pain Scale[13]	Glasgow Composite Measures Pain Scale – Feline[16]
Subscale 1: Pain expression	
Miscellaneous behaviors:	Observer's impression of the cat
A. Lying quietly, moving tail	
B. Contracts & extends pelvic limbs ± trunk muscles	
C. Eyes partially closed	
D. Licks or bites wound	
Reaction to palpation of surgical wound	Attention to wound
Reaction to palpation of abdomen/flank	Response to palpation of wound or painful area
Vocalization	Vocalization
Subscale 2: Psychomotor change	
Posture	Posture
Comfort	Facial expression: ear and whisker position (Figure 7.1)
Activity	Response to assessor when stroked
Attitude	
A. Satisfied	
B. Uninterested	
C. Indifferent	
D. Anxious	
E. Aggressive	
Subscale 3: Physiological variables	
Arterial blood pressure	
Appetite	

To address some of these limitations, Evangelista et al. recently reported development and validation of a Feline Grimace Scale (FGS) to detect naturally occurring acute pain in cats.[20] Thirty-five client-owned cats with acute pain conditions (excluding those with diseases or conditions that could affect facial expressions, or that had received drugs or analgesics within 24 hours of presentation, were excessively shy or feral, or required immediate treatment) and 20 healthy control cats from a teaching colony at the investigators' university were video-recorded undisturbed in their cages as part of a prospective, case-control study. Painful cats then received analgesic treatment and were videoed again after one hour. Four observers, blinded to the groups and time when the images were obtained, independently scored 110 images of the painful and control cats for five facial features: head position, ear position, orbital tightening, muzzle tension, and whisker changes. FGS scores were higher in painful than in control cats, which strongly correlated with another validated instrument.[21] Good overall inter- and intra-rater reliability and excellent internal consistency also were reported. The FGS also detected response to analgesic treatment (scores after analgesia lower than before). The authors concluded, despite the small sample size and validation

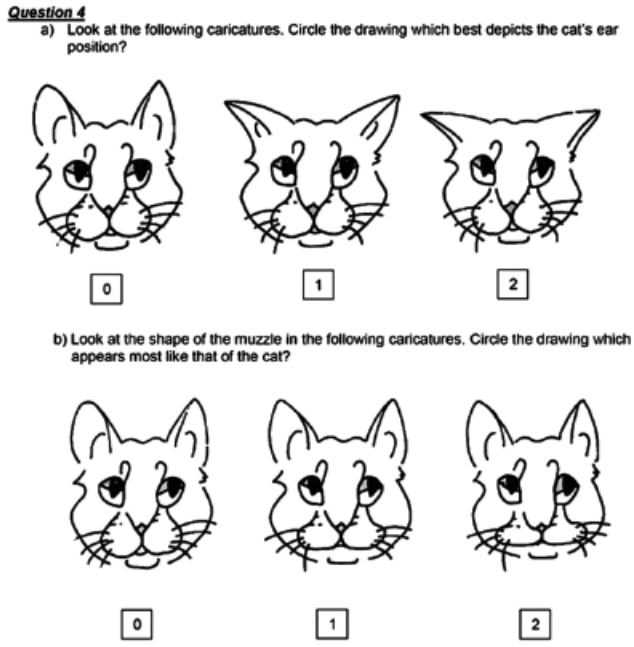

Figure 7.1 Facial expression; ear and whisker position. Glasgow Composite Measures Pain Scale – Feline.[16] John Wiley & Sons.

using experts with years of experience working with cats, that the FGS was a valid and reliable tool for acute pain assessment in cats. They acknowledged that it is unknown, and deserves further investigation, how reliability would be affected by novice raters, and have made a Feline Grimace Scale Training Manual available for this purpose.

Figure 7.2 Pain scales, including facial grimace, may be useful in identifying painful cats and assessing the extent of their pain. Andriy Blokhin / Adobe Stock

Shipley et al.[22] recently reported preliminary appraisal of the reliability and validity of a "Colorado State University Feline Acute Pain Scale," which uses psychological and behavioral signs of pain, facial expressions, and body posture and palpation responses to create a numerical pain score. The scale had moderate-to-good inter-rater reliability when used by expert veterinarians to assess pain intensity or the need to reassess analgesic plan after ovariohysterectomy in cats. Unfortunately, the validity fell short of current guidelines for correlation coefficients, necessitating further refinement and testing to improve its performance before further implementation.

McLennan et al.[23] recently provided discussion of some conceptual and methodological issues relating to pain assessment, including development and utilization of pain facial expression scales (Figure 7.2). They offered guidance for developing valid, reliable facial expression scales, as well as how to use them in clinical practice; their clinical recommendations are presented in Table 7.4.

Table 7.4 Best practices for using facial expression scales in clinical practice.[23] With permission of Elsevier.

- Train personnel with detailed protocols.
- Place protocols in key areas where pain assessment will be required.
- Consider continued training and inter- and intra-observer testing to ensure uniformity in scale implementation.
- Carry out multiple observations over time alongside other behavioral and physiological measures.
- Record scores and display near to patients to monitor progress and effectiveness of treatment.
- Use in combination with other validated indices.
- Do not use in patients with head injuries/trauma.

Behavioral Approaches to Helping Cats Showing Acute Pain or Sickness behaviors[24–26]

{Pharmacological approaches to helping cats in acute pain are available elsewhere.[4,27–29]*}*

Cats tend to form attachments to places rather than to other animals, so confinement in places where they don't feel safe can adversely affect their behavior, physiology, and recovery. Fortunately, effectively enriching these spaces can mitigate these effects.[18,24,30] Enriched conditions permit cats to cope with their surroundings and feel "safer" in their "space." Factors both inside and outside their cage can affect the welfare of cats housed in veterinary facilities.[25,30]

Inside the cage, cats need these resources to cope (Figure 7.3):

a) **A place to hide** – Cats hide to escape threats and to keep warm; place these at the back of the cage to help the cat feel safer. Objects to scratch and to perch on also can be helpful.[31]
b) **Bedding** – Cover the bottom of the cage completely, bare surfaces can be cold and uncomfortable. Bedding with the cat's and owner's scent also may help the cat feel more comfortable. Change bedding only when soiled (rather than daily); most cats prefer familiar bedding.
c) **Food and water** – Provide the cat's usual food if feasible, and put food and water near the back of the cage, as close as possible to its hiding place, to help the cat feel safer.
d) **Litter box** – Place at the front of the cage, since cats use it less frequently than (and only after) they use eating and drinking bowls. Provide the cat's usual litter if feasible.
e) **Door** – Cover as much of the door of the cage as possible to reduce unnecessary stimulation.

Factors outside the cage also can be stressful for confined cats;[18,32] these factors and how to optimize them include:

a) **Lights** – Put on a timer for predictable lighting from day to day if natural light is not available, or turn lights on and off manually at the same time each day. Do NOT turn lights on and off each time someone goes in and out of the space where cats are kept.
b) **Sound –** Minimize (<60 dB – quiet conversational level – can be measured with smartphone apps). Provide music (played softly) cat specific if possible (e.g. https://www.musicforcats.com).[33] There is little research into the effects of white noise on cat stress. It may be useful during especially loud periods of the day to dampen the impact of unpredictable noise with the following caveats:
   i) Prioritize efforts to decrease the source of the noise or to house cats in quieter areas.
   ii) Ensure the volume is set to below 60 dB.

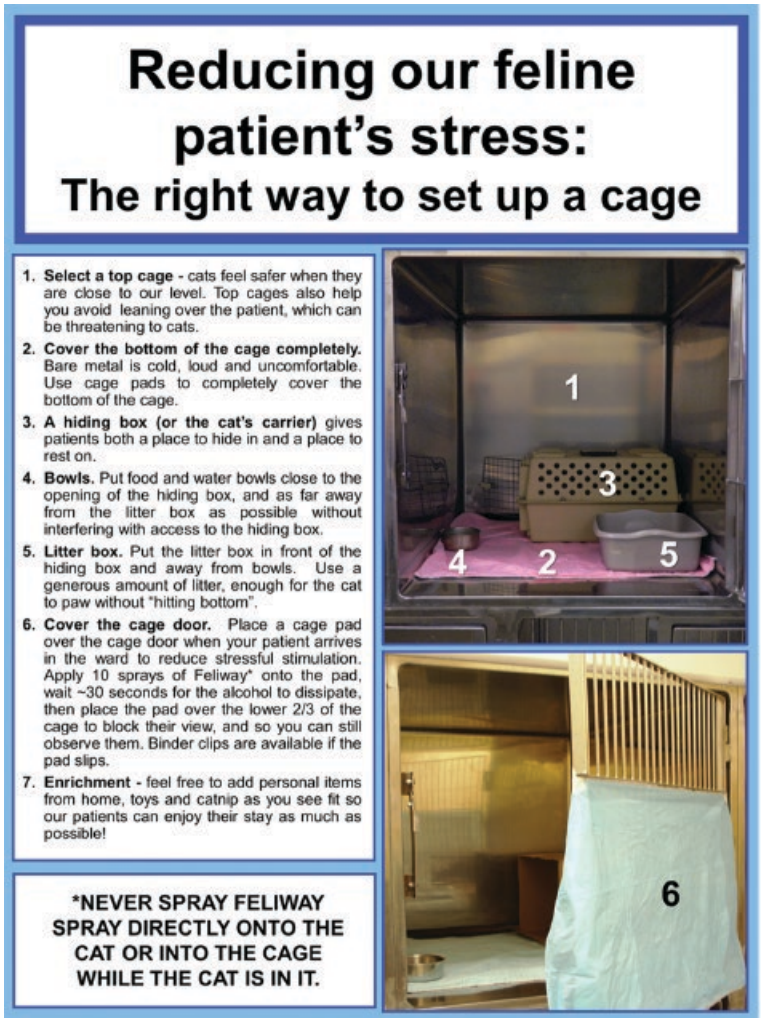

Figure 7.3 Poster of cage set-up recommendations. René Descartes' Traite de l'homme (Treatise of Man).

iii) Place white noise generator near the room door or source of the noise to be masked, not close to an individual cage or housing unit.
iv) Use only intermittently and as needed.
v) Closely monitor cats' behavioral response to use of white noise generators, reassessing use as indicated.

c) **Odors –** Minimize smells from dogs, other cats, perfumes, alcohol (from hand rubs), cigarettes, cleaning chemicals (including laundry detergent), air fresheners, etc.; all can be aversive and stressful, especially to cats confined in a cage where they can't move away from the odors.
d) **Temperature:** Cats prefer warm, 85–100 degrees F, temperatures.[34] Provide bedding that allows cats to "cocoon" to retain warmth if they choose to do so.
e) **Daily routine:** Perform cleaning, feeding, and treatment procedures at the same time each day, preferably by the same person, to increase predictability. Return cage furnishings to the same place after spot-cleaning, and house cats in the same cage throughout their stay.

f) **Low stress handling**[35] – Use these techniques to maximize the cat's perception of safety, predictability, and control. Add extra attention like brushing or playing from a familiar, dedicated person whenever possible.

Behaviors signaling that something may be wrong with caged cats include "resting" in litter boxes, and cages that show no use since the last cleaning or are in disarray. Sickness behaviors also are cause for concern. These include variable combinations of vomiting, diarrhea or soft feces, no eliminations in 24 hours, urinating or defecating out of the litter box, anorexia or decreased appetite, lethargy, and not grooming, which will be discussed later in this chapter.[36]

Acute Pain Resources

How Do I Know if My Cat Is in Pain? https://catfriendly.com/feline-diseases/signs-symptoms/know-cat-pain

2022 AAHA/AAFP Pain Management Guidelines for Dogs and Cats[37]

UNESP-Botucatu Multidimensional Composite Pain Scale https://static1.squarespace.com/static/56c72d078259b517148247e6/t/579dc74744024362eb01bdbc/1469957961939/UNESP+Botucatu+Multidimensional+Composite+Pain+Scale.pdf

Glasgow Composite Measures Pain Scale – Feline (CMPS-Feline).[16] https://www.newmetrica.com/acute-pain-measurement

Fear Free practice[6] https://fearfreepets.com

Cat-friendly practice[38] https://catvets.com/cfp/cfp

Domestic Cat Demeanour Scoring System – https://journals.sagepub.com/doi/suppl/10.1177/1098612X13509081/suppl_file/Annex1.pdf

Chronic Pain (CP)

Acute pain drives behavior in the service of survival. Pain perception usually occurs in the presence of states that threaten physical integrity and survival. Unfortunately, pain can outlive its usefulness, becoming chronic and maladaptive. Pain perception has qualities of both intensity and affect. Intensity describes the physical unpleasantness of the perception, whereas affect describes the feelings that accompany pain perception. These perceptions drive motor activities (withdrawal) and behaviors (guarding) directed toward avoiding continued exposure to the sensory inputs that resulted in the perception, and to protect the individual to permit healing. Acute pain usually results from input from sensory neurons that respond to noxious (nociceptive) stimuli (Figure 7.4), which has influenced thinking about pain for centuries.

In 1979, Patrick Wall,[40] one of the fathers of the gate theory of pain,[41] recognized that the time had come to shift from thinking about pain solely based on the origin of the input and the destination of the output to considering the dynamic stability of the entire interconnected system. He recognized that nociceptive input was but one of many factors evaluated during ongoing analysis of the external and internal environments necessary to permit a response that increased the probability of survival.

Nociceptive input to the central nervous system (CNS) may result in perceptions of immediate unpleasantness, as well as in appraisals of the meaning of the input.[3,42] These appraisals weigh the long-term implications of the presence of the pain state, based on one's genetic and epigenetic history, memory of past events, the environmental context, and imagination of future

possibilities (expectation). Complex interactions between amplifying and inhibitory neuronal networks in the central nervous system also influence pain perception,[43] as do emotional, hormonal, and external environmental influences.[44,45]

The situation becomes even more complex with chronicity, when CP can become a disease in its own right.[46] Moreover, perception of environmental threat ("stress") can exacerbate clinical signs in a variety of CP states, including feline interstitial cystitis (FIC),[42] and exposure to chronic or repeated threats, such as chronic restraint or repeated forced swimming in rodents.[47] In contrast, exposure to acute stress (threat) can inhibit pain perception, called "stress-induced analgesia,"[44,47] possibly in part through corticotropin-releasing factor (CRF_2) and oxytocin receptor signaling.[48]

Figure 7.4 Historical illustration of the "labeled line" pathway from nociceptor to painful perception.[39] René Descartes' Traite de l'homme (Treatise of Man).

Most human and animal patients with CP are managed in primary care. Approximately 20–55% of human primary care consultations are for pain, of which roughly half are for CP. If the figures are anything like this in primary veterinary care, understanding how CP is classified may improve the quality of care for this problem.

Chronic Pain Definitions

A systematic classification coding system for CP in human beings was developed for the first time in the 11th Revision, the International Classification of Diseases, (ICD-11), in 2018.[c] The current (2019) IASP Classification of common CP conditions is presented in Table 7.5.[d]

For many years CP was defined as pain that persists past normal healing time[49] and hence lacks the acute warning function of physiological nociception. Because this definition was difficult to verify in some pain conditions, the IASP currently defines CP as pain that lasts or recurs for longer than 3 months in humans.[46,50] They define primary CP pain in one or more anatomical regions that is associated with emotional distress that interferes with daily life. They differentiate three different kinds of common CP conditions; nociceptive (actual or threatened tissue damage causing the persistent activation of peripheral nociceptors), nociplastic (altered nociceptive function), and neuropathic (disease or lesion of the somatosensory system). In contrast, they consider secondary CP to reflect pathology associated with some other disease (e.g., cancer, some cases of osteoarthritis).

In 2016, the term "nociplastic" pain was proposed as a mechanistic descriptor for chronic pain states not characterized by obvious activation of nociceptors or neuropathy, "but in whom clinical

c https://www.who.int/classifications/icd/en.

d https://www.iasp-pain.org/advocacy/definitions-of-chronic-pain-syndromes. Accessed February 22, 2022.

Table 7.5 IASP Classification of common, clinically relevant chronic pain conditions.[50] Adapted from[44]

Name	Description
1) Chronic primary pain	Chronic pain in one or more anatomical regions that persists or recurs for longer than 3 months, and that is characterized by significant emotional distress (anxiety, anger/frustration or depressed mood) or functional disability (interference in daily life activities and reduced participation in social roles). Chronic primary pain is multifactorial: biological psychological and social factors contribute to the pain syndrome. The diagnosis is appropriate independently of identified biological or psychological contributors unless another diagnosis would better account for the presenting symptoms.
2) Chronic secondary musculoskeletal pain	Persistent or recurrent pain that arises as part of a disease process directly affecting bone(s), joint(s), muscle(s), or related soft tissue(s); may be spontaneous or movement-induced, and is limited to nociceptive pain. It does not include pain perceived in musculoskeletal tissues but not arising therefrom, such as the pain of compression neuropathy or somatic referred pain.
3) Chronic secondary visceral pain	Persistent or recurrent pain originating from internal organs of the head/neck region and the thoracic, abdominal, and pelvic cavities.
4) Chronic secondary headache or orofacial pain	Secondary pain caused by chronic headache and orofacial conditions, include chronic dental pains and temporomandibular disorders.
5) Chronic postsurgical or posttraumatic pain	Pain persisting after surgery or other trauma, where the initiating events and normal healing times are known.
6) Chronic cancer-related pain	Pain caused by the cancer itself (by the primary tumor or by metastases) or by its treatment (surgery, chemotherapy, and radiotherapy)
7) Chronic neuropathic pain	Pain caused by a lesion or disease of the somatosensory nervous system, which may be peripheral or central, and spontaneous or evoked by sensory stimuli (hyperalgesia and allodynia).

and psychophysical findings suggest altered nociceptive function."[51] According to the IASP, nociplastic pain might be involved in symptoms reported by patients with fibromyalgia, nonspecific musculoskeletal pain, and visceral pain disorders such as irritable bowel syndrome, and interstitial cystitis.[51] "In addition, patients suffering initially from nociceptive pain, such as osteoarthritis, may develop alterations in nociceptive processing manifested as altered descending pain inhibition accompanied by spread of hypersensitivity. In such cases, variable combinations of nociceptive and nociplastic input contribute to their pain."[51]

Examples of some common chronic pain conditions in people and domestic cats are presented in Table 7.6. The fact that many of those described in people have not (yet) been described in cats is not meant to imply that they do not occur in cats – just that their occurrence has not been identified to our knowledge at the present time. Certainly animal models of some of the conditions in people exist, but the relevance of models based upon injuries inflicted on healthy animals to naturally occurring diseases is not always obvious.[52]

Behavioral signs of chronic pain can be subtle, non-specific, and progress slowly. Owners may report the appearance of new and the disappearance of any combination of the behaviors described in Table 7.7.[53,56,57]

Table 7.6 Examples of chronic pain conditions in people and domestic cats. Adapted from[44]

Name	Examples in people	Examples in cats
1) Chronic primary pain	a) Widespread pain (e.g., fibromyalgia) b) Complex regional pain syndromes c) Headache and orofacial pain (e.g., chronic migraine or temporomandibular disorder) d) Visceral pain (e.g., irritable bowel syndrome or interstitial cystitis (IC)) e) Musculoskeletal pain (e.g., nonspecific low-back pain)	a) Not described b) Not described c) Orofacial pain d) Feline IC[53] and (some cases of) inflammatory bowel disease e) Not described
2) Chronic secondary musculoskeletal pain	a) Rheumatoid arthritis b) Symptomatic osteoarthritis (OA) c) Spasticity after spinal cord injury d) Rigidity in Parkinson disease	a) Not described b) OA c) Similar d) Not described
3) Chronic secondary visceral pain	a) Inflammatory e.g., esophagitis, gastritis, pancreatitis b) Vascular e.g., thrombosis, hypercoagulability, aneurysm c) Mechanical e.g., e.g., lithiasis, stenosis, traction of a viscus	Similar
4) Chronic secondary headache or orofacial pain	a) Trauma or injury b) Vascular c) Infection d) Dental e) Neuropathic	Similar
6) Chronic postsurgical or posttraumatic pain	Many	Many
7) Chronic cancer-related pain	Many	Many
8) Chronic neuropathic pain	See Scholz, et al.[54]	See Epstein[55]

Table 7.7 Behavioral changes observed in cats with chronic pain. Adapted from[53,56,57]

Behavior	Description
Movement	• Less fluid than usual • Less time spent moving, playing, or exploring • Intensity and vitality decreased (activity intolerance) • Jumps on to or down from elevated surfaces in stages rather than directly
Eating behaviors	• Decreased or increased food intake
Elimination behaviors	• Difficulty getting into or out of the litter box • Difficulty getting into or out of normal elimination postures • Urination or defecation outside of the litter box

(Continued)

Table 7.7 (Continued)

Behavior	Description
Grooming behaviors	• Reduced grooming frequency or duration of grooming bouts • Difficulty in positioning for grooming • Reduced scratching behavior • Excessive grooming due to pain or abnormal sensory sensitivity, which can result in self-induced alopecia
Social behaviors	• Less willing to interact with people and other pets • More hiding • Avoids being stroked or handled
Exploratory behaviors	• Less interest in the environment (e.g., playing, going outside, greeting owners and other pets, jumping onto or between elevated surfaces, sniffing objects, looking under furniture) • Seeks out warm, comfortable resting areas
Sudden vocalizing or agitation	• Suddenly vocalizes or runs, either spontaneously or during attempts to pet or stroke the cat* • Suddenly becomes fixated on a particular part of its body and starts licking it intensively for no obvious reason • Normal behavior may resume shortly after these episodes

*Muscle spasms or skin twitches along the back after being stroked could indicate hypersensitivity.

Chronic Pain Scales

Three owner-based and one veterinarian-based chronic OA pain scales currently exist.[53] These include the Feline Musculoskeletal Pain Index (FMPI), the Client Specific Outcome Measures (CSOM), and the Montreal Instrument for Cat Arthritis Testing for Use by Caretaker (MI-CAT[C]) for clients, and the Montreal Instrument for Cat Arthritis Testing for Use by Veterinarian (MI-CAT[V]) for clinicians (links to scales provided in the Resources section). The owner-based scales were developed to permit evaluation of the cat in its usual context to avoid the confounds associated with transportation and evaluation in a clinical environment. These scales are still undergoing validation, and currently are considered "living documents," subject to ongoing studies to further validate them.[53] Whether or not these or other scales will be incorporated into primary practice will depend on the outcome of these studies.

For comparison with scales used in human medicine, a recent study compared standardized response means, standardized effect sizes, and receiver operating curve analyses to assess change between baseline and 3-month assessments in 250 participants from a randomized clinical effectiveness trial of collaborative telecare management for moderate to severe and persistent musculoskeletal pain between 2-, 3-, 4-, and 11-item scales.[58] They reported that some measures were better able to detect changes than were others, and that post hoc analyses suggested that differences in content or rating scale structure (number of response options or anchoring language) did not adequately explain the observed differences in the detection of change. To the author's knowledge, current veterinary scales have not yet been tested for such sensitivity to change over time.

Health-related Quality of Life (HRQoL) Scales[53]

Scales for both general HRQoL[59–61] and specific conditions[62,63] have been developed and partially validated for cats. The generic scales could be used for chronic pain, but to date have not been sufficiently developed to be incorporated into daily clinical practice. They include (links to scales provided in the Resources section):

- VetMetrica[60] – is web-based, and initial evidence supports its use in cats with OA.[64] It consists of 20 items divided into 3 domains (vitality, comfort, and emotional wellbeing), and currently is available for use in clinical practice and research by paid subscription.
- Feline QoL measure[61] consists of 16 items divided into 2 domains (healthy behaviors and clinical signs). It has been evaluated in healthy cats, but is not yet available.
- Cat HEalth and Wellbeing (CHEW),[65] consists of 33 items in 8 domains including physical (mobility, eyes, coat, fitness, and appetite), mental and emotional (emotions and energy), and social functioning (engagement) domains.

As with the pain scales, whether or not these or other scales will be incorporated into primary practice remains to be seen.

Clinical Assessment of CP

Montiero et al.[53,56] have proposed a step-by step approach to evaluation of chronic pain (please consult the references for additional details).

- Schedule sufficient time, especially for initial consultations.
- Obtain details of patient's environment and daily routine. Recent behavior changes may be particularly significant. Environmental,[66] pain and/or HRQoL scales can be used to obtain additional information.
- Perform low-stress physical examination using feline-friendly handling techniques; carefully observe body language and facial expressions, palpate joints and long bones if OA is suspected, conduct neurological examination when neuropathic pain is suspected. NB: Withdrawal, avoidance, vocalization, etc. during palpation of specific body parts can indicate pain, but lack of behavioral response does not exclude pain presence in a shy/fearful cat.
- Observe the cat moving or assess home videos of the cat provided by the owners.
- Consider laboratory tests to investigate identified signs of concomitant diseases (secondary CP). Imaging may aid the diagnosis of some conditions, e.g., OA, stones, and cancer, but may not correlate with clinical signs of pain.

Sickness Behaviors

Sickness behaviors (SB)[67] are well-documented physiological and behavioral responses to infection that has been found in species across the animal kingdom, including zebrafish,[68] rodents,[69] dairy cattle,[70] cats,[36] and humans.[71] Common SB across species include fever, anorexia, inactivity, and decreased social contact.

Psychological stress also can result in SB, via stress response system (SRS)-induced release of corticotrophin-releasing factor (CRF), which activates the sympathetic nervous (SNS) and immune

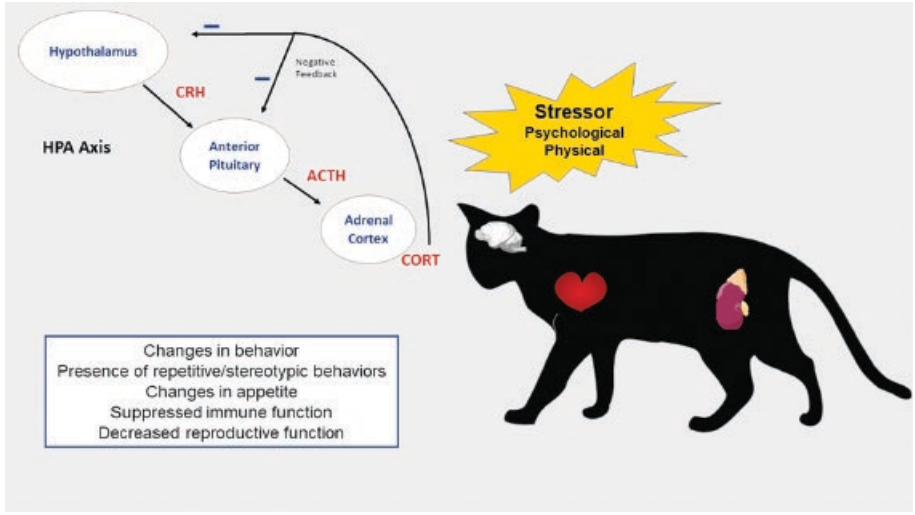

Figure 7.5 Depiction of the stress-induced activation of the HPA-axis and associated behavioral and physiologic responses.

systems, resulting in pro-inflammatory cytokine release.[72,73] This cascade has been linked to SB, mood symptoms, and pathologic pain (Figure 7.5).[74,75]

The associated behavioral response includes suppression of self-care behaviors such as feeding, social contact, and grooming to support processes that conserve energy to boost immune function to fight pathogens,[75,76] along with increased vigilance when exposed to psychological threats.[77,78] These psycho-neuro-immunologic changes are evolutionarily conserved, adaptive, normal responses that helps individuals survive by motivating the animal to change its behavior.

The motivational drive of SB should be considered in welfare assessments, as well as other motivators, such as fear, hunger, and thirst. Seeking rest, withdrawing from the environment, and caring for one's self are evolutionarily adaptive responses to infection that are as normal as arousal and escape are in response to a threat.[79] However, when this motivational state is caused by chronic environmental disturbances that exceed the animal's coping capacity, it is a sign of impaired welfare and should be addressed. Impaired welfare can be considered a chronic imbalance between positive and negative experiences; decreased perception of control and increased perception of threat resulting in chronic activation of the SRS.[80] It is now assumed that, similar to humans, chronic exposure to environmental stressors can induce mental suffering in animals with or without physical health problems.[80]

Clinical Signs of Sickness Behaviors

The most common SB responses to stress in domestic cats include decreased appetite, vomiting of hair, food, or bile, eliminating outside of litter pans, decreased social interactions, decreased grooming behavior, and an increase in the frequency and intensity of attempts to hide (Figure 7.6).[18,30,36,81]

We found increased SB in response to environmental stressors in laboratory-housed cats, which included transient (one-week) discontinuation of contact or interactions with the cats' primary caretaker, changes in time of day of routine husbandry, unfamiliar caretakers, and a delay of three hours

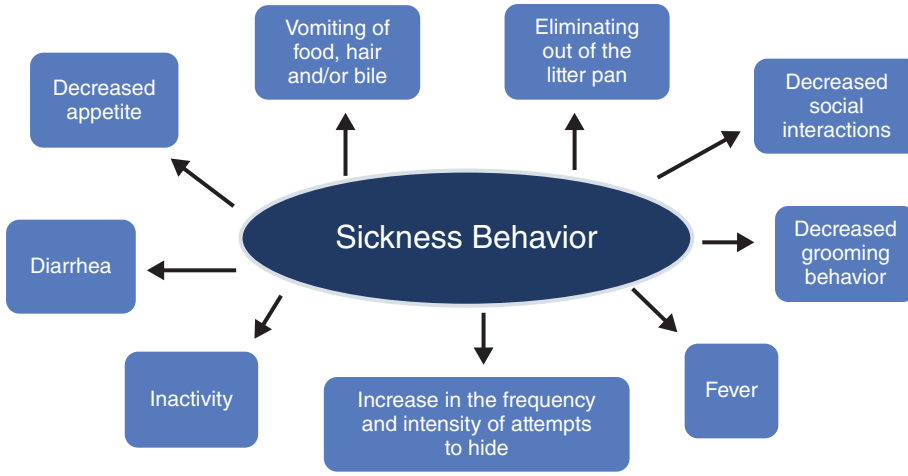

Figure 7.6 Common sickness behaviors observed in domestic cats.

in feeding time.[36] These events resulted in a 3.2-fold increased relative risk (RR) for SB compared to control weeks, and larger increases in risk for decreased food intake (RR = 9.3) and eliminations (RR = 6.4), and an increased risk for elimination of feces (RR = 9.8) and urine (RR = 1.6) outside the litter pan. Subsequently, changes in immune system function associated with stressors were found, including a decrease in circulating lymphocytes and an increase in the neutrophil to lymphocyte ratio from baseline. Additionally, gene expression for the pro-inflammatory cytokines IL-6 and TNF-α were altered.[30]

Figure 7.7 Vomiting is not a normal feline behavior; the cause should be explored.

We have consistently found that the most common SB in response to psychological stressors in confined cats include decreased appetite, increased eliminations out of the litter pan, and vomiting of food, hair, and/or bile (Figure 7.7). The most common owner reported SB include excessive appetite (34%), vomiting of hair, food or bile (25%), nervous/anxious/fearful behavior (22%), and urination or defecating out of the litter pan (11%).[82] These and other SBs also are frequently identified in pet cats brought to veterinarians for evaluation.[83] These results demonstrate that daily monitoring of cats for SB can offer a practical, non-invasive method to assess stress responses and the quality of their environment and thus, gauge overall welfare for cats confined in homes or veterinary hospitals, as well as those housed in shelters or research colonies.

Management

The housing space of confined cats is generally reduced in both quantity and quality in comparison to options available to their free-roaming counterparts. There are many aspects of the captive environment that may impact the welfare of cats. Individuals must adapt to their physical environment, which often does not match the physical environment in which their species evolved. Captive housing environments are typically built and maintained for human comfort and

convenience. Cats perceive their environments very differently from how humans do, so many environmental factors may be aversive or stressful to them. Factors pertaining to the macro-environment (the room), the micro-environment (the individual cage or restricted area available to the cat), predictability and control of the environment, and the quality of the social environment (including the human–cat relationship), as well as interactions with conspecifics and other animals in the environment, such as dogs housed within auditory or olfactory proximity, all influence cats' perception of threat.[18,84–86] The impact of stress caused by human intervention(s) should be minimized to support both the psychological and physiological health of confined cats. Understanding the cats' sensorium and how they are likely to perceive stimuli will aid caretakers in monitoring and improving the housing environment. Finally, the environment should be behaviorally relevant, with the quantity and quality of space provided allowing for the development and normal expression of species-typical behavior patterns.

Perhaps the greatest stressor cats experience when confined in a home or cage is the perception or actual lack of ability to control their surroundings. Confined cats have little or no control over:[32]

- Who their social partners are.
- How much space they can put between themselves and others.
- The type, amount, or availability of food.
- The quality or quantity of environmental stimuli they experience, including
  - Lighting
  - Noise
  - Odor
  - Temperature.

Predictability, or the lack thereof, is another environmental aspect that cats may perceive to be stressful. Studies have shown that, given a choice, animals will choose predictability over unpredictability, especially in relation to aversive events.[32,87,88] Predictability refers both to temporal consistency (the time when events happen), as well as familiarity with caretakers and the environment. A consistent, predictable daily routine is essential, particularly when an animal is confined. Daily cleaning and feeding procedures conducted at the same time of day and performed by a familiar person allow cats to predict potentially aversive events.

Finally, individual personality differences have been identified in cats, indicating that personality traits may play a role in cat preferences for or use of resources. A recent study of coping styles in cats reported that cats housed in an enriched housing environment that was quiet, predictable, and enriched, to minimize stress and promote acclimation, used hiding and perching resources differently. Although hiding decreased and perching increased across days overall, cats that were identified as having a reactive coping style spent more time in the hide box, whereas cats identified as having a proactive coping style spent more time on the perch.[89] These results reinforce the importance of addressing individual differences by providing enriched caging with *both* hiding and perching opportunities to confined cats, as previously reported.[18,31,81,90,91]

Behavioral Approaches to Helping Cats Showing Chronic Pain Or Sickness Behaviors[92,93]

The Client

Owners of cats with chronic pain come to us for a diagnosis for the cause of whatever signs concern them most, and may not know that their cat suffers from chronic pain. In our experience,

the most important consideration for a successful outcome for cats with chronic pain related to FIC (and apparently other chronic pain states as well)[94] is effective and empathic client communication.[92] After performing a complete evaluation of the cat and concluding that chronic pain is likely to be present, we can explain to the client that while no cure currently is available, appropriate therapeutic and palliative procedures can generally keep the cat's clinical signs to a minimum and increase the disease-free interval, and that most of their care can be provided in collaboration with a trained technician. We also demonstrate compassion by listening carefully to the client's story of the effects of having a cat with chronic pain, provide a satisfactory explanation for the sources of the signs, express care and concern for the situation, and enhance the *client's* perception of control. Effective caregiver–client interactions appear to enhance patient adherence to treatments, and quality of life outcomes of therapy.[95] We can then prescribe any therapies appropriate to the presenting manifestation(s), and (when possible) introduce the client to the technician or other staff member trained to care for cats with chronic pain, who will coach the client to implement multimodal environmental modification (MEMO) [66,96] for the patient in an attempt to minimize the effects of perception of environmental threat on the cat's signs. The formality of this introduction demonstrates that we intend to sustain the partnership with the client through our technical support staff to support their efforts to gain and maintain control of the patient's clinical signs.

The Cat

Pharmacotherapy

Choices for drug therapy, if any, depend on the individual cat's manifestation(s) of chronic pain, and are beyond the scope of this chapter. Excellent references are available elsewhere.[28,97] Medicating cats can be challenging and if forced on them will increase fear and distress, damage the cat–owner relationship, and has the potential to shorten their life if the owner is unable to provide the necessary treatment, especially for chronic conditions. Therefore, we recommend utilizing low-stress techniques and training cats to accept examination, medication, and treatments, ideally before they are necessary, to minimize fear and distress and optimize care. A full discussion of cooperative care is beyond the scope of this chapter but can found elsewhere.[98]

Diet and Feeding Management

Some diets are marketed for "stressed" cats, but the evidence for their effectiveness in management of chronic pain has yet to be evaluated, and their salutary effects, if any, seem modest.[99,100] Moreover, studies have shown that many cats with chronic visceral pain (FIC) can be effectively managed without any diet change.[36,96,101,102] In most cases we recommend that owners choose whichever (Association of American Feed Control Officials labeled) diets fit their personal preferences, and then to offer a few examples of these at mealtime so their cat can express its preferences. We recommend this to minimize the effects of their perception of diet on the activation of the SRS of both the client and the cat. A detailed discussion of the pros and cons of diet therapy for all manifestations of chronic pain is beyond the scope of this article, and unfortunately most studies of dietary management of pain have been either supported or conducted by food companies.[103] If a diet change seems appropriate, only attempt to implement it after the cat has returned home and is feeling better to reduce the risk of inducing a learned aversion to the new food.

The Environment

Environmental conditions are known to affect the behavior and health of animals,[104] particularly captive animals.[32,105] Environmental enrichment has been shown to relieve chronic pain in a variety of animal studies.[106–108] If cats with chronic pain have a sensitized SRS, then treatments that increase their perception of control *and* reduce their perception of threat are more likely to be effective than those that do not. Effective MEMO creates conditions that permit the patient to feel safe, and to have unrestricted access to species-appropriate novelty, activity, and interactions with other animals (including humans). Effective MEMO for cats means provision of all "necessary" resources, refinement of interactions with owners, a tolerable intensity of conflict, and thoughtful institution of change(s) to the cat's environment (its "territory"). It also extends the "1+1" rule traditionally applied to litter boxes (one for each cat in the home, plus one more) to all pertinent resources (particularly resting areas, and food, water, and litter containers) in the home.

Space

Each cat needs a safe "refuge"; a cozy carrier in a desirable (to the cat) location in the home and outfitted for the cat's comfort. Habituating the cat to the carrier also facilitates crating the cat for medical care and other travel. Cats also interact with the physical structures in their environment, and need opportunities to scratch (both horizontal and vertical may be necessary), climb, hide, and rest; preferably in multiple locations in the home.

A recent study reported that some cats may enjoy olfactory enrichment, including catnip, silver vine, Tatarian honeysuckle and valerian (a constituent of Feliway spray).[109,110] Another recent study reported pet cats' preferences for social interaction with the owner (50% of cats), food (37%), toys (11%), and scent (2%).[111] Significantly more cats preferred social interaction to toys and food to scent, but no differences were found between social interaction and food, food and toys, or toys and scent.

Food

Cats prefer to eat individually in a safe, quiet location where they will not be startled by other animals, sudden movement, or activity of air ducts or appliances that may begin operation unexpectedly.[112] Some cats also prefer wet foods, possibly due to differences in flavors or the potentially more natural "mouth feel," whereas other cats prefer dry foods. When a diet change is appropriate (and agreed to by the owner), offering the new diet in a separate, adjacent container at mealtime rather than removing the usual food and replacing it with the new food or mixing foods permits cats to express their preferences. Natural cat-feeding behavior also includes predatory activities such as stalking and pouncing. These may be simulated by hiding small amounts of food around the house, or by putting food into food puzzles.[113]

Litter Boxes

Litter box issues may be present even when LUTS are not observed. A detailed discussion of litterbox location (safe), size (big), litter type (ask the cat) and management is beyond the scope of this article; excellent recommendations are available elsewhere.[92,93,114]

Play

Cats may enjoy play interactions with owners, and many can be trained to perform behaviors ("tricks") to the extent that their condition permits.[115] Owners need to understand that while cats readily respond to positive reinforcement (food), they cannot respond to punishment like more group-living social species, because this form of "teaching" apparently never entered their behavioral repertoire.[116] Cats also seem to be more amenable to learning if the behavior is shaped *before* feeding. Many cats appear to like novelty, so providing a variety of toys, rotated or replaced regularly, can sustain their interest. Some cats also seem to have preferences for specific prey. For example, some cats prefer to chase birds, whereas others may prefer to chase mice, lizards, or bugs. Identifying a cat's "prey preferences" allows owners to provide toys that the cat will be most likely to play with.

Not all cats enjoy play; some seem to prefer to be petted and groomed.

Conflict

Like the rest of us, when a cat feels threatened, it often responds by attempting to restore its perception of control. During such responses, some cats become aggressive, some become withdrawn, and some become ill. Inter-cat conflict may be present when multiple cats are housed indoors together.[117] Conflict among cats can develop because of perceived threats to their status in the home, over access to valued (or scarce) resources (food, resting areas, litter boxes, owner attention, etc.), from other animals in the home, or from outside cats. Providing a "house of plenty," one with more resources than all the cats can use at once, may minimize these risks.

Follow-up

All the information clients sometimes need can overwhelm them.[92] One can help support the client by focusing conversations on those changes the client perceives to be most important, and is willing to make, by providing written instructions for implementing the desired changes, and then following up with the client in a few days to see what questions have come to their mind, and what they have managed to do in the interim. We always ask *both*, "How is your cat doing?" and "How are *you* doing?" We then re-contact them in a week or two to learn how things are going and to provide support. If implementation of the changes has been successful, one can move on to additional changes. In our experience, a time usually comes (and often quite quickly) when the client "gets it" and can continue on without additional coaching.

Prevention

Vulnerability for a chronic pain condition can develop after significant adverse experiences, particularly early in life.[118] This vulnerability may be unmasked by chronic and or overwhelming perception of threat later in life, and also may be mitigated by effective MEMO.[119,120] The husbandry implications of this information is clear; to the extent that we can convince ourselves and our clients of the value of effective environmental enrichment for all cats, and then find and implement ways to provide it, we all – cats, clients, and caregivers – are likely to enjoy better health and wellbeing, and may minimize the risk of chronic pain.

Conclusions

Many confined cats appear to cope with less-than-optimal environments. The underlying, early adverse event-mediated, differences in neuro-endocrine-immune responses identified in some cats with chronic pain, however, may limit their adaptive capacity, so these cats may represent a separate population of individuals with increased vulnerability to provocative environments. Moreover, we are concerned more with optimizing the environments of cats than with identifying and implementing minimum requirements for their survival.

Providing an environment that is compatible with cats' behavioral needs often seems to mitigate the effects of at least some manifestations of chronic pain in addition to promoting their general health and welfare. This is not to say that the absence of environmental enrichment causes chronic pain in cats, only that it may unmask an underlying vulnerability in some cats.[121]

Resources for Practices

The science of Feline OA Pain https://www.zoetisus.com/oa-pain/feline-oa-pain.aspx

Degenerative Joint Disease in Cats https://catvets.com/public/PDFs/ClientBrochures/DJD-Webview.pdf

WSAVA Global Pain Council https://wsava.org/committees/global-pain-council

WSAVA Assessment, recognition and treatment of pain, 2022 AAFP/AAHA Pain Management Guidelines Dogs and Cats https://www.aaha.org/aaha-guidelines/2022-aaha-pain-management-guidelines-for-dogs-and-cats/home https://www.wsava.org/WSAVA/media/Documents/CommitteeResources/GlobalPainCouncil/Chronic-Pain_Cats.pdf

Resources for Clients

How do I know if my cat is in pain? https://catfriendly.com/keep-your-cat-healthy/know-cat-pain

How to tell if your cat is in pain https://www.aaha.org/globalassets/02-guidelines/pain-management/painmanagement_cats_web.pdf

Chronic pain in cats Owner webinar – www.youtube.com/watch?v=_f18kjTbuCc

Degenerative Joint Disease (Arthritis) in cats https://catfriendly.com/feline-diseases/degenerative-joint-disease-arthritis

Joint pain in cats – http://painfreecats.org/for-owners/#diagnosing

References

1 Aydede M. Does the IASP definition of pain need updating? *Pain Rep*. 2019;4(5):e777.

2 Merola I, Mills DS. Behavioural signs of pain in cats: An expert consensus. *PLoS One*. 2016;11(2):e0150040.

3 Merola I, Mills DS. Systematic review of the behavioural assessment of pain in cats. *J Feline Med Surg*. 2016;18(2):60–76.

4 Steagall P, Robertson SA, Taylor P. *Feline anesthesia and pain management*. Hoboken, NJ: John Wiley & Sons; 2017.

5 Lascelles B, Cripps P, Mirchandani S, Waterman A. Carprofen as an analgesic for postoperative pain in cats: Dose titration and assessment of efficacy in comparison to pethidine hydrochloride. *J Small Anim Pract*. 1995;36(12):535–541.
6 Demaline B. Fear in the veterinary clinic: History and development of the fear free℠ initiative. *Conspectus Borealis*. 2018;4(1):2.
7 Steagall PV, Monteiro BP. Acute pain in cats: Recent advances in clinical assessment. *J Feline Med Surg*. 2018;21(1):25–34.
8 Robertson S. How do we know they hurt? Assessing acute pain in cats. *In Practice*. 2018;40(10):440–448.
9 Mathews K, Kronen PW, Lascelles D, et al. Guidelines for recognition, assessment and treatment of pain: WSAVA Global Pain Council members and co-authors of this document. *J Small Anim Pract*. 2014;55(6):E10–E68.
10 Waran N, Best L, Williams V, Salinsky J, Dale A, Clarke N. A preliminary study of behaviour-based indicators of pain in cats. *Anim Welfare*. 2007;16(S):105–108.
11 Robertson S. Assessment and recognition of acute (adaptive) pain. In: Steagall P, Robertson S, Taylor P, eds. *Feline anesthesia and pain management*. Hoboken, New Jersey; 2017:199–220.
12 Corletto F. *Using acute pain scales for cats*. British Medical Journal Publishing Group; 2017.
13 Brondani JT, Mama KR, Luna SP, et al. Validation of the English version of the UNESP-Botucatu multidimensional composite pain scale for assessing postoperative pain in cats. *BMC Vet Res*. 2013;9(1):143.
14 Benito J, Monteiro BP, Beauchamp G, Lascelles BDX, Steagall PV. Evaluation of interobserver agreement for postoperative pain and sedation assessment in cats. *J Am Vet Med Assoc*. 2017;251(5):544–551.
15 Doodnaught GM, Benito J, Monteiro BP, Beauchamp G, Grasso SC, Steagall PV. Agreement among undergraduate and graduate veterinary students and veterinary anesthesiologists on pain assessment in cats and dogs: A preliminary study. *Can Vet J*. 2017;58(8):805.
16 Reid J, Scott E, Calvo G, Nolan A. Definitive Glasgow acute pain scale for cats: Validation and intervention level. *Vet Rec*. 2017;108(18):449.
17 Zeiler GE, Fosgate GT, Van Vollenhoven E, Rioja E. Assessment of behavioural changes in domestic cats during short-term hospitalisation. *J Feline Med Surg*. 2014;16(6):499–503.
18 Stella J, Croney C, Buffington T. Environmental factors that affect the behavior and welfare of domestic cats (Felis silvestris catus) housed in cages. *App Anim Behav Sci*. 2014;160:94–105.
19 Buisman M, Hasiuk MM, Gunn M, Pang DS. The influence of demeanor on scores from two validated feline pain assessment scales during the perioperative period. *Vet Anaesth Analg*. 2017;44(3):646–655.
20 Evangelista MC, Watanabe R, Leung VS, et al. Facial expressions of pain in cats: The development and validation of a Feline Grimace Scale. *Sci Rep*. 2019;9(1):1–11.
21 Calvo G, Holden E, Reid J, et al. Development of a behaviour-based measurement tool with defined intervention level for assessing acute pain in cats. *J Small Anim Pract*. 2014;55(12):622–629.
22 Shipley H, Guedes A, Graham L, Goudie-deangelis E, Wendt-Hornickle E. Preliminary appraisal of the reliability and validity of the Colorado State University Feline Acute Pain Scale. *J Feline Med Surg*. 2019;21(4):335–339.
23 McLennan KM., Miller AL, Dalla Costa E, et al. Conceptual and methodological issues relating to pain assessment in mammals: The development and utilisation of pain facial expression scales. *App Anim Behav Sci*. 2019;217:1–5.
24 Carney HC, Little S, Brownlee-Tomasso D, et al. AAFP and ISFM feline-friendly nursing care guidelines. *J Feline Med Surg*. 2012;14(5):337–349. doi:10.1177/1098612X12445002.

25 Lefman SH, Prittie JE. Psychogenic stress in hospitalized veterinary patients: Causation, implications, and therapies. *J Vet Emerg Crit Care*. 2019;29(2):107–120.
26 Grubb T, Sager J, Gaynor JS, et al. AAHA anesthesia and monitoring guidelines for dogs and cats. *J Am Anim Hosp Assoc*. 2020;56(2):59–82.
27 Steagall PV. Analgesia: What makes cats different/challenging and what is critical for cats? *Vet Clin Small Anim Pract*. 2020;50(4):749–767.
28 Self I. *BSAVA guide to pain management in small animal practice*, 1st ed. Gloucester, UK: British Small Animal Veterinary Association; 2019.
29 Epstein ME, Rodan I, Griffenhagen G, et al. AAHA/AAFP pain management guidelines for dogs and cats. *J Feline Med Surg*. 2015;17(3):251–272.
30 Stella J, Croney C, Buffington T. Effects of stressors on the behavior and physiology of domestic cats. *App Anim Behav Sci*. 2013;143(2):157–163. doi:10.1016/j.applanim.2012.10.014.
31 Gourkow N, Fraser D. The effects of housing and handling practices on the welfare, behaviour and selection of domestic cats (Felis sylvestris catus) by adopters in an animal shelter. *Anim Welfare*. 2006;15:371–377.
32 Morgan KN, Tromborg CT. Sources of stress in captivity. *App Anim Behav Sci*. 2007;102(3–4):262–302. doi:10.1016/j.applanim.2006.05.032.
33 Snowdon CT, Teie D, Savage M. Cats prefer species-appropriate music. *App Anim Behav Sci*. 2015;166:106–111. doi:10.1016/j.applanim.2015.02.012.
34 NRC. Thermoregulation in Cats. In: *Nutrient requirements of dogs and cats*. Washington, DC: The National Academies Press; 2006:270–271. https://doi.org/10.17226/10668.
35 Herron ME, Shreyer T. The pet-friendly veterinary practice: A guide for practitioners. *Vet Clin North Am Small Anim Pract*. 2014;44(3):451–481.
36 Stella JL, Lord LK, Buffington CA. Sickness behaviors in response to unusual external events in healthy cats and cats with feline interstitial cystitis. *J Am Vet Med Assoc*. 2011;238(1):67–73. doi:10.2460/javma.238.1.67.
37 Gruen ME, Lascelles BDX, Colleran E, et al. AAHA pain management guidelines for dogs and cats. *J Am Anim Hosp Assoc*. 2022;58(2):55–76.
38 Burns K. Cat friendly practice program takes off: American Association of Feline Practitioners growing with program. *J Am Vet Med Assoc*. 2012;241(10):1264.
39 Duncan G. Mind-body dualism and the biopsychosocial model of pain: What did Descartes really say? *J Med Philos*.
40 Wall PD. On the relation of injury to pain the John J. Bonica Lecture. *Pain*. 1979;6(3):253–264.
41 Melzack R, Wall PD. *Pain mechanisms: A new theory*. 1965.
42 Westropp JL, Kass PH, Buffington CA. Evaluation of the effects of stress in cats with idiopathic cystitis. *Am J Vet Res*. 2006;67(4):731–736.
43 Harte SE, Harris RE, Clauw DJ. The neurobiology of central sensitization. *J Appl Biobehav Res*. 2018;23(2):e12137.
44 Vachon-Presseau E. Effects of stress on the corticolimbic system: Implications for chronic pain. *Prog Neuro-Psychopharmacol Biol Psychiatry*. 2018;87:216–223.
45 Timmers I, Quaedflieg CW, Hsu C, Heathcote LC, Rovnaghi CR, Simons LE. The interaction between stress and chronic pain through the lens of threat learning. *Neurosci Biobehav Rev*. 2019;107:641–655.
46 Treede R-D, Rief W, Barke A, et al. Chronic pain as a symptom or a disease: The IASP classification of chronic pain for the: International classification of diseases:(: ICD-11:). *Pain* 2019;160(1):19–27.
47 Bravo L, Llorca-Torralba M, Suárez-Pereira I, Berrocoso E. Pain in neuropsychiatry: Insights from animal models. *Neurosci Biobehav Rev*. 2020;115:96–115.

48 Larauche M, Moussaoui N, Biraud M, et al. Brain corticotropin-releasing factor signaling: Involvement in acute stress-induced visceral analgesia in male rats. *Neurogastroenterol Motil*. 2019;31(2):e13489.

49 Bonica JJ. *The management of pain*. Philadelphia: Lea and Febiger; 1953:1243–1244.

50 Treede R-D, Rief W, Barke A, et al. A classification of chronic pain for ICD-11. *Pain*. 2015;156(6):1003.

51 Kosek E, Cohen M, Baron R, et al. Do we need a third mechanistic descriptor for chronic pain states? *Pain*. 2016;157(7):1382–1386.

52 Buffington CAT. Bladder pain syndrome/interstitial cystitis – Etiology and animal research. In: Baranowski A, Abrams P, Fall M eds. *Urogenital pain in clinical practice*. New York: Informa; 2007:169–183:chap19.

53 Monteiro BP, Steagall PV. Chronic pain in cats: Recent advances in clinical assessment. *J Feline Med Surg*. 2019;21(7):601–614.

54 Scholz J, Finnerup NB, Attal N, et al. The IASP classification of chronic pain for ICD-11: Chronic neuropathic pain. *Pain*. 2019;160(1):53.

55 Epstein ME. Feline neuropathic pain. *Vet Clin North Am Small Anim Pract*. 2020;50(4):789–809.

56 Monteiro B, Lascelles B. Assessment and recognition of chronic (maladaptive) pain. In: Steagall PVM, Robertson SA, Taylor PM, eds, *Feline anesthesia and pain management*. Hoboken, NJ: Wiley/Blackwell; 2017:241–256.

57 Monteiro BP. Feline chronic pain and osteoarthritis. *Vet Clin North Am Small Anim Pract*. 2020;50(4):769–788.

58 Kean J, Monahan P, Kroenke K, et al. Comparative responsiveness of the PROMIS pain interference short forms, brief pain inventory, PEG, and SF-36 bodily pain subscale. *Med Care*. 2016;54(4):414.

59 Reid J, Nolan A, Scott E. Measuring pain in dogs and cats using structured behavioural observation. *Vet J*. 2018;236:72–79.

60 Noble CE, Wiseman-Orr LM, Scott ME, Nolan AM, Reid J. Development, initial validation and reliability testing of a web-based, generic feline health-related quality-of-life instrument. *J Feline Med Surg*. 2019;21(2):84–94.

61 Tatlock S, Gober M, Williamson N, Arbuckle R. Development and preliminary psychometric evaluation of an owner-completed measure of feline quality of life. *Vet J*. 2017;228:22–32. doi:10.1016/j.tvjl.2017.10.005.

62 Niessen S, Powney S, Guitian J, et al. Evaluation of a quality-of-life tool for cats with diabetes mellitus. *J Vet Int Med*. 2010;24(5):1098–1105.

63 Noli C, Borio S, Varina A, Schievano C. Development and validation of a questionnaire to evaluate the Quality of Life of cats with skin disease and their owners, and its use in 185 cats with skin disease. *Vet Dermatol*. 2016;27(4):247.

64 Scott EM, Davies V, Nolan AM, et al. Validity and responsiveness of the generic health-related quality of life instrument (VetMetrica™) in cats with osteoarthritis. Comparison of vet and owner impressions of quality of life impact. *Front Vet Sci*. 2021;8:1124.

65 Freeman LM, Rodenberg C, Narayanan A, Olding J, Gooding MA, Koochaki PE. Development and initial validation of the Cat HEalth and Wellbeing (CHEW) Questionnaire: A generic health-related quality of life instrument for cats. *J Feline Med Surg*. 2016;18(9):689–701.

66 Westropp JL, Delgado M, Buffington C. Chronic lower urinary tract signs in cats: Current understanding of pathophysiology and management. *Vet Clin Small Anim Pract*. 2019;49(2):187–209. doi:10.1016/j.cvsm.2018.11.001.

67 Hart BL. Biological basis of the behavior of sick animals. *Neurosci Biobehav Rev*. 1988;12(2):123–137. doi:10.1016/S0149-7634(88)80004-6.

68 Kirsten K, Soares SM, Koakoski G, Kreutz LC, Barcellos LJG. Characterization of sickness behavior in zebrafish. *Brain Behav Immun*. 2018;73:596–602.

69 Broom DM. Behaviour and welfare in relation to pathology. *App Anim Behav Sci*. 2006;97(1):73–83. doi:10.1016/j.applanim.2005.11.019.

70 Fogsgaard KK, Røntved CM, Sørensen P, Herskin MS. Sickness behavior in dairy cows during Escherichia coli mastitis. *J Dairy Sci*. 2012;95(2):630–638.

71 Shattuck EC, Muehlenbein MP. Towards an integrative picture of human sickness behavior. *Brain Behav Immun*. 2016;57:255–262.

72 Marques-Deak A, Cizza G, Sternberg E. Brain-immune interactions and disease susceptibility. *Mol Psychiatry*. 2005;10(3):239–250.

73 Dantzer R. Neuroimmune interactions: From the brain to the immune system and vice versa. *Physiol Rev*. 2018;98(1):477–504.

74 Danese A, McEwen BS. Adverse childhood experiences, allostasis, allostatic load, and age-related disease. *Physiol Behav*. 2012;106(1):29–39. doi:10.1016/j.physbeh.2011.08.019.

75 Raison CL, Miller AH. When not enough is too much: The role of insufficient glucocorticoid signaling in the pathophysiology of stress-related disorders. *Am J Psychiatry*. 2003;160(9):1554–1565. doi:10.1176/appi.ajp.160.9.1554.

76 Dantzer R, O'Connor JC, Freund GG, Johnson RW, Kelley KW. From inflammation to sickness and depression: When the immune system subjugates the brain. *Nat Rev Neurosci*. 2008;9(1):46–56. doi:10.1038/nrn2297.

77 Sapolsky RM. *Why zebras don't get ulcers*, 3rd ed. New York, NY: Holt paperbacks; 2004.

78 Marques-Deak A, Cizza G, Sternberg E. Brain-immune interactions and disease susceptibility. *Mol Psychiatry*. 2005;10(3):239–250. doi:10.1038/sj.mp.4001643.

79 Dantzer R, Kelley KW. Twenty years of research on cytokine-induced sickness behavior. *Brain Behav Immun*. 2007;21(2):153–160.

80 Bain MJ, Buffington CT. The relationship between mental and physical health. In: McMillan FD ed. *Mental health and well-being in animals*, 2nd ed. Oxfordshire, UK: CABI; 2019:33–49.

81 Stella JL, Croney CC, Buffington CT. Behavior and welfare of domestic cats housed in cages larger than US norm. *J Appl Anim Welfare Sci*. 2017;20(3):296–312.

82 Stella JL, Croney CC. Management practices of cats owned by faculty, staff, and students at two Midwest veterinary schools. *Sci World J*. 2016;2016.

83 Buffington CA, Westropp JL, Chew DJ, Bolus RR. Risk factors associated with clinical signs of lower urinary tract disease in indoor-housed cats. Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't. *J Am Vet Med Assoc*. 2006;228(5):722–725. doi:10.2460/javma.228.5.722.

84 Amat M, Camps T, Manteca X. Stress in owned cats: Behavioural changes and welfare implications. *J Feline Med Surg*. 2016;18(8):577–586. doi:10.1177/1098612X15590867.

85 Stella JL, Croney CC. Environmental aspects of domestic cat care and management: Implications for cat welfare. *Sci World J*. 2016;ArticleID: 6296315. doi:10.1155/2016/6296315.

86 Vinke C, Godijn L, Van der Leij W. Will a hiding box provide stress reduction for shelter cats? *App Anim Behav Sci*. 2014;160:86–93.

87 Weiss JM. Psychological factors in stress and disease. *Sci Am*. 1972;226(6):104–113.

88 Weiss JM. Effects of coping behavior in different warning signal conditions on stress pathology in rats. *J Comp Physiol Psychol*. 1971;77(1):1–13. doi:10.1037/h0031583.

89 Stella J, Croney C. Coping styles in the domestic cat (Felis silvestris catus) and implications for cat welfare. *Animals*. 2019;9(6):370.

90 Kry K, Casey R. The effect of hiding enrichment on stress levels and behaviour of domestic cats (Felis sylvestris catus) in a shelter setting and the implications for adoption potential. *Anim Welfare*. 2007;16(3):375–383.

91 Rochlitz I. Feline welfare issues. In: Turner DC, Bateson P, eds. *The domestic cat – The biology of its b*ehavior. Cambridge, UK: Cambridge University Press; 2000:208–226.
92 Herron ME, Buffington CA. Environmental enrichment for indoor cats: Implementing enrichment. *Compend Contin Educ Vet*. 2012;34(1):E1–E5.
93 Ellis SL, Rodan I, Carney HC, et al. AAFP and ISFM feline environmental needs guidelines. *J Feline Med Surg*. 2013;15(3):219–230. doi:10.1177/1098612X13477537.
94 Monteiro B, Troncy E. Treatment of chronic (Maladaptive) pain. In: Steagall PV, Robertson SA, Taylor P eds. *Feline anesthesia and pain management*. Hoboken, NJ: John Wiley & Sons; 2018:257–280:chap 15.
95 Frankel RM. Pets, vets, and frets: What relationship-centered care research has to offer veterinary medicine. *J Vet Med Educ.* Spring 2006;33(1):20–27.
96 Buffington CAT, Westropp JL, Chew DJ, Bolus RR. Clinical evaluation of multimodal environmental modification in the management of cats with lower urinary tract signs. *J Feline Med Surg*. 2006;8:261–268.
97 Steagall PV, Robertson SA, Taylor P. *Feline anesthesia and pain management*. Hoboken, NJ: John Wiley & Sons; 2018:301.
98 Howell A, Feyrecilde M. *Cooperative veterinary care*. Hoboken, NJ: John Wiley & Sons; 2018.
99 Kruger JM, Lulich JP, MacLeay J, et al. Comparison of foods with differing nutritional profiles for long-term management of acute nonobstructive idiopathic cystitis in cats. *J Am Vet Med Assoc*. 2015;247(5):508–517. doi:10.2460/javma.247.5.508.
100 Landsberg G, Milgram B, Mougeot I, Kelly S, de Rivera C. Therapeutic effects of an alpha-casozepine and L-tryptophan supplemented diet on fear and anxiety in the cat. *J Feline Med Surg*. 2017;19(6):594–602. 1098612X16669399.
101 Seawright A. A case of recurrent feline idiopathic cystitis: The control of clinical signs with behavior therapy. *J Vet Behav Clin Appl Res*. 2008;3(1):32–38. doi:10.1016/j.jveb.2007.09.008.
102 Chew DJ, Bartges JW, Adams LG, Kruger JM, Buffington CAT. *Randomized, placebo-controlled clinical trial of pentosan polysulfate sodium for treatment of feline interstitial (idiopathic) cystitis presented at: 2009 ACVIM Forum*; June 4, 2009; Montreal, Quebec.
103 Mozaffarian D. Conflict of interest and the role of the food industry in nutrition research. *JAMA* 2017;317(17):1755–1756.
104 Hannan AJ. Review: Environmental enrichment and brain repair: Harnessing the therapeutic effects of cognitive stimulation and physical activity to enhance experience-dependent plasticity. *Neuropathol Appl Neurobiol*. 2014;40(1):13–25. doi:10.1111/nan.12102.
105 Hoy JM, Murray PJ, Tribe A. Thirty years later: Enrichment practices for captive mammals. *Zoo Biol*. 2010;29(3):303–316. doi:10.1002/zoo.20254.
106 Vachon P, Millecamps M, Low L, et al. Alleviation of chronic neuropathic pain by environmental enrichment in mice well after the establishment of chronic pain. *Behav Brain Funct*. 2013;9:22. doi:10.1186/1744-9081-9-22.
107 Bushnell MC, Case LK, Ceko M, et al. Effect of environment on the long-term consequences of chronic pain. *Pain* 2015;156(4):S42–S49. doi:10.1097/01.j.pain.0000460347.77341.bd.
108 Tai LW, Yeung SC, Cheung CW. Enriched environment and effects on neuropathic pain: Experimental findings and mechanisms. *Pain Pract*. 2018(8):1068–1082. doi:10.1111/papr.12706.
109 Pageat P. Properties of cats' facial pheromones. *Google Patents*; 1998.
110 Bol S, Caspers J, Buckingham L, et al. Behavioral responsiveness of cats (Felidae) to silver vine (Actinidia polygama), Tatarian honeysuckle (Lonicera tatarica), valerian (Valeriana officinalis) and catnip (Nepeta cataria). *BMC Vet Res*. 2017;13(70):1–15.
111 Shreve KRV, Mehrkam LR, Udell MA. Social interaction, food, scent or toys? A formal assessment of domestic pet and shelter cat (Felis silvestris catus) preferences. *Behav Processes* 2017;141:322–328.

112 Masserman JH. Experimental neuroses. *Sci Am*. 1950;182:38–43.
113 Dantas LM, Delgado MM, Johnson I, Buffington CT. Food puzzles for cats: Feeding for physical and emotional wellbeing. *J Feline Med Surg*. 2016;18(9):723–732. doi:10.1177/1098612X16643753.
114 de Souza Dantas LM. Vertical or horizontal? Diagnosing and treating cats who urinate outside the box. *Vet Clin North Am Small Anim Pract*. 2018;48(3):403–417.
115 Bradshaw J, Ellis S. *The trainable cat: A practical guide to making life happier for you and your cat*. New York, NY: Basic Books; 2016.
116 Barnett S. The "instinct to teach". *Nature*. 1968;220(5169):747–749.
117 Elzerman AL, DePorter TL, Beck A, Collin J-F. Conflict and affiliative behavior frequency between cats in multi-cat households: A survey-based study. *J Feline Med Surg*. 2019;22(8):705–717. 1098612X19877988.
118 Williams MD, Lascelles BDX. Early neonatal pain-A review of clinical and experimental implications on painful conditions later in life. *Front Pediatr*. 2020;8:30. doi:10.3389/fped.2020.00030.
119 Buffington CA. Idiopathic cystitis in domestic cats – beyond the lower urinary tract. *J Vet Int Med*. 2011;25(4):784–796. doi:10.1111/j.1939-1676.2011.0732.x.
120 Withey SL, Maguire DR, Kangas BD. Developing improved translational models of pain: A role for the behavioral scientist. *Perspect Behav Sci*. 2020;43(1):39–55.
121 Buffington CA. Developmental influences on medically unexplained symptoms. *Psychother Psychosom*. 2009;78(3):139–144. doi:10.1159/000206866.