

NUTRITION

Dealing With Dysrexia

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The term **dysrexia** refers to a disruption in food intake, including anorexia (not eating), **hyporexia** (eating less) and eating an unbalanced diet (eg, the patient that will eat roast beef but not a prescribed low-protein diet). Although a short period of inadequate intake (1 or 2 days) is generally well tolerated, longer periods of hyporexia may slow recovery and put patients at risk of other complications. These include changes in the gastrointestinal (GI) microbiome (ie, dysbiosis), delayed gastric emptying and intestinal hypomotility, and compromise to enterocyte health and mucosal integrity. Hyporexia and anorexia are known to predispose vulnerable patients to translocation of potential pathogens from the GI tract. Cats, particularly those with a robust body condition score (BCS), will begin to accumulate fat within their hepatocytes after just a few days of anorexia, with overt compromise due to hepatic lipidosis noted within 10-14 days. In addition to all the physiological consequences of poor food intake, this takes a toll on the pet owner and can lead to premature decisions about discontinuation of therapy or euthanasia. Owners are often disinclined or unable to administer oral medications if the pet is not eating.

The mechanisms by which illness suppresses appetite are complex, and we do not yet have a clear picture of them all. Changes in messaging within the

hypothalamus likely play a key role, with a disturbance of the usual signals regarding satiety. In healthy animals, two distinct neuronal populations regulate this process, with one set (the orexigenic neurons) driving food-seeking behaviors, while the other (the anorexigenic neurons) depress appetite. Activity within these centers also impacts metabolic rate, so that energy stores are conserved when food is scarce. Some diseases, primarily those associated with inflammation, can essentially hijack the anorexigenic neurons, so that appetite is suppressed but the metabolic rate is concurrently increased. This is one of the pathways behind the cachexic conditions, in which weight loss can occur alarmingly quickly, and at a much faster rate than we would expect simply from a lack of intake. Cachexia is sometimes referred to as “protein-energy wasting syndrome,” a phrase that effectively captures the underlying metabolic derangement.

There are several neuroendocrine systems that drive satiety and satiation, but only one hormone specifically drives hunger, ghrelin, which is produced primarily in the stomach. Ghrelin is essential for survival, as it is the primary trigger for activity in the orexigenic (food seeking/hunger) center within the hypothalamus. Other hormones, such as cortisol and thyroxine, may also support food-seeking behaviors, but have other more complex metabolic effects.



It may be helpful to have the owner come in and hand feed the patient or place an object such as a piece of clothing in the cage to provide comforting familiar scents.

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INITIAL APPROACH TO THE INAPPETANT PATIENT

Start with a global assessment of the reason(s) for poor intake and address the most likely possibilities first. In many patients, hyporexia is a multifactorial process, and is shaped by psychological, environmental, nociceptive, pharmacological and physiological influences. Some of these are easier to fix than others, and a multimodal approach is often necessary.

Psychological influences

Hospitalized patients are unavoidably disoriented by the change in their environment and may experience substantial amounts of anxiety. This is often clearly apparent in our feline patients that often retreat under a towel and refuse to re-emerge. Appetite is suppressed by stress, particularly if patients are fearful, so we need to think of ways to mitigate the psychological impact of hospitalization. It may be helpful to have the owner come in and hand feed the patient or place an object such as a piece of clothing in the cage to provide comforting familiar scents. Depending on your staffing

levels, try to have one person focus on food intake with a particular patient, while others do the “mean” tasks like placing catheters, administering injections, etc. Assigning one person to be the comforter and feeder may provide a feeling of safety for our anxious patients.

Ask owners about food preferences and follow these when possible. If a diet change is medically indicated (eg, for renal or GI disease), do not make a radical change. Instead, gradually introduce the appropriate diet when the patient is eating consistently. In the short term, eating some of the wrong food is better than eating none of the right one.

Ideally, cats should be housed in a separate room from dogs. If this is not possible, hang a towel over the front of the cat’s cage and provide a hiding place (even a cardboard box will suffice!) within the cage. The feline pheromone diffusers are also helpful and one should be placed nearby. For cats, it is important that feeding areas are clearly separated from toileting areas. Feline-specific housing with raised platforms and separate rooms is ideal and can markedly improve well-being. An existing set of steel cages can be easily transformed into a condo with a simple plastic tube, allowing the cat to rest and eat in one side and eliminate in the other.

Environmental influences

Many people think that human hospitals smell bad, and I am sure that many of our patients think the vet hospital smells dreadful. If you are aware of a whiff of bleach or other disinfectants in your treatment areas or wards, this is probably overpowering to our patients. Consider changing products or cleaning cages with a chemical-free steam cleaner. Noises can also affect patient well-being and should be modulated as much as possible. Isolate barking dogs and try to keep sick patients away from boarding areas that tend to be loud. Simple additional sound proofing efforts can be rewarding. Also pay attention to background music.

Nociceptive influences

Pain is a powerful appetite suppressant and may impede a patient’s ability to seek orprehend food. Even in the absence of overt manifestations of pain, it can be helpful to consider that discomfort is impacting intake and intervene appropriately. Choices about pain control can be challenging, as opioids can suppress intake and non-steroidal drugs are problematic in patients with renal or GI compromise.

Pharmacological influences

Numerous therapeutic drugs can impact appetite, most often by triggering feelings of nausea (eg, various antibiotics) or by causing ileus or delayed gastric emptying (opioids). If a patient is hyporexic, it can be very helpful to look critically at its current medication list and see if anything can be discontinued or switched.

In people, opioid-induced constipation is a major issue. We do not tend to pay that much attention to our patients' stools (or lack thereof!) unless we note diarrhea, but I believe that iatrogenic constipation can affect comfort and appetite. Drugs are a common cause, but lack of activity and reluctance to defecate in a strange environment also play a role.

Physiological influences

This category includes sensations of nausea, gastric discomfort, gastroesophageal reflux and constipation. All of these processes are likely to impact food intake, and effective management may make a substantial difference to appetite. Maropitant (1 mg/kg SQ q24h; 2 mg/kg PO q24h) is my first choice for nausea, as it is well tolerated and may reduce visceral pain. Persistent gastric ileus may be mitigated with a prokinetic agent; metoclopramide has some effect on gastric emptying, but erythromycin (1 mg/kg IV or PO q8-12h) is generally superior.

As our patients cannot describe their symptoms, it can be hard to identify gastric discomfort or gastroesophageal reflux. Lip smacking and exaggerated swallowing motions are suggestive but are usually associated with severe compromise and may not be noted in animals with milder changes. Although there is appropriate concern about overuse of proton pump inhibitors in critically ill animals, a short trial with pantoprazole (1 mg/kg IV q24h) or omeprazole (0.7 mg/kg PO q12h) may be worthwhile.

If imaging or physical examination indicates fecal retention, a glycerin enema (3-5 mls) may trigger defecation, improve patient comfort and increase food intake. There is a strong neurological relationship between the stomach and colon, and studies in children have shown that constipation can suppress appetite.

PHARMACOLOGIC INTERVENTIONS FOR INAPPETENCE

Although numerous drugs have been used off-label for appetite stimulation in both dogs and cats, their

effects are unpredictable and often disappointing. However, the ghrelin agonist class of drugs shows tremendous promise in this regard and are used for this purpose in people. The FDA has recently approved a ghrelin receptor agonist for use as an appetite stimulant in dogs (capromorelin; Entyce®). A feline-specific version is currently in development. We do not have time to discuss all the agents used to stimulate food intake, so the list below covers only the most widely used.

Mirtazapine

This is a noradrenergic/serotonergic agent and is licensed for use in people as an antidepressant. It stimulates 5-HT₁ receptors and strongly antagonizes 5-HT₂ and 5-HT₃ receptors. It has been shown to be a potent appetite stimulant in some cats. The therapeutic window is small, and overdose can result in hyperexcitability, crying and tremors. It should not be combined with cyproheptadine (see below). Based on pharmacokinetic studies, it can be given daily in cats, although many do well with 2 mg PO or transdermally q2-3d. In addition to promoting food intake, mirtazapine may also decrease nausea and have a modest prokinetic effect.

Cyproheptadine

This is an antihistamine drug with antiserotonergic effects. Increased food intake is a recognized side effect, likely through antagonism of 5-HT receptors in the hypothalamus. I have found it to be less predictable than mirtazapine with respect to appetite stimulation, and it must be given twice daily. It can take a few days to see an effect, and the drug should be tapered rather than discontinued abruptly. Side effects can be worrisome, and include CNS depression, paradoxical excitement, anticholinergic effects and a lowering of the seizure threshold.

Diazepam

This is a benzodiazepine and enhances GABA neuro-transmission. It was routinely used in cats for appetite stimulation until an association between oral diazepam and acute hepatotoxicity emerged. A single IV dose may be considered, in an effort to 'kick start' intake but long-term use in cats is unwise. The effect in dogs is often less dramatic.

Tetrahydrocannabinol (THC)

A synthetic form of TCH (dronabinol) is used in people for appetite stimulation. It also has anti-emetic and anti-nausea effects. The dose in dogs and cats is unclear, and there is limited information regarding effectiveness in companion animals. There is a risk of toxicity with this drug, and it is a Class III-controlled drug.

Glucocorticoids

These drugs stimulate appetite via increasing neuropeptide Y and decreasing pro-inflammatory cytokine production. Many dogs will increase intake while receiving glucocorticoids, but cats are relatively resistant to their appetite stimulating effects. Side effects are substantial, with muscle wasting, delayed healing, immunocompromise and diabetes mellitus. As a general rule, steroids should not be given to an anorexic animal prior to establishing a definitive diagnosis as these drugs will hide lymphoma but let infectious agents such as *Histoplasma* run rampant.

Capromorelin (Entyce®)

This drug is currently approved for use in dogs and is the first ghrelin receptor agonist approved for use in veterinary medicine. A feline product is also in development. Safety and field studies indicate that this drug is a potent appetite stimulant, with a wide safety margin. This drug is likely to have wide applications for the management of both transient and sustained hyporexia in companion animals.

In addition to stimulating the orexigenic neurons and promoting food intake, ghrelin also triggers the release of growth hormone (GH) from the pituitary. This supports muscle growth along with

weight gain. Negative feedback from insulin-like growth factor-1 limits GH production so that levels remain robust but are not excessive.

Numerous ghrelin receptor agonists are under investigation for use in people. Preliminary data shows substantially longer survival times in patients with metastatic neoplasia, mitigation of gastroparesis in those with Parkinson's disease, and beneficial anti-inflammatory effects. This drug class offers substantial promise in the management of various conditions in both human and veterinary medicine.

Feeding tubes

There are numerous options for assisted parenteral feeding using food delivery tubes. Some can be placed in awake patients with minimal or no sedation (nasoesophageal, nasogastric, nasojejunal), while others require general anesthesia (esophageal, gastric, gastrojejunal, jejunal). As a broad guideline, I use nasal tubes for transient support, as these are often uncomfortable and should be regarded as a temporary bridge to self-feeding or placement of another device when the patient is stabilized. I tend to place a longer-lasting feeding tube pretty promptly in my patients (particularly cats), and generally chose an esophageal tube. These can be placed very quickly and are well-tolerated, but the patient must be under anesthesia with an endotracheal tube in place.

SUMMARY

Managing hyporexia can be challenging and a multimodal approach is often needed. Pharmacological agents can play a key role in improving intake, and the new ghrelin agonist drugs show tremendous promise in this regard. Although the consequences of prolonged inadequate intake may be insidious, dysrexia can markedly impact patient outcomes and must be promptly addressed. **TVP**

Recommended Reading

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