AMERICAN ASSOCIATION OF FELINE PRACTITIONERS

The Ins and Outs of Feline **Nutrition** and **Gastroenterology**

7th WORLD FELINE VETERINARY CONFERENCE

PROCEEDINGS

October 12 – 15, 2023

Renasant Convention Center ▪ Memphis, TN

www.catvets.com/conference2023

We would like to recognize and thank the following companies for their sponsorships.

Platinum Partnership Sponsors

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Thursday Welcome Reception; Pre-conference Day Seminar & Social - Diabetes Masterclass, Drs. Ellen Behrend, Audrey Cook, Patty Lathan, Thomas Schermerhorn, Catharine Scott-Moncrieff & Cynthia Ward; Lunch & Learn with Diabetes Masterclass Speakers; Nutritional Management of Diabetes Mellitus, Dr. Audrey Cook; Discussing Diabetes Mellitus: Empowering Technicians, Dr. Ken Yagi; All Coffee Breaks; Tote Bags; Hotel Key Cards

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Breakfast Symposium on Constipation, Dr. Ashlie Saffire; Early Career Veterinarian Scholarship Program; Student Award Program; Cat Friendly Interactions & Handling Workshop, Dr. Ilona Rodan; Nursing & Nutrition for the Critical Feline Patient Who Just Won't Eat!, Dr. Ashlie Saffire; Feline Chronic Enteropathy, Dr. Craig Webb; Nutritional Management of the Comorbid CKD Patient & Harnessing the Power of Fiber to Manage GI Disease, Dr. Valerie Parker; Approach to the Vomiting Cat: Causes, Treatment, & Management & Approach to Diarrhea in Kittens, Dr. Adam Rudinsky; No Way Out! Constipation, Obstipation, Megacolon: Panel Discussion, Drs. Adam Rudinsky, Betsy Swanson, and Craig Webb

zoetis

Hands-on Feline Orthopedic Evaluation Workshop with Drs. Duncan Lascelles and Margaret Gruen; Lunch & Learn with Speaker Dr. Tracey Deiss; Breakfast Symposium on Osteoarthritis, Drs. Joyce Login and Michelle Meyer

Gold Partnership Sponsors

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Friday Happy Hour Reception; Lunch & Learn, Dr. Cynthia Ward

Dechra

Lunch & Learn, Dr. Jessica Pritchard; Nutritional Management of Hypercalcemia, Dr. Valerie Parker; Nuanced Nutrition: Calcium Oxalate Urolithiasis & Cobalamin: Diagnostic & Therapeutic Implications, Dr. Audrey Cook; Conference Wi-Fi in Convention Center; Notepad & Pen

IDEXX

Lunch & Learn, Drs. Elizabeth Schooley & Kelly St. Denis; The Feline Philosophy Behind Diagnosing GI Disease & Diagnostic Dilemmas: The History, Mystery, & Bemoaning of Feline Triaditis, Dr. Craig Webb; Interpreting Liver Biopsies, Feline Pancreatic Disease: Familiar Friends & Missed Connections, & Approach to the Yellow Cat, Dr. Adam Rudinsky

ceva

Pre-conference Day Early Morning Learning Sessions with Speakers Drs. Melissa Hall & Natalie Marks; Cat Friendly Interactions & Handling Workshop, Dr. Ilona Rodan

MERCK Animal Health

Lunch & Learn, Dr. Sheryl Gamble; Water Bottles

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Hill's Transforming Lives

Food for Thought Luncheon, Dr. Vicky Ograin; Critical Nutritional Foundations for Every Cat & Use of Assisted Enteral Nutrition, Dr. Valerie Parker; Treating the Itchy Cat: A Review & Update on Treatment Options, Dr. Sara Ramos; Oncology Nutrition Management Cats with Cancer, Dr. Catherine Ruggiero

PURINA PRO PLAN VETERINARY DIETS

Lunch & Learn, Dr. Alison Manchester; Nutritional Management of Chronic Enteropathies, Dr. Valerie Parker; Diagnostic Testing in Feline Chronic Enteropathy Demonstrates Evolution from Inflammatory Bowel Disease to Intestinal Lymphoma, Dr. Anne Avery; Speaker, Dr. Michael Lappin

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Lunch & Learn, Dr. Matt McGlasson

ZOMEDICA

Lunch & Learn, Dr. Kelly St. Denis; The Cat is Losing Weight: Is it GI or FHT, or Both?, Dr. Kelly St. Denis

sleepypod safe travels

Cat Friendly Interactions & Handling Workshop, Dr. Ilona Rodan; Speaker Ms. Ellen Carozza

VetStem

Stem Cells in Feline GI Disease & FMT: What's Coming Down the Pipeline, Dr. Craig Webb

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Friday Morning Breakfast

wedgewood PHARMACY

Management of Liver Disease, Dr. Adam Rudinsky

BLUE NATURAL Veterinary Diet

Emerging or Just Ignored: Ductal Plate Malformations, Dr. Adam Rudinsky

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Modifying the Microbiome: The Role of Probiotics in Feline Practice, Dr. Audrey Cook

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The Feline Pyramid of Poop, Dr. Craig Webb

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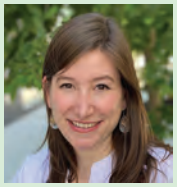
President's Welcome 2023



Welcome to the 2023 AAFP Annual Conference and 7th World Feline Veterinary Conference! I am thrilled to extend a warm 'meowdy' to everyone attending in-person and virtually for *The Ins and Outs of Feline Nutrition and Gastroenterology.*

As we embark on this enlightening journey through the intricate world of our feline companions' digestive tracts, I hope you will be captivated by discussions on the nutritional management of disease and uncovering the mysteries of feeding tubes – those slender lifelines that keep our whiskered friends thriving. We will get the chance to delve into the depths of the feline microbiome, where the tiniest inhabitants wield the mightiest influence, and explore the complexities of matters both unpleasant and common: vomiting and constipation. Our speakers are truly the cat's pajamas, presenting insights that will have us typing furiously in OneNote to share some pearls with all our associates. A huge thank you to our Conference Planning Task Force for developing the schedule, topics, and speakers lineup for us all to enjoy.

Between lectures I encourage you to visit our exhibit hall, a treasure trove of innovations and insights that might leave whiskers quivering. And don't miss our social events, including the Welcome Reception and Happy Hour Reception– the best opportunities to mingle, network, and forge new connections. New this year is the Student Social, which goes hand in hand with efforts by our new Student Engagement Committee to relaunch Student Chapters of the AAFP at every school.

These fun events would not be possible without our generous Sponsors. A heartfelt thank you goes out to: Boehringer Ingelheim, Royal Canin, Zoetis, Elanco, Dechra, IDEXX, Ceva, Merck Animal Health, Hill's Pet Nutrition, Purina ProPlan Veterinary Diets, Basepaws, Zomedica, Sleepypod, VetStem, Trivium Vet, Wedgewood Pharmacy, Blue Natural Veterinary Diet, Visbiome Vet, Banfield Pet Hospital, Endoscopy Support Services, and Brakke Consulting. Your support is a cornerstone of this event and we are truly grateful. We also extend our appreciation to our Conference Partners - ABVP, EveryCat, IVAPM, NAVTA, and TICA - for standing by us in our pursuit of feline excellence.

Speaking of excellence, I'd also like to take this time to introduce our incoming President, Dr. Tammy Sadek. With her straightforward, decisive, and supportive approach, Tammy is the purr-fect leader to steer our ship. Her steadfast commitment to feline patients and the field of feline medicine is unwavering.

As you leave our meeting with newfound knowledge, and hopefully many fond new memories and cat camaraderie, we ask that you mark your calendars for next year's Conference, themed *Dermatology, Cardiology, and Diagnostic Methodology,* which is scheduled for September 26 - 29, 2024 in the charming city of Minneapolis, Minnesota. I always look forward to visiting family there, and riding some roller coasters in the great Midwest Mall of America, don't 'cha know. ;)

Thank you for your dedication to feline wellbeing, and here's to an enriching and enlightening Conference!

Kira Ramdas, DVM
2022-23 AAFP President

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AAFP MEMBER EXCLUSIVE

POUNCE ON THIS SPECIAL RENEWAL OFFER

Renew your AAFP Membership for 2024 by 12/31/23 for a chance to win 1 of 5 complimentary registrations to the 2024 Spring into Feline Medicine eConference!

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Your membership gives you free access to live and on-demand CE webinars, discounts on popular AAFP conferences, and more.

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Renew Today!

Membership in the AAFP gives you access to a thriving community, and offers practical resources and educational materials designed to improve feline health and wellbeing.

Renew your membership by December 31, 2023 for your chance to win one of five complimentary registrations to the 2024 Spring into Feline Medicine eConference, coming to computers everywhere on Sunday, April 21; Wednesday, May 1; and Saturday, May 11.

How to Renew

- Renewing your AAFP membership is easy! Visit **catvets.com/renew** and follow the instructions.
- Forget your password? Click on the "Forgot Password" link to reset it.
- Contact the AAFP if you have any questions about your login, how to renew, or for details about your member benefits.

THURSDAY, OCTOBER 12, 2023

Pre-conference Day*

Schedule is in Central Daylight Time

TIME	SESSION TITLE		SPEAKER	ROOM	SPONSOR/ PARTNER
7:45 - 11:45 am	Hands-on Feline Orthopedic Evaluation Workshop**	IPO	Drs. Duncan Lascelles & Margaret Gruen	110 & 111	zoetis
	PRE-CONFERENCE DAY*				
10:00 - 11:45 am	**Early Morning Learning Sessions**				
10:00 - 10:50 am	The Allergic Patient: New Insights in Skin Barrier Science	LS	Dr. Melissa Hall	Ballroom B	Ceva
10:55 - 11:45 am	Serenity Now! A Deeper Dive into the Peaceful Practice	LS	Dr. Natalie Marks	Ballroom B	Ceva
11:45 - 1:15 pm	**Food for Thought Luncheon**				
12:15 - 1:15 pm	Nutritional Counselor Program: Get Inspired to Run your Own Nutritional Consultations	LS	Vicky Ograin	Ballroom B	Hill's
1:30 - 5:30 pm	**Seminar & Social**				ABVP
1:30 - 2:00 pm	Diabetes Masterclass: Oral Hypoglycemics - An Overview	LS	Dr. Audrey Cook	Ballroom B	Boehringer Ingelheim
2:00 - 3:15 pm	Diabetes Masterclass: SGLT-2 Inhibitors - Safety & Efficacy Data	LS	Drs. Ellen Behrend & Patty Lathan	Ballroom B	Boehringer Ingelheim
3:15 - 3:45 pm	**Refreshment Break**			Ballroom C	
3:45 - 4:10 pm	Diabetes Masterclass: Getting Started & Monitoring	LS	Dr. Cynthia Ward	Ballroom B	Boehringer Ingelheim
4:10 - 5:00 pm	Diabetes Masterclass: Troubleshooting & Complications	LS	Drs. Thomas Schermerhorn & Catharine Scott-Moncrieff	Ballroom B	Boehringer Ingelheim
5:00 - 5:30 pm	Diabetes Masterclass: Panel Discussion		Diabetes Masterclass Speakers	Ballroom B	Boehringer Ingelheim
5:30 - 7:00 pm	Welcome Reception *All attendees invited*			Riverview Lobby	Boehringer Ingelheim

LS Live Streamed

IPO In-person Only

Sessions and speakers are subject to change.

*In-person attendees need to register for Pre-conference Day if they would like to attend. Additional fees apply.

**Separate Registration Required from Pre-conference Day. Additional fees apply.

FRIDAY, OCTOBER 13, 2023

Schedule is in Central Daylight Time

TIME	SESSION TITLE		SPEAKER	ROOM	SPONSOR/ PARTNER
6:00 - 7:00 am	Early Riser Yoga Class*	IPO		Sheraton Hotel - Heritage Ballroom	
7:15 - 8:00 am	Continental Breakfast			Ballroom Foyer	TRIVIUM VET
8:00 - 8:15 am	President's Address	LS	Dr. Kira Ramdas	Ballroom A & B	
8:15 - 9:30 am	Critical Nutritional Foundations for Every Cat	LS	Dr. Valerie Parker	Ballroom A & B	Hills
9:30 - 11:00 am	Networking Refreshment Break			Exhibit Hall	Boehringer Ingelheim
11:00 - 11:50 am	Nutritional Management of the Comorbid CKD Patient	LS	Dr. Valerie Parker	Ballroom A	ROYAL CANIN
	Nutritional Idiosyncrasies & the Role in Obesity, Diabetes Mellitus, & Hepatic Lipidosis	LS	Dr. Adronie Verbrugghe	Ballroom B	EveryCAT
11:55 - 12:45 pm	Use of Assisted Enteral Nutrition	LS	Dr. Valerie Parker	Ballroom A	Hills
	Do Nutrients & Ingredients Matter for Weight Loss? How to Select a Diet	LS	Dr. Adronie Verbrugghe	Ballroom B	EveryCAT
12:45 - 2:10 pm	Lunch			Exhibit Hall	
1:00 - 2:00 pm	*Lunch & Learn #1:** Velagliflozin: An Oral Solution for the Diabetic Cat	IPO	Diabetes Masterclass Speakers	102 - 104	Boehringer Ingelheim
1:00 - 2:00 pm	*Lunch & Learn #2:** Evolving the Feline MDB: Purrfect Balance for Your Patient Assessment	IPO	Drs. Elizabeth Schooley & Kelly St. Denis	105 - 107	IDEXX
1:00 - 2:00 pm	*Lunch & Learn #3:** Calming Cats: The Impact of Transport & Anxiety on Our Cats, Cat Caregivers, & Practices	IPO	Dr. Tracey Deiss	113 - 115	zoetis
2:10 - 3:00 pm	Nutritional Management of Chronic Enteropathies	LS	Dr. Valerie Parker	Ballroom A	PRO PLAN VETERINARY DIETS
	Feeding Comorbidities: Obese Cats with Other Diseases	LS	Dr. Adronie Verbrugghe	Ballroom B	
3:05 - 3:55 pm	Harnessing the Power of Fiber to Manage GI Disease	LS	Dr. Valerie Parker	Ballroom A	ROYAL CANIN
	Navigating Alternative Cat Foods: Intersection Between Cat Needs & Client Preferences	LS	Dr. Adronie Verbrugghe	Ballroom B	
3:55 - 4:40 pm	Networking Refreshment Break			Exhibit Hall	Boehringer Ingelheim
3:55 - 4:40 pm	Student Social **All Students Invited to Attend*			Memphis Board Room	
4:40 - 5:30 pm	Nutritional Management of Hypercalcemia	LS	Dr. Valerie Parker	Ballroom A	Dechra
	Feeding the Allergic Cat	LS	Dr. Sara Ramos	Ballroom B	Hills
5:30 - 6:45 pm	Happy Hour Reception			Exhibit Hall	Elanco

LS Live Streamed
IPO In-person Only

*Separate registration required. No fees associated.

Senvelgo®
(velagliflozin
oral solution)

NEW!

JUST WHAT CATS ORDERED

A convenient, once-daily liquid oral solution for feline diabetes

Simplify feline diabetes treatment for cats and their owners with the liberating convenience of a once-daily liquid oral solution.

- Delivers sustained glycemic control starting as soon as 1 week for most cats[1,2]
- Precise dosing tailored to the cat's weight
- Minimal risk of clinical hypoglycemic events[1-3]
- Well accepted by most cats[1]

Scan for more details!

*3 Months' Supply**

*Based on average cat weight of 11 lbs

1. Data on file at Boehringer Ingelheim.
2. SENVELGO® (velagliflozin oral solution) [Freedom of Information Summary; NADA 141-568]. St. Joseph, MO: Boehringer Ingelheim Vetmedica, Inc.; 2023.
3. SENVELGO® (velagliflozin oral solution) prescribing information.

IMPORTANT SAFETY INFORMATION: SENVELGO® (velagliflozin oral solution) is indicated to improve glycemic control in otherwise healthy cats with diabetes mellitus not previously treated with insulin. **Before using this product, it is important to read the entire product insert, including the boxed warning.**

Cats treated with SENVELGO may be at an increased risk of diabetic ketoacidosis or euglycemic diabetic ketoacidosis, both of which may result in death. Development of these conditions should be treated promptly, including insulin administration and discontinuation of SENVELGO.

Do not use SENVELGO in cats with diabetes mellitus who have previously been treated with insulin, who are receiving insulin, or in cats with insulin-dependent diabetes mellitus. The use of SENVELGO in cats with insulin-dependent diabetes mellitus, or the withdrawal of insulin and initiation of SENVELGO, is associated with an increased risk of diabetic ketoacidosis or euglycemic diabetic ketoacidosis and death.

Sudden onset of hyporexia/anorexia, lethargy, dehydration, or weight loss in cats receiving SENVELGO should prompt immediate discontinuation of SENVELGO and assessment for diabetic ketoacidosis, regardless of blood glucose level. SENVELGO should not be initiated in cats with ketonuria, ketonemia, pancreatitis, anorexia, dehydration, or lethargy at the time of diagnosis of diabetes mellitus, as it may indicate the presence of other concurrent disease and increase the risk of diabetic ketoacidosis.

Keep SENVELGO in a secure location out of reach of **children**, dogs, cats, and other animals to avoid accidental ingestion or overdose. **For more information, please refer to the enclosed package insert or visit SENVELGOClinic.com.**

Boehringer Ingelheim

L6528
Package Insert

Senvelgo®
(velagliflozin oral solution)

15mg/ mL

For oral use in cats only

Sodium-glucose cotransporter 2 (SGLT2) inhibitor

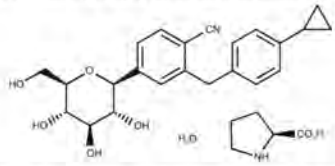
Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

WARNING: DIABETIC KETOACIDOSIS/EUGLYCEMIC DIABETIC KETOACIDOSIS

- **Cats treated with SENVELGO may be at an increased risk of diabetic ketoacidosis or euglycemic ketoacidosis (see Adverse Reactions). As diabetic ketoacidosis and euglycemic ketoacidosis in cats treated with SENVELGO may result in death, development of these conditions should be treated promptly, including insulin administration and discontinuation of SENVELGO (see Monitoring).**
- **Due to the risk of developing diabetic ketoacidosis or euglycemic ketoacidosis, do not use SENVELGO in cats with diabetes mellitus who have previously been treated with insulin, who are receiving insulin, or in cats with insulin-dependent diabetes mellitus (see Contraindications).**
- **SENVELGO should not be initiated in cats with anorexia, dehydration, or lethargy at the time of diagnosis of diabetes mellitus or without appropriate screening tests (see Animal Safety Warnings).**

Description: SENVELGO® (velagliflozin oral solution) equal to velagliflozin L-proline H_2O 20.051 mg/mL, is a clear, colorless to slightly yellow, to slightly brown, liquid multi-dose preparation consisting of 1.5% w/v velagliflozin in an aqueous mixture of propylene glycol and ethanol intended for oral use in cats. SENVELGO is an orally active, sodium-glucose cotransporter 2 (SGLT2) inhibitor.

The chemical name of velagliflozin is 2-(4-cyclopropyl-benzyl)-4-((2S,3R,4R,5S,6R)- 3,4,5-trihydroxy-6-hydroxymethyltetrahydropyran-2-yl)-benzonitrile. It forms a co-crystal with L-proline ((S)-pyrrolidine-2-carboxylic acid) as a monohydrate and velagliflozin, L-proline and H2O are in 1:1:1 ratios. Its empirical formula is $C_{21}H_{25}NO_6 \times C_5H_9NO_2 \times H_2O$, its molecular formula is $C_{26}H_{34}N_2O_9$, and its structural formula is:



Indication: SENVELGO is indicated to improve glycemic control in otherwise healthy cats with diabetes mellitus not previously treated with insulin.

Dosage and Administration: Always provide the Client Information Sheet with each prescription.

Dosing Instructions:
The SENVELGO dose is 0.45 mg/lb of body weight (1 mg/kg), once daily regardless of blood glucose level. The dose may be administered directly into the mouth or with a small amount of wet food. Do not mix into food. The solution should be given at approximately the same time every day. If a dose is missed, it should be given as soon as possible on the same day. If the cat vomits within 30 minutes of dosing, the dose can be repeated.

SENVELGO should be administered using the dosing syringe provided in the package. The dosing syringe fits onto the bottle and has a body weight scale with increments per pound of body weight. The dose should be rounded down to the nearest pound. After administration, close the bottle tightly with the cap. If needed, the syringe can be cleaned with a clean, dry cloth.

Prior to initiation of treatment:
Prior to initiation of SENVELGO, the veterinarian should ensure the cat is alert, active, eating, and drinking. The veterinarian should conduct a physical examination, obtain a medical history, CBC, serum chemistry, serum fructosamine, and urinalysis including evaluation for ketonuria (see **Animal Safety Warnings**).

If there is a delay of more than a week between diagnosis of diabetes mellitus and initiation of SENVELGO, the veterinarian should re-evaluate the cat with a full physical examination and updated history to ensure the cat still meets the criteria described above. A delay of more than a week between diagnosis and starting SENVELGO may increase the risk of developing diabetic ketoacidosis.

Monitoring of cats receiving SENVELGO:
- Sudden onset of hyporexia/anorexia, lethargy, dehydration, or weight loss in cats receiving SENVELGO should prompt immediate discontinuation of SENVELGO and assessment of diabetic ketoacidosis, regardless of blood glucose level.
- **Evaluate for ketonuria 2 to 3 days after initiation of treatment and approximately 7 days after initiation of treatment and anytime the cat shows signs of illness.** If ketonuria is present, discontinue SENVELGO and promptly treat with insulin, even if blood glucose is normal.
- During the first 4 weeks after initiation of SENVELGO, glycemic control and clinical improvement should be evaluated.
  - A physical examination, blood glucose curve, serum fructosamine, and body weight should be assessed at 1 and 4 weeks after initiating SENVELGO.
  - SENVELGO should be discontinued, and initiation of insulin considered, in cats demonstrating poor glycemic control (weight loss, average blood glucose from a glucose curve > 300 mg/dL or fructosamine values suggesting poor control (> 450 µmol/L) after 4 weeks of treatment.
- During ongoing treatment with SENVELGO, blood glucose, fructosamine, urinary ketones, serum chemistry, body weight, hydration status, and clinical signs of diabetes mellitus should be routinely monitored.
  - Presence of ketonuria should prompt discontinuation of SENVELGO and transition to insulin.
  - Cats with increasing or persistently elevated triglyceride or cholesterol levels may have declining glycemic control or pancreatitis, and may be at risk of developing diabetic ketoacidosis or euglycemic diabetic ketoacidosis (diabetic ketoacidosis with normal blood glucose levels). Consider further evaluation and discontinuation of SENVELGO in these cats.
  - Increasing or persistently elevated feline pancreas-specific lipase (fPL) should prompt further evaluation for pancreatitis and consideration of discontinuation of SENVELGO.
  - Initial mild weight loss may be seen with SENVELGO associated with its mode of action (glucosuria and caloric wasting). Unintentional weight loss which doesn't improve or stabilize within 7 days may indicate the need to evaluate for concurrent disease and consideration of discontinuation of SENVELGO (see **Adverse Reactions**).
  - If clinical signs of illness occur, evaluate the cat as soon as possible to ensure it is not at risk for diabetic ketoacidosis or euglycemic diabetic ketoacidosis (see **Animal Safety Warnings**).
  - SENVELGO should be discontinued if the cat's clinical condition declines and/or glycemic control worsens after initial improvement.
- Cats may present with diabetic ketoacidosis and a normal blood glucose concentration (euglycemic diabetic ketoacidosis). Delay in recognition and treatment of diabetic ketoacidosis and euglycemic diabetic ketoacidosis may result in increased morbidity and mortality.
- Development of diabetic ketoacidosis or euglycemic ketoacidosis requires the following actions:
  - Discontinuation of SENVELGO
  - Prompt initiation of insulin therapy
  - Administration of dextrose or other carbohydrate source, regardless of blood glucose concentration
  - Appropriate nutritional support should be promptly initiated to prevent or treat hepatic lipidosis.

Contraindications: Do not use SENVELGO in cats with diabetes mellitus who have previously been treated with insulin, who are receiving insulin, or in cats with insulin-dependent diabetes mellitus. The use of SENVELGO in cats with insulin-dependent diabetes mellitus, or the withdrawal of insulin and initiation of SENVELGO, is associated with an increased risk of diabetic ketoacidosis or euglycemic diabetic ketoacidosis and death.

Warnings:
User Safety Warnings: Not for use in humans. Keep out of reach of children.

Wash hands after use. This product may cause mild eye irritation. Avoid contact with eyes. If the product accidentally gets into the eyes, rinse eyes immediately with plenty of water; if wearing contact lenses, rinse the eyes first then remove contact lens(es) and continue to rinse for 5-10 minutes. If eye irritation continues or accidental ingestion occurs, seek medical advice and provide this product information to the physician. Exposure to product may induce local or systemic allergic reaction in sensitized individuals. Oral exposure to velagliflozin may cause transient effects such as increased renal glucose excretion, increased urine volume, and hypoglycemia.

Animal Safety Warnings:
- SENVELGO should not be initiated in cats with:
  - Anorexia, dehydration, or lethargy at the time of diagnosis of diabetes mellitus as it may indicate the presence of other concurrent disease and increase the risk of diabetic ketoacidosis.
  - Ketonuria, ketonemia, or suspected diabetic ketoacidosis or a history of the same
  - Clinical suspicion of pancreatitis within the last month based on clinical signs, serum fPL > 12 mcg/L, and/or diagnostic imaging consistent with pancreatitis.
  - Chronic or unresponsive diarrhea
  - Cachexia
  - Bilirubin > 0.5 mg/dL
  - Creatinine > 2 mg/dL
- SENVELGO may cause a mild increase in serum creatinine, blood urea nitrogen (BUN), phosphorus, and sodium in cats with or without chronic kidney disease within weeks of starting therapy, followed by a stabilization of values.
- Cats with baseline creatinine between 1.6 and 2 mg/dL when SENVELGO treatment is started should be closely monitored for signs of volume depletion/dehydration and body weight loss. Renal function should be monitored within the first week of treatment initiation and then according to standard chronic kidney disease guidelines. SENVELGO has not been evaluated in cats with baseline creatinine > 2 mg/dL.
- Cats should be screened for urinary tract infections and treated, if indicated, when initiating SENVELGO. Cats treated with SENVELGO should be monitored for urinary tract infections and treated promptly.
- Cats should be evaluated for concurrent disease including pancreatitis, infectious disease, urinary tract infection, neoplasia, and hypersomatotropism (acromegaly) before initiating and while receiving SENVELGO as these conditions may increase the risk of developing diabetic ketoacidosis.
- Persistently low or worsening serum chloride values compared to the pre-treatment value may indicate the development of diabetic ketoacidosis or euglycemic diabetic ketoacidosis.
- SENVELGO may cause increased serum calcium and persistent elevations may require additional diagnostics. Persistent elevated calcium has been associated with increased risk of calcium-containing urolith formation in other SGLT2 inhibitors.
- Cats should be closely monitored for development of diabetic ketoacidosis or euglycemic diabetic ketoacidosis (for example, ketonuria or anorexia) after stopping SENVELGO. Euglycemia may persist for 2 to 3 days after stopping SENVELGO.
- Keep SENVELGO in a secure location out of reach of dogs, cats, and other animals to avoid accidental ingestion or overdose.

Precautions:
- Consider temporarily discontinuing SENVELGO during times of decreased caloric intake, such as surgery or decreased appetite, as continued administration of SENVLEGO may increase the risk of diabetic ketoacidosis.
- SENVELGO contains propylene glycol. When cats are administered SENVELGO at the 1 mg/kg/day dose, cats receive 40 mg/kg/day of propylene glycol. Exceeding 80 mg/kg/day of propylene glycol may result in excess hepatic glycogen stores. Use caution when administering SENVELGO to cats receiving other products that contain propylene glycol.
- Glucosuria may persist for 2-3 days after stopping SENVELGO. In cats receiving SENVELGO, glucosuria is not a reliable indicator for monitoring glycemic control.
- The safety and effectiveness of SENVELGO has not been evaluated in cats with chronic kidney disease (IRIS (International Renal Interest Society) Stages 3 and 4).
- The concurrent use of volume depleting drugs in cats treated with SENVELGO has not been evaluated.
- SENVELGO has not been evaluated with concurrent use of insulin or other blood glucose lowering treatments.
- The safety and effectiveness of SENVELGO in breeding, pregnant, and lactating cats has not been evaluated.

Adverse Reactions:
Two hundred fifty-two (252) cats with diabetes mellitus were enrolled in a 180-day multicenter field study. Safety data were evaluated in 252 cats treated with at least one dose of SENVELGO. Regardless of blood glucose level, cats received SENVELGO at a dose of 0.45 mg/lb once daily. The most common adverse reactions were diarrhea or loose stool, weight loss, vomiting, polyuria, polydipsia, and elevated blood urea nitrogen (BUN). The table below summarizes the adverse reactions reported in the study.

Adverse Reactions	Frequency (N=252) Number (%)
Diarrhea (including loose stool)	132 (52.3%)
Weight loss*	111 (44%)
Vomiting	92 (36.5%)
Polyuria	46 (18.3%)
Polydipsia	42 (16.7%)
BUN†	39 (15.5%)
Anorexia or hyporexia	34 (13.5%)
Hypersalivation and/or gagging	33 (13.1%)
Urine specific gravity > 1.060	29 (11.5%)
Dehydration	28 (11.1%)
Lethargy	20 (7.9%)
Polyphagia	19 (7.5%)
Urinary tract infections/cystitis	18 (7.1%)
Diabetic ketoacidosis or euglycemic diabetic ketoacidosis‡	18 (7.1%)
Hypercalcemia	16 (6.3%)
Ketonuria§	14 (5.6%)
Inappropriate urination	14 (5.6%)
Death or euthanasia	13 (5.2%)
Elevated AST and/or ALT**	12 (4.8%)
Hypertriglyceridemia††	12 (4.8%)
Hyperphosphatemia	12 (4.8%)
Elevated fPL	11 (4.4%)
Pancreatitis	10 (4.0%)
Elevated creatinine	9 (3.6%)
Hepatic lipidosis	6 (2.4%)
Urinary incontinence	3 (1.2%)

* Approximately 80 cats had weight loss during the first week of treatment, likely due to dehydration and/or caloric wasting from glucosuria.

† Most cats had elevations ≤ 1.5X upper limit of normal (ULN).

‡ All but 5 cases occurred within 2 weeks of starting SENVELGO. Twelve of these cats had euglycemic diabetic ketoacidosis.

§ These cats did not progress to diabetic ketoacidosis and all but one developed ketonuria within a week of starting SENVELGO. The cats discontinued SENVELGO and transitioned to insulin.

** Four of these cats had AST (aspartate aminotransferase) and/or ALT (alanine aminotransferase) > 2X ULN.

†† These cats sometimes also had elevated cholesterol.

The following adverse reactions were seen in the study with < 1% frequency: elevated creatine kinase (> 3X ULN), hypoglycemia without clinical signs (glucose ≤ 50 mg/dL), anemia, abnormal behavior, bradycardia, and dermatitis.

Ketonuria and diabetic ketoacidosis: Thirty-two (32) cats developed ketonuria, diabetic ketoacidosis or euglycemic diabetic ketoacidosis and were removed from the study. Twenty-six (26) of these cats developed ketonuria, diabetic ketoacidosis, or euglycemic diabetic ketoacidosis within the first 7 days of treatment with SENVELGO. Thirteen (13) of these cats developed ketonuria without further progression to diabetic ketoacidosis or euglycemic ketoacidosis and were transitioned to insulin. An additional thirteen (13) cats developed diabetic ketoacidosis or euglycemic ketoacidosis. Nine cats recovered after hospitalization and intensive treatment. Three of the 9 cats had concurrent conditions: hepatopathy (1), hepatic lipidosis (1), and pancreatitis and hepatic lipidosis (1). Four of the 13 cats were euthanized; three because the owners declined treatment and one cat was euthanized after not responding to hospitalization and intensive treatment.

Six cats developed ketonuria, diabetic ketoacidosis or euglycemic diabetic ketoacidosis after the first 7 days of treatment. One cat developed ketonuria without progression to diabetic ketoacidosis or euglycemic ketoacidosis after more than 4 months on SENVELGO. Five cats developed diabetic ketoacidosis or euglycemic ketoacidosis. Two cats (one with concurrent pancreatitis and hepatic lipidosis) were treated and recovered. One with concurrent pancreatitis was treated and recovered but died several days later. Two of the five cats were euthanized; one cat was euthanized after poor response to hospitalization and intensive therapy; and one was euthanized due to declining condition unrelated to diabetic ketoacidosis.

Thirty-eight enrolled cats had been previously treated with insulin. Of those 38 cats, 12 (32%) developed ketonuria, diabetic ketoacidosis, or euglycemic diabetic ketoacidosis during the first week and were removed from the study. These 12 cats are included in the 26 cases reported above and represent 46% of the cases removed in the first week of treatment due to ketonuria or ketoacidosis.

Death and euthanasia: Nineteen cats died (3) or were euthanized (16) during the study, or shortly following removal from the study, with thirteen possibly related to SENVELGO use or declining glycemic control. In addition to 6 of the cases associated with diabetic ketoacidosis described above, euthanasia was associated with the following conditions (number of cats): acute renal failure within a week of starting SENVELGO (1), worsening or emergent urinary incontinence associated with poor glycemic control (2), worsening polyuria/polydipsia and inappropriate urination (1), progressive signs of diabetes mellitus (1), declining condition and suspected pancreatitis (1), azotemia and lack of effect within a week of starting SENVELGO and possible concurrent hypersomatotropism (1).

Contact Information: To report suspected adverse drug events, for technical assistance, or to obtain a copy of the Safety Data Sheet (SDS), contact Boehringer Ingelheim Animal Health at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae.

Information for Cat Owners: Please provide and review the Client Information Sheet with cat owners to ensure they understand the entire contents before SENVELGO is administered. The Client Information Sheet contains important information regarding the use of SENVELGO. Owners should be advised to discontinue SENVELGO and contact a veterinarian immediately if their cat develops anorexia, lethargy, vomiting, diarrhea, or weakness.

Clinical Pharmacology:

Mechanism of Action:

Velagliflozin is an inhibitor of sodium-glucose cotransporter 2 (SGLT2), the renal transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation. By inhibiting SGLT2, velagliflozin reduces the reabsorption of filtered glucose and lowers the renal threshold for glucose, thereby increasing urinary glucose excretion.

Pharmacokinetics: In a laboratory study conducted to determine the prandial state of maximum exposure, systemic exposure for velagliflozin was greater in the fasted state than in the fed state by 170% for the mean maximum observed plasma concentration (C_{max}), and by 45% for the mean area under the plasma concentration versus time curve (AUC) from dosing (time 0) to the last quantifiable concentration ($AUC_{0\text{-}last}$), respectively.

In a well-controlled, laboratory margin of safety study in healthy, adult cats (see **Target Animal Safety**), after repeat daily oral dosing for six months, a slight to moderate increase in exposure to velagliflozin was observed. In addition, a tendency for a less than dose proportional increase of maximum plasma concentration (C_{max}) and exposure (AUC) over the tested dose range was noted.

Following oral administration of SENVELGO in cats at 1 mg/kg, velagliflozin was rapidly absorbed with a median time to maximum concentration of 0.25 hours. The velagliflozin mean (± standard deviation) C_{max} was 1030 (± 361) ng/mL and the mean $AUC_{0\text{-}last}$ to the last quantifiable plasma concentration was 3295 (± 1098) day*ng/mL. The elimination half-life of velagliflozin was 3.68 (± 0.34) hours.

Effectiveness: Two hundred and fifty-two (252) cats diagnosed with diabetes mellitus were enrolled in a 180-day multicenter field study. The cats included various purebred and mixed breed cats ranging in age from 4 to 18 years and in weight from 5.7 to 26.5 lbs (2.6 to 12 kg). Cats were administered SENVELGO at a dose of 0.45 mg/lb (1 mg/kg) orally, once daily, regardless of blood glucose level, beginning on Day 0. Cats were evaluated at Days 2 or 3, and Days 7 and 30 and then monthly.

Treatment success was evaluated on Day 30 and was defined as improvement in at least one clinical sign of diabetes mellitus (polyuria, polydipsia, unintended weight loss, polyphagia, or diabetic neuropathy) and improvement in at least one blood glucose variable (blood glucose curve mean or serum fructosamine).

Of 198 cats included in the effectiveness-evaluable population:

- 175 cats (88.4%) were considered a treatment success on Day 30 (lower bound of the two-sided 90% confidence interval was 84%).
- Mean blood glucose decreased from 446.4 mg/dL (single fasted sample) prior to Day 0 to 169.8 mg/dL (blood glucose curve mean) on Day 30
- Mean fructosamine levels decreased from 551.4 µmol/L prior to Day 0 to 332.0 µmol/L on Day 30.
- Improvements in the clinical signs of polyuria, polydipsia, body weight, polyphagia, and diabetic neuropathy on Day 30 were observed in 125/177 (71%), 128/176 (73%), 133/167 (80%), 33/80 (41%), and 7/30 cats (23%), respectively.
- 157 cats completed the 180-day study

Target Animal Safety: In a well-controlled laboratory margin of safety study, SENVELGO was administered orally to fasted, healthy, 8 to 9 month old cats at 0, 1, 3, or 5 mg/kg body weight (corresponding to 1X, 3X or 5X the intended labeled point dose of 1 mg/kg) once daily for 26 weeks (6 months). Control cats (0 mg/kg) received saline at a volume equal to the 5 mg/kg dose. There were eight cats per group (4 females, 4 males). All cats survived the study and there were no SENVELGO-related effects on ophthalmic examinations, indirect systolic blood pressure measurements, and blood coagulation parameters. Hypersalivation and vomiting after dose administration occurred infrequently and was only observed in the groups that received SENVELGO.

During physical examinations on Days 14 and 28, there was a drug-related decrease in heart rate (< 140 bpm) in the cats that received SENVELGO compared to the control cats. There were no other drug-related effects on physical examinations.

Polydipsia, glucosuria, decreased urine creatinine, and diarrhea were reported more frequently in cats that received SENVELGO than in control cats.

Reddish, mucoid feces were observed in three instances in the 1X group cats. One cat in the 5X group had decreased activity, vomiting, and reduced feed consumption for one day, and reddened rectal mucous membranes were observed over the next 5 days. Two cats (3X and 5X groups) were each observed to have a reddened prepuce with white-yellow discharge twice during the study that was not associated with abnormal urinalyses.

Food consumption was higher in the cats that received SENVELGO compared to the control cats. The rate of body weight gain was lower in the 5X group cats compared to cats in the control, 1X and 3X groups.

There were drug-related increases in reticulocyte count, mean corpuscular hemoglobin, mean corpuscular volume, and Heinz body percentage, and a decrease in mean corpuscular hemoglobin concentration in the cats that received SENVELGO compared to control cats. None of the cats showed any clinical signs of anemia and the number of erythrocytes, hemoglobin, and hematocrit values were normal. There was no effect of SENVELGO on white blood cells and platelets.

There were drug-related increases in serum magnesium, albumin, cholesterol, and triglycerides in the cats that received SENVELGO, with some magnesium, serum albumin and triglyceride values above the reference range. There was a drug-related decrease in mean BUN in the cats that received SENVELGO. There were no other treatment-related changes in serum chemistry parameters, including serum glucose and symmetric dimethylarginine (SDMA).

A reticular pattern was observed on the surface of the liver of one control, three 1X, four 3X, and three 5X group cats.

How Supplied: SENVELGO (velagliflozin oral solution) 15 mg/mL, 30 mL nominal fill volume is supplied in a 45 mL plastic bottle with dosing syringe.

NDC 0010-4614-01

Storage Information: SENVELGO can be stored at or below 77°F (25°C) with excursions permitted up to 104°F (40°C). Once the bottle is opened, use the contents within six months.

Approved by FDA under NADA # 141-568

Marketed by:
Boehringer Ingelheim Animal Health USA Inc.
Duluth, GA 30096

Revised 06/2023

Boehringer Ingelheim

SATURDAY, OCTOBER 14, 2023

Schedule is in Central Daylight Time

TIME	SESSION TITLE		SPEAKER	ROOM	SPONSOR/ PARTNER
6:00 - 7:00 am	Early Riser Yoga Class*	IPO		Sheraton Hotel - Heritage Ballroom	
6:45 - 8:00 am	Breakfast			Ballroom Foyer	
7:00 - 7:50 am	*Breakfast Symposium*: Controlling OA Pain in Cats: Where Do I Start?	LS	Drs. Joyce Login & Michelle Meyer	Ballroom B	zoetis
8:00 - 8:50 am	Nutritional Management of Diabetes Mellitus	LS	Dr. Audrey Cook	Ballroom A	Boehringer Ingelheim
	The Feline Philosophy Behind Diagnosing GI Disease	LS	Dr. Craig Webb	Ballroom B	IDEXX
	Technician: Sippin' Through Straws: Taking the Stress Out of Feline Neonate Tube Feeding	LS	Ellen Carozza	Ballroom C	sleepypod
8:55 - 9:45 am	Nuanced Nutrition: Calcium Oxalate Urolithiasis	LS	Dr. Audrey Cook	Ballroom A	Dechra
	The Feline Pyramid of Poop	LS	Dr. Craig Webb	Ballroom B	endoscopy support services, inc.
	Technician: Chew With Your Mouth Closed! Preventing Food Phobias & Fighting at the Dinner Table in the Multi-cat Household	LS	Ellen Carozza	Ballroom C	sleepypod
9:45 - 11:00 am	Networking Refreshment Break			Exhibit Hall	Boehringer Ingelheim
9:50 - 10:15 am	AAFP Membership Meeting	LS		Ballroom C	
10:20 - 10:50 am	ABVP: Is it for Me?	LS		Ballroom C	ABVP
11:00 - 11:25 am	Cobalamin: Diagnostic & Therapeutic Implications	LS	Dr. Audrey Cook	Ballroom A	Dechra
11:00 - 12:15 pm	No Way Out! Constipation, Obstipation, Megacolon: Panel Discussion	LS	Drs. Adam Rudinsky, Betsy Swanson, & Craig Webb	Ballroom B	ROYAL CANIN
	Technician: RECOVER CPR Guideline Updates: Feline Focus	LS	Ken Yagi	Ballroom C	NAVTA
11:25 - 12:15 pm	Modifying the Microbiome: The Role of Probiotics in Feline Practice	LS	Dr. Audrey Cook	Ballroom A	visbiome vet.
12:15 - 1:40 pm	Lunch			Exhibit Hall	
12:30 - 1:30 pm	*Lunch & Learn #1:** Feline GI Immunity's Inextricable Links to Dietary & Microbiome Components	IPO	Dr. Alison Manchester	102 - 104	PRO PLAN VETERINARY DIETS
12:30 - 1:30 pm	*Lunch & Learn #2:** Why is This Kitty Skinny? What Should I Do About It?	IPO	Dr. Jessica Pritchard	105 - 107	Dechra
12:30 - 1:30 pm	*Lunch & Learn #3:** Let's Get Digital: How Smart Pet Tech Can Make a Big Impact on Cat Care	IPO	Dr. Sheryl Gamble	113 - 115	MERCK Animal Health
1:40 - 2:30 pm	Management of Liver Disease	LS	Dr. Adam Rudinsky	Ballroom A	wedgewood PHARMACY
	Diagnostic Testing in Feline Chronic Enteropathy Demonstrates Evolution from Inflammatory Bowel Disease to Intestinal Lymphoma	LS	Dr. Anne Avery	Ballroom B	PRO PLAN VETERINARY DIETS
	Technician: Nursing & Nutrition for the Critical Feline Patient Who Just Won't Eat!	LS	Dr. Ashlie Saffire	Ballroom C	ROYAL CANIN
2:30 - 3:15 pm	Networking Refreshment Break			Exhibit Hall	Boehringer Ingelheim
3:15 - 4:05 pm	Liver & Biliary System: Peri-Operative Care, Surgical Evaluation, & Diagnostic Sampling	LS	Dr. Betsy Swanson	Ballroom A	
	The Role of Microbiome: Supporting, Immune Modulating, & Stress Lessening Probiotics in GI Diseases	LS	Dr. Michael Lappin	Ballroom B	PRO PLAN VETERINARY DIETS
	Technician: Discussing Diabetes Mellitus: Empowering Technicians	LS	Ken Yagi	Ballroom C	Boehringer Ingelheim
4:10 - 5:00 pm	Interpreting Liver Biopsies	LS	Dr. Adam Rudinsky	Ballroom A	IDEXX
	Update on the Diagnosis & Management of Infectious GI Diseases	LS	Dr. Michael Lappin	Ballroom B	PRO PLAN VETERINARY DIETS
	Technician: Practical Application of Feline Emergency Transfusions	LS	Ken Yagi	Ballroom C	NAVTA
5:00 - 5:30 pm	Cat Friendly Practice®: Because You're Worth It	LS	Dr. Kelly St. Denis	Ballroom C	Cat Friendly Practice

LS Live Streamed

IPO In-person Only

*Separate registration required. No fees associated.

SUNDAY, OCTOBER 15, 2023

Schedule is in Central Daylight Time

TIME	SESSION TITLE		SPEAKER	ROOM	SPONSOR/ PARTNER
6:45 - 8:00 am	Breakfast			Ballroom Foyer	
7:00 - 7:50 am	*Breakfast Symposium*: Feline Constipation: Updates on Acute & Chronic Treatment Modalities	LS	Dr. Ashlie Saffire	Ballroom B	ROYAL CANIN
7:30 - 10:00 am	Cat Friendly Interactions & Handling Workshop**	IPO	Dr. Ilona Rodan	110 & 111	Ceva, ROYAL CANIN, sleepypod, TICA
8:00 - 8:50 am	Approach to the Vomiting Cat: Causes, Treatment, & Management	LS	Dr. Adam Rudinsky	Ballroom A	ROYAL CANIN
	Stem Cells in Feline GI Disease	LS	Dr. Craig Webb	Ballroom B	VetStem, EveryCAT
8:55 - 9:45 am	Approach to Diarrhea in Kittens	LS	Dr. Adam Rudinsky	Ballroom A	ROYAL CANIN
	Diagnostic Dilemmas: The History, Mystery, & Bemoaning of Feline Triaditis	LS	Dr. Craig Webb	Ballroom B	IDEXX
9:45 - 10:45 am	Networking Refreshment Break			Exhibit Hall	Boehringer Ingelheim
10:45 - 11:35 am	Feline Pancreatic Disease: Familiar Friends & Missed Connections	LS	Dr. Adam Rudinsky	Ballroom A	IDEXX
	Feline Chronic Enteropathy	LS	Dr. Craig Webb	Ballroom B	ROYAL CANIN
11:40 - 12:30 pm	Approach to the Yellow Cat	LS	Dr. Adam Rudinsky	Ballroom A	IDEXX
	FMT: What's Coming Down the Pipeline	LS	Dr. Craig Webb	Ballroom B	VetStem
12:30 - 1:45 pm	Lunch			Exhibit Hall	
12:40 - 1:40 pm	*Lunch & Learn #1:* * Elevate Your Practice's Feline Wellness at Every Life Stage	IPO	Dr. Matt McGlasson	102 - 104	basepaws
12:40 - 1:40 pm	*Lunch & Learn #2:* * Cats Don't Read Textbooks: The Conundrums of Diagnosing Feline Hyperthyroidism	IPO	Dr. Kelly St. Denis	105 - 107	ZOMEDICA
12:40 - 1:40 pm	*Lunch & Learn #3:** Don't Sugar Coat It: Treatment Options for the Diabetic Cat	IPO	Dr. Cynthia Ward	113 - 115	Elanco
1:45 - 2:35 pm	Emerging or Just Ignored: Ductal Plate Malformations	LS	Dr. Adam Rudinsky	Ballroom A	Blue Buffalo Natural Veterinary Diet
	The Vomiting Cat: Probing for Answers in the Older Cat	LS	Dr. Jennifer Babineaux	Ballroom B	
2:40 - 3:30 pm	Feline Gastrointestinal Eosinophilic Sclerosing Fibroplasia	LS	Dr. Petra Cerna	Ballroom A	
	The Vomiting Cat: Probing for Answers in the Younger Cat	LS	Dr. Jennifer Babineaux	Ballroom B	
3:30 pm	Conclusion of Conference				

LS Live Streamed

IPO In-person Only

*Separate registration required. No fees associated.

**Separate registration required. Additional fees apply.

NEW

Varenzin™-CA1

A REVOLUTIONARY NEW TREATMENT IN THE FIGHT AGAINST CKD-RELATED ANEMIA

The innovative, easy-to-administer oral option that safely treats anemia in cats with chronic kidney disease.

Indication: Varenzin-CA1 is indicated for the control of nonregenerative anemia associated with chronic kidney disease (CKD) in cats.

Important Safety Information: For oral use in cats only. Keep this drug, including used syringes, out of reach of children. Wash hands immediately after use. In case of accidental ingestion, seek medical advice immediately. Women who are pregnant or may become pregnant should administer the product with caution. Varenzin-CA1 should not be administered to cats that are pregnant, lactating or intended for breeding or to cats with known hypersensitivity to molidustat. Use with caution in cats with a history of seizures and in cats predisposed to thromboembolic disease. Hematocrit (HCT) or packed cell volume (PCV) levels should be monitored regularly as polycythemia may result from use of Varenzin-CA1. Varenzin-CA1 has not been evaluated in cats less than 1 year of age. The most common adverse reactions included vomiting, increases in systolic blood pressure and mild transient increase in serum potassium. For full prescribing information visit the Elanco Booth or call 1-888-545-5973.

Elanco™

Elanco

Varenzin™-CA1

(molidustat oral suspension)

Hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor

25 mg/mL

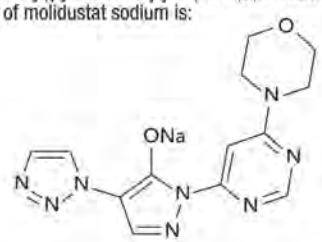
For oral use in cats only

Conditionally approved by FDA pending a full demonstration of effectiveness under application number 141-571. It is a violation of Federal law to use this product other than as directed in the labeling.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION

Varenzin-CA1 (molidustat oral suspension) is a white to yellow-white oily suspension. Each mL of Varenzin-CA1 contains 25 mg of molidustat sodium. The inactive ingredients are glycerol dibehenate, fish oil, sunflower oil, butylhydroxytoluene, and sorbic acid. The empirical formula is $C_{13}H_{13}N_8O_2Na$ and the molecular weight is 336.28. The chemical name is Sodium 1-[6-(morpholin-4-yl)pyrimidin-4-yl]-4-(1H-1,2,3-triazol-1-yl)-1H-pyrazol-5-olate. The chemical structure of molidustat sodium is:



INDICATION

Varenzin-CA1 is indicated for the control of nonregenerative anemia associated with chronic kidney disease (CKD) in cats.

DOSAGE AND ADMINISTRATION

Shake well before use.

The dosage of Varenzin-CA1 is 2.3 mg/lb (5 mg/kg) body weight (bw) administered orally once daily for up to 28 consecutive days. Treatment may be repeated after a minimum 7-day pause (see **Monitoring and Repeating Treatment**). Varenzin-CA1 should be administered using the dosing syringe provided in the package. The dosing syringe is marked in increments of 0.1 mL. The dose should be rounded up to the nearest 0.1 mL.

Dosing Information

To ensure the correct dose is administered, body weight should be determined prior to starting treatment.

Table 1. Dosing Chart

Weight Range in pounds (lb)	Volume of Varenzin-CA1 (mL)
3.4 to 4.4	0.4
4.5 to 5.5	0.5
5.6 to 6.6	0.6
6.7 to 7.7	0.7
7.8 to 8.8	0.8
8.9 to 9.9	0.9
10 to 11	1
11.1 to 12.1	1.1
12.2 to 13.2	1.2

Note: The syringe included with the Varenzin-CA1 product cannot be used to accurately dose cats weighing under 3.4 pounds. Cats greater than 13.2 lb bw should be treated with a dose of 2.3 mg/lb bw rounded up to the nearest 0.1 mL.

Administration

Shake well before use. Remove screw cap. Use the enclosed syringe for each treatment. Place the syringe nozzle firmly into the opening of the bottle. Turn the bottle upside down and withdraw the necessary volume. Turn the bottle back into an upright position before removing the syringe. The product should be administered with the syringe into the cat's mouth. See illustrations 1 through 4 below for administration steps:

Step 1:

Step 2:

Step 3:

Step 4:

After administration, close bottle tightly with cap and store syringe in the carton together with the product. Do not disassemble or wash the syringe.

The product should be given once daily for up to 28 consecutive days. If the cat vomits after consuming any portion of the dose, the cat should not be re-dosed and should be considered as dosed for the day.

Monitoring and Repeating Treatment

Treated cats should initially have their hematocrit (HCT) or packed cell volume (PCV) levels monitored weekly beginning about the 14th day of the 28-day treatment cycle to ensure HCT or PCV does not exceed the upper limit of the reference range. Discontinue Varenzin-CA1 if HCT or PCV exceeds the upper limit of the reference range.

After treatment cessation the hematocrit level should be periodically checked (for example, weekly, every 2 weeks or monthly). When the HCT or PCV level declines below the lower limit of the reference range, a new treatment cycle should be started. The interval between treatment cycles will vary between cats and may change over time for an individual cat but should be at least 7 days.

If a cat does not respond to treatment after 3 weeks (see **REASONABLE EXPECTATION OF EFFECTIVENESS**), it is recommended to re-examine the animal for any other underlying condition that may contribute to anemia, such as iron deficiency, inflammatory diseases or blood loss. It is advised to treat the underlying condition before restarting treatment with Varenzin-CA1.

CONTRAINDICATIONS

Varenzin-CA1 should not be administered to cats with known hypersensitivity to molidustat or to any of the inactive ingredients.

Varenzin-CA1 should not be administered to cats that are pregnant, lactating, or intended for breeding. In an embryo-fetal-developmental toxicity study in rats, an increase incidence of ocular malformations such as flat eye rudiments and microphthalmia were observed at doses of 30 mg/kg bw per day. These effects may be due to an increase in oxygen availability, caused by molidustat-induced polycythemia. Localized hypoxia is an important factor in normal eye development. Developmental toxicity studies have not been conducted in cats. Available animal data have shown excretion of other HIF-PH inhibitors into milk. It is unknown whether molidustat is excreted into the milk of lactating cats.

WARNINGS

User Safety Warnings

Not for use in humans.

Keep this drug, including used syringes, out of reach of children. Wash hands immediately after use and/or spillage.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician. Symptoms of exposure to molidustat may include the following: gastrointestinal effects (nausea, vomiting, diarrhea), blood and clotting effects (increases in reticulocytes, erythropoietin, and hemoglobin), dizziness, fainting, hypertension, changes in cardiac output and cardiac index, and increases in heart rate.

Symptoms may not occur immediately; therefore, the exposed individual should be monitored. People with known hypersensitivity to molidustat sodium should avoid direct contact with this product and should administer the product with caution.

Women who are pregnant or may become pregnant should administer the product with caution. Molidustat administered orally to pregnant rats during the period of organogenesis was associated with adverse fetal outcomes (see **CONTRAINDICATIONS**).

Do not eat, drink, or smoke while handling this product.

Animal Safety Warnings

Keep Varenzin-CA1 in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

PRECAUTIONS

Varenzin-CA1 has been associated with thromboembolic disease (see **ADVERSE REACTIONS**).

Use with caution in cats that may be predisposed to thromboembolic disease.

Use with caution in cats with a history of seizures (see **ADVERSE REACTIONS**).

Phosphate binders or other products containing multivalent cations such as calcium, iron, magnesium or aluminum have been shown to chelate with other HIF-PH inhibitors. Based on information in humans, consider staggered administration of Varenzin-CA1 and phosphate binders and iron supplements (at least 1 hour apart), if possible, to prevent potentially decreasing absorption of molidustat.

Polycythemia may result from use of Varenzin-CA1. When starting Varenzin-CA1, cats should have their hematocrit (HCT) or packed cell volume (PCV) levels monitored regularly during the treatment cycle to ensure HCT or PCV does not exceed the upper limit of the reference range (see **DOSAGE AND ADMINISTRATION**). Clinical signs associated with polycythemia found in preapproval studies in healthy cats included changes in mucous membrane color, slightly prolonged capillary refill time, heart pounding, and tachycardia (see **TARGET ANIMAL SAFETY**). Polycythemia after Varenzin-CA1 administration was also associated with increases in serum potassium, creatinine, serum phosphorus, and systolic blood pressure, which were not associated with clinical signs (see **ADVERSE REACTIONS** and **TARGET ANIMAL SAFETY**).

The use of Varenzin-CA1 administered concurrently with other erythropoiesis-stimulating agents, including recombinant erythropoietin drugs, has not been studied.

The safe use of Varenzin-CA1 has not been evaluated in cats less than 1 year of age.

ADVERSE REACTIONS

The safety of Varenzin-CA1 was evaluated in a masked, controlled 28-day field study to evaluate the effectiveness of molidustat oral suspension (not commercial formulation) for the control of nonregenerative anemia associated with CKD in cats (see **REASONABLE EXPECTATION OF EFFECTIVENESS**). Enrollment included 21 cats; 15 cats were treated with Varenzin-CA1, and 6 cats were administered a vehicle control. Eight of these cats were subsequently enrolled in an extended open-label safety study for up to 8 additional weeks. Cats were dosed daily for 28 days. Vomiting was the most frequently reported adverse event, observed in 6/15 (40%) cats in the molidustat group and no cats in the control group. Increases in systolic blood pressure and mild transient increases in serum potassium were also observed. The most serious adverse event was a cat in the molidustat group that presented, after 28 days of treatment, in lateral recumbency with a cold front leg from a suspected thromboembolism and was euthanized.

The safety of Varenzin-CA1 was evaluated in an interim analysis of data collected in an open label safety phase of an ongoing clinical field effectiveness and safety study. Varenzin-CA1 was administered for 28 consecutive days, followed by a treatment pause of at least 7 days, then treatment was repeated for up to 4 treatment cycles. The study evaluated 55 client-owned cats with nonregenerative anemia (PCV < 28%) secondary to CKD that had received at least one dose of Varenzin-CA1 at 5 mg/kg bw in the safety phase. Cats had a mean age of 13 years (range 5.2 to 23.4) and initial body weights between 2.3 to 5.9 kilograms. At baseline just prior to enrollment into the study, 31%, 47%, and 22% of cats were in International Renal Interest Society (IRIS) Stage 2, 3, and 4 CKD, respectively (to learn more about IRIS staging, visit http://www.iris-kidney.com/index.html).

Vomiting was the most frequently reported adverse event, either alone or with other events, and was reported at least once in 29/55 (52.7%) of the cats in the study. Vomiting was more frequent on treatment days than during treatment pause.

Two cats had seizures during the study. One cat had a seizure associated with severe uremia, severe anemia, and dehydration. One cat, which had a history of a seizure about 1 year prior, had a seizure during the study and severe hypertension.

Nineteen cats died or were euthanized before completion of the safety phase of the study due to worsening CKD or declining quality of life, and one cat was euthanized due to an abdominal mass.

CONTACT INFORMATION

To report suspected adverse drug reactions, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Elanco US Inc. at 1-888-545-5973.

For additional information about reporting adverse drug experiences for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae.

CLINICAL PHARMACOLOGY

Mechanism of Action

Varenzin-CA1 (molidustat oral suspension) is a competitive and reversible inhibitor of hypoxia-inducible factor prolyl hydroxylase (HIF-PH). The inhibition of HIF-PH induces a dose-dependent increase of endogenous erythropoietin (EPO) by stabilizing HIF, resulting in increased erythropoiesis (red blood cell production).

Pharmacokinetics

The pharmacokinetic parameters of Varenzin-CA1 after a single oral dose of 2.5, 5, and 10 mg/kg bw and intravenous dose of 5 mg/kg bw were evaluated in a laboratory study in which 8 healthy, young adult cats (4 neutered males, 4 spayed females) received Varenzin-CA1 orally or molidustat sodium aqueous suspension intravenously, utilizing a crossover study design. Following oral administration, molidustat was rapidly absorbed.

Table 2: Mean (± standard deviation) pharmacokinetic parameters of molidustat following a single oral or intravenous dose of 5 mg/kg in cats:

Route	Oral	Intravenous
T_{max}† (hour)	1 (0.67 – 1.5)	Not Applicable
C_{max} (µg/mL)	3.86 ± 0.495	26.0 ± 8.42††
AUC_{last} (hour*µg/mL)	13.0 ± 2.98	16.5 ± 2.97
AUC_{inf} (hour*µg/mL)	13.1 ± 2.99	16.6 ± 3.01
$T_{1/2}$ (hour)	4.68 ± 0.661	6.28 ± 4.43

† Median and range are reported for T_{max} instead of arithmetic mean and standard deviation

†† C_0 back-extrapolated concentration at time 0 by a log-linear regression of first 2 data points following intravenous administration

C_{max}: Maximum observed plasma concentration

T_{max}: Time to maximum observed plasma concentration

AUC_{last}: Area under the plasma concentration versus time curve from time of dosing to the last quantifiable concentration

AUC_{inf}: Area under the plasma concentration versus time curve from time of dosing extrapolated to infinity

$T_{1/2}$: Terminal elimination half-life

The pharmacokinetic parameters of molidustat after 6 daily oral doses of 5 mg/kg bw were evaluated in a second laboratory study using 8 healthy, young adult cats (4 neutered males, 4 spayed females). Minimal accumulation of molidustat in the plasma pharmacokinetic profile was observed in the study.

REASONABLE EXPECTATION OF EFFECTIVENESS

A reasonable expectation of effectiveness may be demonstrated based on evidence such as, but not limited to, pilot data in the target species or studies from published literature.

Varenzin-CA1 is conditionally approved pending a full demonstration of effectiveness.

Additional information for Conditional Approvals can be found at www.fda.gov/animalca.

A reasonable expectation of effectiveness for Varenzin-CA1 for the control of nonregenerative anemia associated with CKD in cats is supported by a 28-day, masked, randomized, controlled field study. The study was conducted at 23 U.S. and 10 European Union veterinary clinics. The study included 21 client-owned cats with nonregenerative anemia associated with CKD. The enrolled cats weighed 2 to 6 kg and ranged from 4 to 17 years of age. The enrolled cats were randomized to treatment with molidustat oral suspension (not commercial formulation) (n=15) or vehicle control (n=6). Cats were dosed based on body weight at a minimum dose of 5 mg molidustat/kg bw or an equivalent volume of vehicle control, administered orally once daily for 28 days. One molidustat-treated cat, which was dehydrated on Study Day 28, was excluded from the Study Day 28 effectiveness analysis because the dehydration may have affected the cat's HCT results. Treatment success was based on an absolute increase of ≥4 percentage points in HCT observed on Study Day 28 compared to Study Day 0, or a relative increase of 25% in HCT on Study Day 28 compared to Study Day 0. The treatment success rate in the molidustat-treated group was numerically superior to the vehicle control group on Study Day 28 (50% [7/14] vs. 16.7% [1/6]). Eight cats from the effectiveness phase were enrolled in a continuation phase, which lasted an additional 56 days, and received, depending on their PCV, either 2.5 mg/kg or 5 mg/kg bw of the same molidustat oral suspension formulation. The continuation phase was a multi-center, unmasked, non-randomized, uncontrolled field safety and effectiveness study. During the continuation phase of the study, PCV was evaluated weekly, and HCT was evaluated on Study Days 56 and 84 (± 2 days). Treatment success for each cat during the continuation phase was defined the same as during the 28-day study. On Study Day 56, 75% (6/8) of the cats were considered successes and on Study Day 84, 62.5% (5/8) of the cats were considered successes.

TARGET ANIMAL SAFETY

The safety of Varenzin-CA1 was established in 2 laboratory studies and 2 field safety and effectiveness studies (see **REASONABLE EXPECTATION OF EFFECTIVENESS** for details on the first field study).

Target Animal Safety Study

In a laboratory study, molidustat oral suspension (not commercial formulation) was administered orally to healthy 10 to 11-month-old male cats (6 cats per group) at doses of 2.5 mg/kg bw or 5 mg/kg bw daily for 56 or 28 consecutive days, respectively. Cats administered 2.5 mg molidustat/kg bw were euthanized on Study Day 57, and cats administered 5 mg molidustat/kg bw were euthanized on Study Day 29. Due to HCT values over the threshold of 60%, 2 cats dosed at 2.5 mg/kg bw and 1 dosed at 5 mg/kg were euthanized on Study Day 23; another cat dosed at 5 mg/kg bw was euthanized on Study Day 25. The control group (4 cats) were untreated. No clinically relevant changes related to molidustat were observed among the cats for food consumption and body weight. The most common physical exam findings included abnormal mucous membrane color, prolongation of capillary refill time (about 3 seconds), heart pounding, and tachycardia in the molidustat oral suspension groups. Polycythemia was noted in conjunction with these exam findings (all cats had HCTs greater than 50%).

Abnormal clinical pathology findings included a mild increase in serum potassium above baseline values in the 5 mg/kg bw group and a mild increase in serum creatinine above baseline in most cats in the molidustat groups (up to 21.6% in one 5 mg/kg bw cat). At necropsy, there was an apparent dose-dependent decrease in the mean kidney to brain ratio in the molidustat groups. Numerically lower (57.17% of control) mean thymus weight was recorded in cats administered molidustat at 5 mg/kg bw. Lower thymus weights were also noted in cats administered molidustat at 2.5 mg/kg bw. The administration of molidustat was associated with histopathological findings of congestion of the vasculature in the brain, thrombosis/hemostasis in the heart, prominent myocardial vessels, minimal edematous change of valves in the heart, and acute thrombosis of large pulmonary arteries in the lung. These findings were attributed to the pharmacologic mode of action (erythropoiesis via HIF-PH inhibition) of molidustat oral suspension.

Exploratory Pharmacokinetic and Pharmacodynamic Study

Molidustat oral suspension (not commercial formulation) was administered orally to 10 male and 12 female, healthy 22 to 24-month-old cats at doses of 5 mg/kg bw (5% oily suspension, 6 cats) or 10 mg/kg bw (10% oily suspension, 5 cats; or 10% aqueous suspension, 5 cats) daily for 24, 16, or 16 consecutive days, respectively.

The control group (6 cats) were administered an oily suspension vehicle-only control for 24 days. Study Day 0 was the first day of drug administration, and all cats remained on study for evaluation until Study Day 104. No clinically relevant changes related to molidustat were observed among the cats for food consumption, body weight, and physical examination. Molidustat oral suspension administration was associated with an apparent dose-related increase in vomiting. All cats in the 10 mg/kg bw groups showed a clinically relevant increase in serum creatinine on Study Day 12. One cat in the 10 mg/kg bw oily suspension group had an 86% increase in creatinine levels, which was just above the reference range, at Study Day 12. Similar increases in blood urea nitrogen were not found. All creatinine values in the 10 mg/kg bw groups returned to baseline by Study Day 97. A transient, mild increase in serum phosphorus was also noted on Study Day 12 (10 mg/kg bw groups) or Study Day 23 (5 mg/kg bw group). The increased values did not exceed the reference range for any cat and generally returned to baseline by Study Day 97. One cat in the 10 mg/kg bw oily suspension group showed a mild but clinically relevant increase in serum alanine aminotransferase (ALT) and alkaline phosphatase (ALP) levels on Study Day 12. There were no clinically relevant changes in other liver enzymes or total bilirubin. The cat also showed a concurrent 50% increase in creatinine on Study Day 12 that was at the upper end of the reference range. The rises in ALT, ALP, and creatinine on Study Day 12 values decreased by Study Day 97. There were no clinical signs related to hepatic or renal disease in this cat. The cause for the changes was not identified, but a direct drug effect or an indirect effect secondary to polycythemia could not be ruled out.

STORAGE CONDITIONS

Store at controlled room temperature 20°C – 25°C (68°F – 77°F). Excursions permitted between 15°C and 30°C (59°F – 86°F).

HOW SUPPLIED

27 mL of a 25 mg/mL oral suspension in a bottle with an oral dosing syringe.

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Revision date - 05/2023

The additional CE Sessions below will be available on-demand through the Virtual Platform at catvets.com/conference2023. Both in-person and virtual attendees will have access to these CE Sessions.

Virtual-only Sessions

SESSION TITLE	SPEAKER	SPONSOR/PARTNER
Feline GI Pain: Underappreciated & Over-Represented	Dr. Jennifer Slovak	IVAPM
Nutritional Support for Cats with Cancer	Dr. Catherine Ruggiero	Hill's
The Cat is Losing Weight: Is it GI or FHT, or Both?	Dr. Kelly St. Denis	ZOMEDICA
Using Ultrasound to Collect Fine Needle Aspirates	Dr. Jennifer Babineaux	

Virtual-only Session Abstracts

Feline GI Pain: Underappreciated & Over-Represented, *Dr. Jennifer Slovak*
Veterinary medicine has evolved in recent years regarding the recognition and appreciation of osteoarthritis and peri-surgical pain in our companion animals, especially cats. Unfortunately, there is a commonly under-appreciated aspect of feline discomfort—abdominal/GI pain. Generally, abdominal pain is felt below the ribs and extends to the pelvis, an area largely encompassing the gastrointestinal tract and its associated organs such as the pancreas and hepatobiliary system. Visceral nociceptors within the mesentery or serosal surfaces and within the mucosal walls of hollow organs respond to chemical or mechanical stimuli. Unfortunately, visceral pain can be diffuse and poorly localized due to sparse afferent innervation relative to somatic innervation, making GI pain challenging to detect in our feline patients. This is relevant in clinical medicine as many diseases involving the GI tract occur in cats such as: chronic enteropathies (inflammatory and lymphoma), cholangiohepatitis, constipation, and pancreatitis. With continued diligent patient assessment and evolution of pain scales and analgesia options, we can improve our patients' quality of life.

Nutritional Support for Cats with Cancer, *Dr. Catherine Ruggiero*
Neoplasia is prevalent in the feline population and can have a significant impact on nutritional status. There is risk of malnutrition from cancer, especially when the neoplastic process interferes with prehension, chewing, and/or swallowing. Additionally, some cancer therapies can contribute to malnutrition. To help mitigate this risk, certain food features should be prioritized when feeding cats with cancer, including taste. A new food, Hill's Prescription Diet ONC Care, can benefit feline patients with neoplasia.

The Cat is Losing Weight: Is it GI or FHT, or Both?, *Dr. Kelly St. Denis*
Unexplained weight loss can be a challenge in the aging feline species. A minimum database, including total T4 can be enlightening, but what if the results are equivocal? If the results seem clear, how do we rule out other contributing comorbidities? In this seminar we will review the ins and outs of diagnosis, management, and monitoring these two common feline health issues.

Using Ultrasound to Collect Fine Needle Aspirates, *Dr. Jennifer Babineaux*
Percutaneous ultrasound-guided aspiration is a safe procedure that improves medical diagnoses, is minimally invasive, and may help avoid more costly procedures such as laparoscopic or surgical biopsies. This lecture will discuss the approach to percutaneous ultrasound-guided fine needle aspirates (FNA) for the general practitioner, including risks and benefits, case selection, and how to perform the procedure safely.

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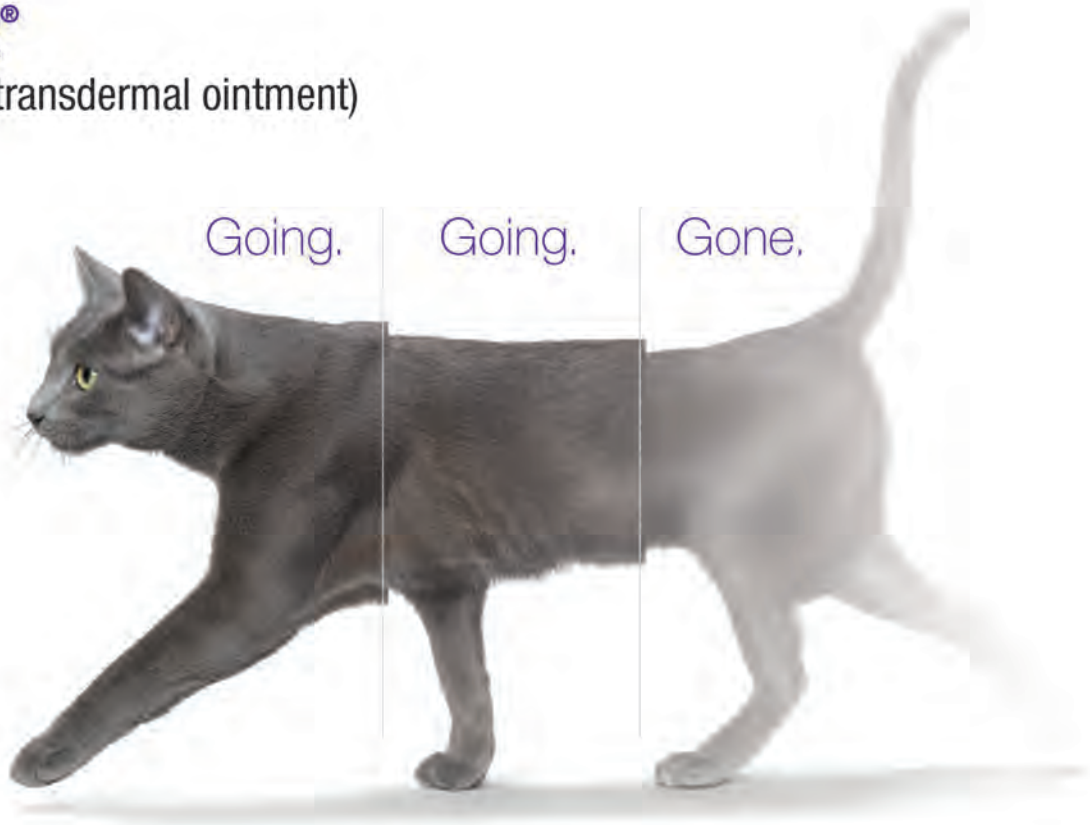

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CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Mirataz (mirtazapine transdermal ointment) is a white to off-white ointment containing 2% (w/w) of mirtazapine suitable for transdermal (topical) administration. The active ingredient, mirtazapine, is a *a2*-adrenergic receptor antagonist, nor-adrenergic and serotonergic drug.

INDICATION: For the management of weight loss in cats.

CONTRAINDICATIONS: Mirataz is contraindicated in cats with a known hypersensitivity to mirtazapine or to any of the excipients. Mirataz should not be given in combination, or within 14 days before or after treatment with a monoamine oxidase inhibitor (MAOI) [e.g. selegiline hydrochloride (L-deprenyl), amitraz], as there may be an increased risk of serotonin syndrome.

HUMAN WARNINGS: **Not for human use. Keep out of reach of children. Wear disposable gloves when handling or applying Mirataz to prevent accidental topical exposure.** After application, dispose of used gloves and wash hands with soap and water. After application, care should be taken that people or other animals in the household do not come in contact with the treated cat for 2 hours because mirtazapine can be absorbed transdermally and orally. However, negligible residues are present at the application site and the body of the cat at 2 hours after dosing. In case of accidental skin exposure, wash thoroughly with soap and warm water.
In case of accidental eye exposure, flush eyes with water.
If skin or eye irritation occurs seek medical attention.
In case of accidental ingestion, or if skin or eye irritation occurs,
seek medical attention.

PRECAUTIONS: Do not administer orally or to the eye. Use with caution in cats with hepatic disease. Mirtazapine may cause elevated serum liver enzymes (See **Animal Safety** in the product insert). Use with caution in cats with kidney disease. Kidney disease may cause reduced clearance of mirtazapine which may result in higher drug exposure. Upon discontinuation of Mirataz, it is important to monitor the cat's food intake. Food intake may lessen after discontinuation of mirtazapine transdermal ointment. If food intake diminishes dramatically (>75%) for several days, or if the cat stops eating for more than 48 hours, reevaluate the cat. Mirataz has not been evaluated in cats < 2 kg or less than 6 months of age. The safe use of Mirataz has not been evaluated in cats that are intended for breeding, pregnant, or lactating cats.

ADVERSE REACTIONS: The most common adverse reactions reported in the field study were application site reactions, behavioral abnormalities (vocalization and hyperactivity), and vomiting. **See Product Insert for complete Adverse Reaction information.**

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Anne Avery, VMD, PhD

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Colorado State University, Fort Collins, Colorado

Dr. Anne Avery is the Director of the Clinical Hematopathology Laboratory at Colorado State University and a Professor in the Department of Microbiology, Immunology, and Pathology. The primary focus of the Clinical Hematopathology Laboratory is the understanding of lymphoproliferative disorders at the clinical and molecular level, and how those disorders relate to the normal functions of cells of the immune system. She received her VMD from University of Pennsylvania where she also did a one-year small animal internship, a PhD from Cornell, and completed a 3-year post-doctoral fellowship at the Dana Farber Cancer Institute in Boston before moving to Colorado State University.

Jennifer Babineaux, MBA, DVM, DABVP (Feline)

Inner Visions Veterinary Ultrasound LLC, Ashland, Oregon

Dr. Jennifer Babineaux graduated from the UC Davis School of Veterinary Medicine in 2005 and completed an internal medicine residency at VCA East Bay Veterinary Specialists in 2009. During her residency, she developed an interest in feline medicine as well as in using ultrasound as a daily diagnostic tool for challenging internal medicine cases. Dr. Babineaux worked in the internal medicine departments of the San Francisco SPCA and VCA San Francisco Veterinary Specialists. She became an ABVP Diplomate (Feline) in 2014. Dr. Babineaux moved to Philadelphia in 2014 where she developed a mobile ultrasound and internal medicine consulting practice serving more than 25 hospitals, including 4 feline-only practices. Dr. Babineaux currently provides mobile ultrasound and internal medicine consulting in Ashland, Oregon. She enjoys teaching veterinarians ultrasound skills and advocates for the routine use of ultrasound to diagnose challenging internal medicine cases in general practice. Dr. Babineaux considers cats an especially ultrasound-deficient species.

Ellen Behrend, VMD, PhD, DACVIM (SAIM)

Sponsor

Auburn University, Auburn, Alabama

Dr. Ellen Behrend is the Joezy Griffin Professor in the Department of Clinical Sciences at Auburn University. Dr. Behrend received her VMD degree from the University of Pennsylvania in 1988 and her PhD from Auburn University in 2001. She has received the Dean's Award for Excellence in Teaching and has won the Zoetis Distinguished Teaching Award three times. In 2021, she was named Clinician of the Year for the Auburn University College of Veterinary Medicine. Dr. Behrend has authored more than 200 scientific publications, including journal articles, book chapters, and abstracts, served as Endocrine section editor for editions of *Consultations in Feline Internal Medicine, Kirk's Current Veterinary Therapy,* and *Coté's Clinical Veterinary Advisor,* and was the editor for the canine chapters of *Clinical Endocrinology of Companion Animals.* In addition, she has provided more than 100 continuing education lectures at national and international conferences. Dr. Behrend was previously the Director of the Auburn Endocrine Diagnostic Laboratory.

Ellen Carozza, LVT, VTS (CP-Feline)

Sponsor

The Cat LVT LLC., Herndon, Virginia

As a 1996 SUNY Delhi graduate, Ellen Carozza has worked in many sectors in veterinary medicine. She started out in veterinary technology as a student primate biohazard technician at LEMSIP under the direction of the late Dr. James Mahoney in Sterling Forest, NY. After the closing of the lab, she moved to shelter medicine at the Washington Animal Rescue League (now the Humane Rescue Alliance in Washington DC), as well as a few corporate small animal hospitals in the DC metro area. Ellen has spent more than twenty years in a feline practice helping enhance, evolve, and empower the veterinary technicians' skills and role in feline medicine. She currently runs the Chris Griffey Memorial Feline Foundation (criticalkittens.org) and holds the title of Veterinary Technician Specialist–Feline. Ellen has co-authored several guidelines and toolkits for the AAFP, AAHA, and ISFM. Known for her no nonsense, practical teaching skills, she aims to ensure you will take home valuable material for use in practice after each lecture.

Petra Cerna, MRCVS, AFHEA, AdvCertFB

Colorado State University, Fort Collins, Colorado

Dr. Petra Cerna completed a Small Animal Internal Medicine residency at Colorado State University. She graduated from the University of Veterinary and Pharmaceutical Sciences, Brno, Czech Republic in 2018. She completed a Small Animal Rotating Internship at Vets Now Referral Hospital, Glasgow, UK in 2019 and Small Animal Medicine Internship at The Royal (Dick) School of Veterinary Studies, University of Edinburgh, UK in 2020. Dr. Cerna obtained an ISFM Advanced Certificate in Feline Behavior with Distinction in 2018. She has particular interest in feline medicine and is currently pursuing a Ph.D. in Feline Infectious Peritonitis (FIP) from Colorado State University.

Audrey Cook, BVM&S, FRCVS, MScVetEd, DACVIM (SAIM), DECVIM, DABVP (Feline)

Sponsors

Texas A&M University, College Station, Texas

Dr. Audrey Cook graduated from the University of Edinburgh, Scotland. She completed her internship at North Carolina State University and her residency in small animal internal medicine at University of California, Davis. Dr. Cook is a Diplomate of both the American and European Colleges of Veterinary Internal Medicine, and is also recognized as a specialist in feline practice by the American Board of Veterinary Practitioners. After a decade in private referral practice, Dr. Cook joined the faculty at Texas A&M. She is now Professor of Small Animal Internal Medicine and Chief of the Medicine Service, with particular interests in endocrinology, gastroenterology, and interventional radiology.

Tracey Deiss, DVM

Sponsor

Zoetis, Texas

Dr. Tracey Deiss attended Texas A&M pursuing a BS in Biochemistry and Genetics with a Chemistry minor. She received her DVM from Texas A&M University in 1998. During veterinary school, she worked at MD Anderson Cancer Center, Department of Lab Animal Medicine and Surgery. Dr. Deiss completed an internship in small animal medicine and surgery prior to practicing emergency medicine for 15 years in Grapevine, Texas. She returned to her hometown of Rosenberg, TX joining a large SA practice where her special interests included ultrasonography, soft tissue surgery, and pain management. Dr. Deiss joined Zoetis as the professional services veterinarian for the Houston and surrounding areas in 2018 and is the current medical lead for Core Therapeutics and Feline Pain.

Sheryl Gamble, DVM, MS

Sponsor MERCK Animal Health

Merck Animal Health, Georgia

A triple alumnus of Auburn University, Dr. Sheryl Gamble holds three Summa Cum Laude degrees, including a Bachelor and Master of Science in Zoology and a Doctor of Veterinary Medicine. Her Auburn roots run strong, as she was an award-winning instructor of general biology and physiology in the College of Science and Mathematics. After graduating with her DVM, Dr. Gamble did a preceptorship at the San Diego Zoo in the pathology department, then for two years became involved in full-time small animal private practice. Before joining the team at Merck Animal Health in 2019, Dr. Gamble spent the majority of her professional career focused on human health in the areas of vaccines, cardiology, and oncology. She is currently working on a Masters of Public Health from the University of Iowa. Zoonitic disease prevention is her clinical passion. Dr. Gamble is IBHRE Board certified in Cardiac Rhythm Device Therapy. She is licensed to practice veterinary medicine and surgery in Georgia. She is also a member of the AVMA, the GVMA, the South Georgia Veterinary Medical Association, and the American Association of Industry Veterinarians. Outside of work, Dr. Gamble adores spending time with her extended family, which includes her husband, two kids, six dogs, three cats, two pigs, a horse, a pony, a donkey, three chickens, a fancy leopard gecko, and one lucky fish. Because her care for animals is second to none, she still spends a portion of her Saturdays devoted to treating veterinary patients.

Margaret Gruen, DVM, MVPH, PhD, DACVB

Sponsor zoetis

North Carolina State University College of Veterinary Medicine, Raleigh, North Carolina

Dr. Margaret Gruen is an Associate Professor of behavioral medicine at North Carolina State University. She graduated from the University of Illinois and completed an internship, residency in Veterinary Behavioral Medicine, and PhD in Comparative Biomedical Sciences at North Carolina State University with work focused on the assessment of pain in cats with degenerative joint disease. Her current research focuses on topics of human-animal interaction – how animals communicate through their behavior and how we understand and quantify those behaviors. This includes quantification of chronic pain, and the effects of pain on aspects of daily life including activity, anxiety, and cognitive function. Dr. Gruen is also the Co-director of the Feline Health Center at the NC State University College of Veterinary Medicine.

Melissa Hall, DVM, DACVD

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Animal Dermatology Clinic, Los Angeles, California

Dr. Melissa Hall graduated with a Bachelor of Science in Animal Physiology and Neuroscience from University of California, San Diego prior to achieving her Doctorate of Veterinary Medicine from the University of California, Davis. Dr. Hall's veterinary studies led her to a passion for veterinary dermatology that carried her through a three-year residency with Animal Dermatologic Clinic in Southern California. In 2011, Dr. Hall became a board-certified veterinary dermatologist and diplomate of the American College of Veterinary Dermatologists. Dr. Hall shares her passion for all aspects of skin and ear disease by lecturing all over the world and training residents.

Michael Lappin, DVM, PhD, DACVIM

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Colorado State University, Fort Collins, Colorado

Dr. Michael Lappin graduated from Oklahoma State University and then completed an internship, internal medicine residency, and PhD program in Parasitology at the University of Georgia. Dr. Lappin is the Kenneth W. Smith Professor in Small Animal Clinical Veterinary Medicine at Colorado State University, is the director of the "Center for Companion Animal Studies," and he helps direct the shelter medicine program. He is the chair of the WSAVA One Health Committee. His principal areas of interest are prevention of infectious diseases, the upper respiratory disease complex, infectious causes of fever, infectious causes of diarrhea, and zoonoses. His research group has published more than 300 primary papers or book chapters concerning small animal infectious diseases. Awards include the Norden Distinguished Teaching Award, NAVC Small Animal Speaker of the Year, the European Society of Feline Medicine International Award for Outstanding Contribution to Feline Medicine, the Winn Feline Research Award, the ACVIM Robert W. Kirk Award for Professional Excellence, the WSAVA Scientific Achievement Award, and the AVMA Clinical Research Award.

Duncan Lascelles, BSc, BVSc, CVA, PhD, FRCVS, DSAS(ST), DECVS, DACVS

Sponsor zoetis

North Carolina State University, Raleigh, NC

After graduating from the veterinary program at the University of Bristol, UK, with honors, in 1991, Dr. Lascelles completed a PhD in aspects of pre-emptive/perioperative analgesia at the University of Bristol. After an internship, he completed his surgical residency at the University of Cambridge, UK. He moved to Colorado for the Fellowship in Oncological Surgery at Colorado State University. He is currently Professor in Small Animal Surgery and Pain Management at North Carolina State University. He is board-certified in small animal surgery by the Royal College of Veterinary Surgeons, the European College of Veterinary Surgeons, and the American College of Veterinary Surgeons. He is director of the Comparative Pain Research and Education Centre (CPREC). His research program (Translational Research in Pain [TRiP]) is dedicated to answering critical questions about pain control and pain mechanisms through high quality, innovative research. His career has been focused on developing algometry methods (methods to measure pain) in spontaneous disease animal models (pets with naturally occurring disease), and probing tissues from well-phenotyped animals with spontaneous disease to understand the neurobiology, with a strong translational focus. The aim of his research is to improve pain control in companion animals and facilitate analgesic development in human medicine. He has authored more than 200 peer reviewed research papers and reviews and 350 research abstracts, as well as more than 30 book chapters. He is co-founder of AniV8, a company dedicated to developing innovative methods of measuring pain.

Patricia Lathan, VMD, MS, DACVIM (SAIM)

Sponsor Boehringer Ingelheim

Mississippi State University CVM, Starkville, Mississippi

Dr. Patty Lathan is a professor of small animal internal medicine at Mississippi State University. Her primary interest is endocrinology, specifically the management of adrenal disease and diabetes mellitus. She has published several articles and book chapters, given lectures throughout the United States and internationally, and currently serves as the President of the Society for Comparative Endocrinology. Her students also publish educational endocrine music videos as an assignment for her elective, and those can be viewed on her YouTube channel.

Joyce Login, DVM, CPH

Sponsor zoetis

Zoetis, Princeton, New Jersey

Dr. Joyce Login received her veterinary degree from The Ohio State University and began her career practicing at a small animal hospital in New Jersey. She left private practice to work in the animal health corporate world and has had the opportunity to work for various animal health companies including Hill's, Novartis, and Bayer. In 2010, she joined Zoetis as a specialty hospital liaison and then moved to HQ to be the medical lead for the parasitology. She is currently the Senior Medical Affairs Manager supporting Feline Pain. In 2019, she received her certification in Public Health and is also Fear Free, HAB, and Cat Friendly Certified. She has special interests in the areas of veterinary communication, pain, and vector-borne diseases.

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Alison Manchester, DVM, DACVIM (SAIM)
Colorado State University, Fort Collins, Colorado

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Dr. Alison Manchester grew up in Rochester, NY and studied art history at Tufts University before veterinary school at Cornell. After an internship at the University of Wisconsin, she completed her Internal Medicine training at Colorado State University. Dr. Manchester became board-certified by the ACVIM in 2018. She is currently a post-doctoral fellow at CSU, serving time on clinics and finishing a PhD focused on immune dysregulation in cats and dogs with chronic intestinal inflammation. Her studies involve utilizing novel platforms and non-invasive samples to expand understanding of the gastrointestinal tract in health and disease. When not in the lab or the clinic, she enjoys her red female cat, hiking, cooking, reading fiction, listening to music, and spending time with loved ones in Downeast Maine.

Natalie Marks, DVM, MS, CVJ
VCA Blum Animal Hospital, Chicago, Illinois

Sponsor

Dr. Natalie Marks obtained her bachelor's degree with High Honors in Animal Science from the University of Illinois in 1998, and then proceeded to obtain a Masters in Veterinary Medicine and a Doctorate of Veterinary Medicine degree with High Honors from the University of Illinois College of Veterinary Medicine. She became a Certified Veterinary Journalist in 2018. She has been a veterinarian at Blum Animal Hospital since 2006, was co-owner until 2019, and still practices as an associate. Prior to 2006, Dr. Marks worked at a small animal practice north of Atlanta, GA. Upon her return to Chicago, Dr. Marks became very active in the Chicago VMA, serving on the executive board. She was a past board member of the Illinois State VMA and an active volunteer to the AVMA. Dr. Marks received the prestigious Dr. Erwin Small First Decade Award. In 2012, Dr. Marks was awarded Petplan's nationally-recognized Veterinarian of the Year. In 2015, she was awarded America's Favorite Veterinarian by the American Veterinary Medical Foundation. And, most recently in 2017, she was awarded Nobivac's Veterinarian of the Year for her work on canine Influenza. Dr. Marks led her practice certification to becoming a Cat Friendly Practice hospital and Fear Free hospital. She is a passionate advocate for feline wellness, emotional health, and enrichment, lecturing nationally and internationally.

Matt McGlasson, DVM, CVPM
Noah's Ark Animal Clinics, Fort Mitchell, Kentucky

Sponsor

Dr. Matt McGlasson is a Certified Fear Free Practitioner, Cat Friendly Veterinarian by the AAFP, and a member of the AVMA, VHMA, and AAFP. He currently serves on the Executive Board of the KVMA, serves on the Veterinary Advisory Board for BasePaws, and the editorial advisory board for DVM360. In 2022, Dr. McGlasson was awarded the "Veterinary Hero Award" presented by DVM360 in the category of Practice Management. Most importantly, he is a world-famous cat-dad on several social media channels. His videos featuring his personal special-needs cats as well as patients at the office have been viewed more than 100 million times!

Michelle Meyer, DVM
Serenity Animal Hospital, Sterling Heights, Michigan

Sponsor

Dr. Michelle Meyer earned her DVM degree from Purdue University in 2007 and since graduation works as a clinician in a very busy mixed (dog/cat) private practice in southeastern Michigan. She is actively involved in organized veterinary medicine and is currently serving on three veterinary boards (Michigan VMA, Southeastern Michigan VMA, and AAFP). She has a strong love for feline medicine and loves sharing cases with other fellow general practitioners.

Vicky Ograin, MBA, RVT, VTS (Nutrition)
Hill's Pet Nutrition, Topeka, Kansas

Sponsor

Vicky Ograin is a Registered Veterinary Technician with a MBA and is a Veterinary Technician Specialist (VTS) in Nutrition. She has worked for Hill's Pet Nutrition for 21 years, where she is a Scientific Communication Specialist VHCT, in the U.S. Professional Veterinary Affairs department. At Hill's she focuses on education for the veterinary health care team. Vicky is a proud cat lady and has two rescue cats from the local humane society, Tabatha and Sabrina.

Valerie Parker, DVM, DACVIM (SAIM, Nutrition)
The Ohio State University, Columbus, Ohio

Sponsors

Dr. Valerie Parker is currently a Professor, Clinical at The Ohio State University. She received her DVM from Tufts University, followed by a small animal internship at the Animal Medical Center in New York City. She then completed a small animal internal medicine residency at Iowa State University and a nutrition residency at Tufts University. She is a diplomate of the American College of Veterinary Internal Medicine (SAIM and Nutrition). Dr. Parker's primary areas of interest include kidney disease, gastrointestinal disease, obesity, and vitamin D metabolism, as well as nutritional management of a variety of diseases.

Jessica Pritchard, VMD, MS, DACVIM (SAIM)
University of Wisconsin, Madison, Wisconsin

Sponsor

Dr. Jessica Pritchard is a Clinical Assistant Professor in Small Animal Internal Medicine and the Director of Clinical Assessment at the University of Wisconsin School of Veterinary Medicine. She also co-directs the school's Rotating Internship program. Her research and clinical interests include infectious and gastrointestinal diseases of dogs and cats, skills assessment in veterinary students, and house officer wellbeing. Dr. Pritchard has shared more than 100 hours of continuing education at various national and state conferences. She shares her home with a rambunctious Labrador retriever, Frieda. Her clinical office at work is actually the cat ward, which brings with it a lot of joy (and kittens).

Visit the Ceva Booth #307 to learn more

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Clinically proven performance in cats[1,2]

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In a feline study, DOUXO® S3 CALM demonstrated improvement in signs of pruritus in cats[1]

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Thursday, October 12th

The Allergic Patient: New Insights in Skin Barrier Science

Featured Speaker: Dr. Melissa Hall

10:00 AM - 10:55 AM | Ballroom B

Chlorhexidine can cause rare, but serious allergic reactions in humans. If you experience allergy symptoms, discontinue use immediately and seek medical treatment. Do not use DOUXO® S3 PYO Mousse in cats. Do not use DOUXO® S3 PYO Pads between the toes of the cats.

1. Cózar A. et al. (2023) Performance of a protocol combining applications of Ophytrium-containing Shampoo and Mousse in cats with non-flea induced hypersensitivity dermatitis: a multicentric prospective field trial. Proceedings of the 2023 BSAVA Congress. Manchester, UK, March 23rd-25th. 2. Cózar A. et al.(2023) Performance of a protocol combining applications of Ophytrium and Clorhexidine-containing Shampoo and Pads in cats with bacterial and Malassezia disturbances: a multicentric prospective field trial. Proceedings of the 2023 NAVDF Congress. Seattle, May 9th-12th.

Ceva

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Sara Ramos, DVM, ACVD

Sponsor Hill's

Veterinary Specialists of Greater New Orleans, Prairieville, Louisiana

Dr. Sara Ramos grew up in Louisiana and graduated in 2015 from the LSU School of Veterinary Medicine. Following graduation, she completed a one-year rotating internship at the University of Georgia College of Veterinary Medicine, which is where she was inspired to pursue a career in dermatology. She then returned to LSU where she completed both a one-year dermatology internship and a three-year dermatology residency. Dr. Ramos became a diplomate of the American College of Veterinary Dermatology in 2020 and now serves the dermatology needs of pets in the New Orleans and Baton Rouge area working at Veterinary Specialist of Greater New Orleans and Capital Area Veterinary Specialists. Dr. Ramos is very passionate about continuing to learn and teaching others within the field of dermatology.

Ilona Rodan, DVM, DABVP (Feline), AdvCertFB

Sponsors ROYAL CANIN, Ceva, sleepypod Partner TICA

Cat Behavior Solutions, LLC, Madison, Wisconsin

Dr. Ilona Rodan is the founder and director of Cat Behavior Solutions from 2015. She was the founder and medical director of Care Clinic in Madison, WI for almost three decades before starting her feline behavior focused practice. She is ABVP Feline Certified since 1985. Dr. Rodan is passionate about teaching veterinarians and veterinary teams about feline behavior and how best to interact with and handle cats in veterinary practices to enhance feline welfare and human safety. She had presented nationally and internationally on feline medicine and behavior over the past 10 years. She is also an active AAFP volunteer, a past-president, and former chair of the AAFP Cat Friendly Practice® program. She co-chaired several guidelines and welfare position statements, including the *AAFP/ISFM Cat Friendly Interactions and Handling Guidelines* and the upcoming *AAFP Feline Environmental Needs and Pain Management Guidelines.* She presents nationally and internationally on feline medicine and behavior, and leads workshops on feline-friendly handling. In 2005, she was awarded the AVMA Animal Welfare Award for her leadership and contributions to advancing feline medicine and behavior. Dr. Rodan has written journal articles and book chapters, and is a co-editor and co-author of the veterinary textbook, *Feline Behavioral Health and Welfare,* published in 2015.

Adam Rudinsky, DVM, MS, DACVIM

Sponsors ROYAL CANIN, IDEXX, wedgewood PHARMACY, Blue Natural Veterinary Diet

The Ohio State University College of Veterinary Medicine, Columbus, Ohio

Dr. Adam Rudinsky is an Associate Professor–Tenure in the Small Animal Internal Medicine service at The Ohio State University Veterinary Medical Center. He received his DVM degree from The Ohio State University, completed a small animal rotating internship at Purdue University, and then a combined residency in internal medicine and MS degree at The Ohio State University. Following residency training, he completed two post-doctoral research fellowships in Mucosal Immunology at The Ohio State University and Microbial Pathogenesis at Nationwide Children's Hospital. He is now on faculty at Ohio State as a staff internist, research scientist, and member of the American College of Veterinary Internal Medicine. His current clinical and research interests include gastrointestinal endocrinology, chronic enteropathies, pancreatic and hepatic disease, mucosal immunology, and the intestinal microbiome as it relates to disease pathophysiology and treatment.

Catherine Ruggiero, MS, DVM, DACVIM (Nutrition)

Sponsor Hill's

Hill's Pet Nutrition, Olathe, Kansas

Dr. Catherine Ruggiero is a board-certified veterinary nutritionist® and manager of Scientific Communications at Hill's U.S. She completed her DVM training at the University of Missouri in 2014. Prior to that, she received a Bachelor of Science at St. Lawrence University and a Master of Science in Biological Sciences at Fordham University. She was an associate veterinarian at a small animal veterinary practice in Upstate New York for just over three years before returning to the University of Missouri to pursue residency training in small animal clinical nutrition. Upon completion of an ACVN residency program in 2019, Dr. Ruggiero joined Hill's Pet Nutrition.

Ashlie Saffire, DVM, DABVP (Feline)

Sponsor ROYAL CANIN

Cats Only Veterinary Clinic, Dublin, Ohio

Dr. Ashlie Saffire is a graduate of The Ohio State College of Veterinary Medicine and is board certified in feline practice by the ABVP. She is a published author, serves on the Board of Directors for the AAFP, and is a tutor for the University of Sydney's Feline Medicine Distance Education Course. She is both Fear Free and Cat Friendly Certified. As an invited speaker, Dr. Saffire hopes to share her clinical experience and expertise in feline medicine with the veterinary profession.

Thomas Schermerhorn, VMD, DACVIM (SAIM)

Sponsor Boehringer Ingelheim

Kansas State University, Manhattan, Kansas

Dr. Thomas Schermerhorn is a professor of small animal medicine and holds the Jarvis Chair in Veterinary Medicine at Kansas State University. His clinical interests include all aspects of canine and feline endocrinology, with an emphasis on diabetes. Dr. Schermerhorn's research focuses on cellular and molecular endocrinology, especially the study of diabetes mellitus and related metabolic disorders in dogs and cats. Dr. Schermerhorn earned his veterinary degree at University of Pennsylvania. He also completed a medical internship at South Shore Veterinary Associates in South Weymouth, MA, and a residency in small animal internal medicine at Cornell University, where he also received research training as a graduate fellow in the department of molecular medicine.

Elizabeth Schooley, DVM, MS, DACVIM (SAIM)

Sponsor IDEXX

IDEXX Laboratories Inc., Westbrook, Maine

Dr. Elizabeth Schooley performed both her undergraduate and veterinary education at Colorado State University. After graduation, she completed an internship in small animal medicine and surgery at the Animal Medical Center in New York City. She then completed a residency in small animal internal medicine at the University of Missouri. During this time, she also fulfilled the requirements to obtain a Master's degree in biomedical sciences. She has been board-certified in small animal internal medicine since 2007. Prior to joining IDEXX, Beth worked at a private specialty practice in Richmond, VA. She joined IDEXX in 2010 and her current role is medical affairs specialist for chemistry, endocrinology, and feline infectious disease.

Catharine Scott-Moncrieff, MA, VMB, MS, MRCVS, DACVIM, DECVIM, DSAM

Sponsor Boehringer Ingelheim

Purdue University, Otterbein, Indiana

Dr. J. Catharine Scott-Moncrieff earned her Vet MB from Cambridge University. She later completed a residency at Purdue University College of Veterinary Medicine, where she is now a professor of small animal internal medicine and head of the Department of Veterinary Clinical Sciences. Dr. Scott-Moncrieff is a diplomate of the American College of Veterinary Internal Medicine and European College of Veterinary International Medicine.

Jennifer Slovak, DVM, MS, DACVIM

Zoetis, Wyoming

Partner

Dr. Jennifer Slovak graduated from Iowa State University College of Veterinary Medicine in 2003. For seven years she practiced in Wisconsin, Michigan, and Minnesota as a mixed animal, equine, and small animal veterinarian. She completed a rotating internship and residency in small animal internal medicine at Iowa State University and became ACVIM board-certified in 2014. Since then, Jen has worked at Washington State University, AMC in NYC, and has been an internal medicine locum at five different U.S. veterinary teaching hospitals. Jen values her diverse veterinary experiences and approaches internal medicine with a compassionate, inquisitive, and open mind. Jen has lectured, taught, and published on topics such as pharmacology (mycophenolate & gabapentin), pain awareness and assessment, endocrine diseases, renal conditions, and gastroenterology. She currently lives in Wyoming near Grand Teton National Park with her husband, dogs, cat, and horse.

Kelly St. Denis, MSc, DVM, DABVP (Feline)

St. Denis Veterinary Professional Corporation, Brantford, Ontario

Sponsors

Dr. Kelly St. Denis is board-certified with the ABVP in the specialty of feline practice. In her early career she trained in molecular biology and immunology, and in the field of cancer research. In 1999 she graduated from the Ontario Veterinary College, and owned and operated the Charing Cross Cat Clinic from 2007 to 2020. Dr. St. Denis was President of the AAFP in 2020 and 2021, and continues to be an active volunteer in the organization. Dr. St. Denis is a consultant on the Veterinary Information Network in feline internal medicine.

Betsy Swanson, DVM, MS, DACVS (Small Animal)

Mississippi State University College of Veterinary Medicine, Mississippi State, Mississippi

Sponsor

Dr. Elizabeth Swanson is an Associate Professor of Small Animal Surgery at the Mississippi State University College of Veterinary Medicine. Her clinical and research focus is soft tissue surgery with special interests in wound healing and infection, chronic biofilm infections, minimally invasive surgery, and endourology. She earned her DVM from Iowa State University in 2001. She completed a rotating internship at the Tierärztliche Hochschule Hannover (University of Veterinary Medicine Hannover) in Germany (2002), and later completed surgery specialty internships at Gulf Coat Veterinary Specialists in Houston (2008) and at the University of Missouri (2009, 2010), and her residency in small animal surgery and MS degree at Purdue University 2013. In between the rotating and specialty internships, she practiced for five years as an associate veterinarian in the Chicago area. She has been on faculty at Mississippi State University since 2013. She is actively involved with the American College of Veterinary Surgeons, the Society of Veterinary Soft Tissue Surgery, and the Veterinary Endoscopy Society. In her free time, she enjoys singing, traveling, reading, gardening, and spending time with her pets, including her parents' two cats, Zuzu and Nick.

Adronie Verbrugghe, DVM, PhD, DECVCN

Ontario Veterinary College, University of Guelph, Guelph, Ontario

Partner

Dr. Adronie Verbrugghe graduated as a companion animal veterinarian from Ghent University, Belgium in 2005. She completed her PhD focusing on nutritional modulation of carbohydrate metabolism in cats in 2009. She became board-certified for the European College of Veterinary and Comparative Nutrition (ECVCN) in 2010. In 2011, Dr. Verbrugghe joined the Ontario Veterinary College (OVC), University of Guelph, as Royal Canin Veterinary Diets Endowed Chair in Canine and Feline Clinical Nutrition. As an Associate Professor, Dr. Verbrugghe's academic responsibilities include development and delivery of the small animal clinical nutrition curriculum for the DVM program. Dr. Verbrugghe is also the Service Chief for the OVC Health Science Centre's Clinical Nutrition Service. Her research interests include companion animal nutrition, the link between nutrition, gut microbiota, health and disease, alteration of metabolic pathways through nutrition and nutritional modulation of inflammation, and immunity. Currently pet obesity and unconventional pet foods are the major subjects of her research program. Dr. Verbrugghe has received research funding through the Canadian and Ontario government, charitable organizations, as well as from pet food industry and ingredient suppliers. In 2019, Dr. Verbrugghe received a UofG Research Excellence Award highlighting her governments achievement in canine and feline nutrition research. Dr. Verbrugghe has (co-)authored numerous peer-reviewed publications. She is a regular speaker at local, national, and international conferences. Dr. Verbrugghe has trained many graduate students and ECVCN residents. She is a reviewer for various scientific journals and sits on institutional committees and external scientific advisory boards.

Cynthia Ward, VMD, PhD, DACVIM

University of Georgia, Watkinsville, Georgia

Sponsors

Dr. Cynthia Ward received her VMD and PhD degrees from the University of Pennsylvania. She has been on faculty at the Universities of Pennsylvania and Georgia and was the founder of the University of Georgia Diabetes Clinic. Dr. Ward has authored numerous publications in small animal endocrinology and is a diplomate of the ACVIM (SAIM).

Craig Webb, PhD, DVM, DACVIM

Colorado State University, Fort Collins, Colorado

Sponsors Partner

After completing his PhD in Neuroscience, Dr. Craig Webb earned his DVM from the University of Wisconsin. Following his internship, he joined Colorado State University as a Small Animal Medicine resident with Dr. David Twedt as his mentor, and has remained on faculty at the Veterinary Teaching Hospital for more than two decades. He is the Head of the SAM service and very much enjoys working with bright young students on the clinic floor, seeing patients, and running clinical trials. Dr. Webb's greatest accomplishment was marrying the much better looking and much smarter Dr. Tracy Webb, with whom he collaborates on a number of research projects, and life.

Kenichiro Yagi, MS, RVT, VTS (ECC) (SAIM)

Veterinary Emergency Group, New York, New York

Sponsor Partner

Ken Yagi is a double VTS in emergency and critical care as well as small animal internal medicine, and has a Master's degree in Veterinary Science. He is currently the Chief Veterinary Nursing Officer for Veterinary Emergency Group, and the Program Director for the RECOVER Initiative. Over the years, he has received multiple Veterinary Technician of the Year Awards for his work to bring further recognition of the vital role of the veterinary technicians and nurses through work with organizations like NAVTA. Ken co-edited the *Veterinary Technician and Nurse's Daily Reference Guide for Canine and Feline,* and the *Manual of Veterinary Transfusion Medicine and Blood Banking,* and publishes articles and presents internationally on topics in ECC, transfusion medicine, and the veterinary nursing profession. Ken invites everyone to ask "Why?" to understand the "What" and "How" of our field, and to continually pursue new limits as veterinary professionals and individuals.

Hill's PRESCRIPTION DIET

adventures made possible

time made magical

Powerful nutrition designed for pets fighting cancer.

With taste beyond belief, for adventures beyond imagination.

SCIENCE DID THAT.

Bexacat™
(bexagliflozin tablets)

The search for a non-insulin alternative is over.

ONE TABLET

ONCE A DAY

Give cats the once-daily tablet alternative to insulin that provides effective glycemic control.

Introducing the FIRST non-insulin oral treatment specifically designed for feline diabetes.

INDICATION: Bexacat is indicated to improve glycemic control in otherwise healthy cats with diabetes mellitus not previously treated with insulin.

IMPORTANT SAFETY INFORMATION: Before using this product, it is important to read the entire product insert, including the boxed warning. See the Elanco booth for full prescribing information. Cats treated with Bexacat may be at an increased risk of diabetic ketoacidosis or euglycemic diabetic ketoacidosis, both of which may result in death. Development of these conditions should be treated promptly, including insulin administration and discontinuation of Bexacat. Do not use Bexacat in cats with diabetes mellitus who have previously been treated with insulin, who are receiving insulin, or in cats with insulin-dependent diabetes mellitus. The use of Bexacat in cats with insulin-dependent diabetes mellitus, or the withdrawal of insulin and initiation of Bexacat, is associated with an increased risk of diabetic ketoacidosis or euglycemic diabetic ketoacidosis and death. Sudden onset of hyporexia/anorexia, lethargy, dehydration, diarrhea that is unresponsive to conventional therapy, or weight loss in cats receiving Bexacat should prompt immediate discontinuation of Bexacat and assessment for diabetic ketoacidosis, regardless of blood glucose level. Bexacat should not be initiated in cats with pancreatitis, anorexia, dehydration, or lethargy at the time of diagnosis of diabetes mellitus, as it may indicate the presence of other concurrent disease and increase the risk of diabetic ketoacidosis. Due to risk of severe adverse reactions, do not use Bexacat in cats with evidence of hepatic disease or reduced renal function. Consult a physician in case of accidental ingestion by humans.

Elanco™

Session Abstracts

Schedule is in Central Daylight Time

KEY: W WORKSHOP | C COMBINED TRACK | A TRACK A | B TRACK B | LS LIVE STREAMED | IPO IN-PERSON ONLY

THURSDAY, OCTOBER 12, 2023 – PRE-CONFERENCE DAY

7:45 – 11:45 am W **Hands-on Feline Orthopedic Evaluation Workshop,** *Drs. Duncan Lascelles & Margaret Gruen* IPO
The approach to a clinically meaningful and efficient orthopedic evaluation of the cat will be discussed. The components of capturing a relevant history, observation of the cat, and the hands-on examination will be presented and discussed. Attendees will gain hands-on (yes, live cats) and expert-guided experience in techniques for successful orthopedic/osteoarthritis examinations. Cat Friendly and staff friendly approaches will be emphasized. Learn how to augment your feline practice and build stronger client bonds with caregivers. Review tools and protocols to optimize outcomes for your feline osteoarthritic patients. Read more on page 23.

10:15 – 11:10 am **The Allergic Patient: New Insights in Skin Barrier Science,** *Dr. Melissa Hall* LS
We will review the current understanding of changes which occur in the skin of an allergic patient. We will also discuss the active ingredient Ophytrium and how it works to manage this disruption in the skin barrier. Finally, we will review cases and recent research studies in regards to Ophytrium's use.

11:15 – 11:45 am **Serenity Now! A Deeper Dive into the Peaceful Practice,** *Dr. Natalie Marks* LS
This lecture will start by discussing the pathophysiology of fear and anxiety in cats. Attendees will then refresh about the consequences of stress to our patients, including lab work abnormalities and long-term behavioral changes, as well as how it impacts the human-animal bond. Discussion will continue around the impact of stress to veterinary professionals and how it destroys work culture and longevity. The remainder of the program will focus on ways veterinary teams can use a multi-modal approach to create a calm clinic for patients, cat caregivers, and veterinary professionals.

12:15 – 1:15 pm **Nutritional Counselor Program: Get Inspired to Run your Own Nutritional Consultations,** *Vicky Ograin* LS
Learn how to structure and perform a nutritional consultation and how to address common questions that caregivers may ask. Veterinarians and technicians should be discussing nutrition with caregivers; this session will help start the conversation. We will work through a feline renal case, demonstrating how to do a nutritional consultation and how important it is for the cat to do the consultation, especially when switching to a new food.

1:30 – 2:00 pm **Diabetes Masterclass: Oral Hypoglycemics - An Overview,** *Dr. Audrey Cook* LS
Many cats with diabetes mellitus fit the profile for human type 2 DM, in which chronic insulin resistance results in inadequate insulin secretion. However, oral hypoglycemic agents have traditionally performed very poorly in feline diabetics. In this lecture, we will review the history of oral hypoglycemics in cats, and introduce the SGLT-2 inhibitor drug class. This option represents a true paradigm shift in the management of feline diabetes.

2:00 – 3:15 pm **Diabetes Masterclass: SGLT-2 Inhibitors - Safety & Efficacy Data,** *Drs. Ellen Behrend & Patty Lathan* LS
The most successful oral treatment for feline diabetes is currently sodium glucose transporter 2 (SGLT-2) inhibitors. During this lecture, we will reveal safety and efficacy data regarding velagliflozin, an SGLT-2 inhibitor recently studied in cats. This class of drugs will likely change the landscape of feline diabetes management over the next few years.

3:45 – 4:10 pm **Diabetes Masterclass: Getting Started & Monitoring,** *Dr. Cynthia Ward* LS
There are new and exciting treatments available for feline diabetes mellitus. This talk will focus on how to use the new sodium glucose co-transport protein 2 (SGLT-2) inhibitors (SGLT-2i) in your practice. A brief overview of how the medications work will be presented followed by information on appropriate patient selection and screening protocols for diabetic cats. Initial dosing and monitoring of SGLT2i will be discussed. Information for caregivers about potential adverse events will be highlighted. Specific case examples may be presented.

4:10 – 5:00 pm **Diabetes Masterclass: Troubleshooting & Complications,** *Drs. Thomas Schermerhorn & Catharine Scott-Moncrieff* LS
SGLT-2 inhibitors are an exciting new class of drugs for management of feline diabetes mellitus. This session will address potential adverse effects associated with the use of SGLT-2 inhibitors in cats. The speakers will discuss how to prevent, identify, and treat possible adverse effects.

5:00 – 5:30 pm **Diabetes Masterclass: Panel Discussion,** *Diabetes Masterclass Speakers* LS
A panel of board-certified internists with expertise in endocrinology will answer questions and share insights into the management of feline diabetes mellitus. Attendees are encouraged to bring their questions and share their challenges.

FRIDAY, OCTOBER 13, 2023

8:15 – 9:30 am C ***Critical Nutritional Foundations for Every Cat,*** *Dr. Valerie Parker* LS
During this session, we will review how to feed healthy cats over their lifetimes, including how nutritional requirements for cats change as they progress from kittenhood to senior adulthood. We will review how to determine energy (caloric) requirements for cats. We will review what information is presented on pet food labels, how to effectively use that information, and how to interpret nutrient profiles. Several pet food myths and some tips for effective communication will be discussed.

11:00 – 11:50 am A **Nutritional Management of the Comorbid CKD Patient,** *Dr. Valerie Parker* LS
We will review basic nutritional goals and nutrients of concern for cats with CKD and a few comorbid conditions, including inflammatory bowel disease, diabetes mellitus, and obesity. This will be a case-based discussion with emphasis on practical clinical decision making.

B **Nutritional Idiosyncrasies & the Role in Obesity, Diabetes Mellitus, & Hepatic Lipidosis,** *Dr. Adronie Verbrugghe* LS
Metabolic idiosyncrasies result in specific and unique nutritional requirements of cats. Peculiarities of carbohydrate, protein, and fat metabolism will be discussed. Moreover, we will explore if and how these idiosyncrasies predispose cats to metabolic diseases, including obesity, diabetes mellitus, and feline hepatic lipidosis.

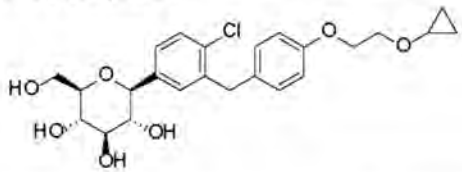
Bexacat™
(bexagliflozin tablets)

15 mg flavored tablets
For oral use in cats only
Sodium-glucose cotransporter 2 (SGLT2) inhibitor

CAUTION
Federal law restricts this drug to use by or on the order of a licensed veterinarian.

WARNING: DIABETIC KETOACIDOSIS/EUGLYCEMIC DIABETIC KETOACIDOSIS
- **Cats treated with Bexacat may be at an increased risk of diabetic ketoacidosis or euglycemic diabetic ketoacidosis (see Adverse Reactions). As diabetic ketoacidosis and euglycemic diabetic ketoacidosis in cats treated with Bexacat may result in death, development of these conditions should be treated promptly, including insulin administration and discontinuation of Bexacat (see Monitoring).**
- **Due to the risk of developing diabetic ketoacidosis or euglycemic diabetic ketoacidosis, do not use Bexacat in cats with diabetes mellitus who have previously been treated with insulin, who are receiving insulin, or in cats with insulin-dependent diabetes mellitus (see Contraindications).**
- **Bexacat should not be initiated in cats with anorexia, dehydration or lethargy at the time of diagnosis of diabetes mellitus or without appropriate screening tests (see Animal Safety Warnings).**

DESCRIPTION
Bexacat (bexagliflozin tablets) are flavored pentagonal, 10 mm, speckled white, brown, or tan biconvex with a characteristic odor. The empirical formula is $C_{24}H_{29}ClO_7$ and the molecular weight is 464.94 g/mol. The chemical name is (2S,3R,4R,5S,6R)-2-(4-chloro-3-(4-(2-cyclopropoxyethoxy)benzyl)phenyl)-6-(hydroxymethyl)tetrahydro-2H-pyran-3,4,5-triol.
The chemical structure of bexagliflozin is:



INDICATION
Bexacat is indicated to improve glycemic control in otherwise healthy cats with diabetes mellitus not previously treated with insulin.

DOSAGE AND ADMINISTRATION
Always provide the Client Information Sheet with the prescription.

Dosing Instructions
Administer one tablet by mouth to cats weighing 6.6 lbs (3.0 kg) or greater once daily, at approximately the same time each day, with or without food, and regardless of blood glucose level.

Monitoring
- Sudden onset of hyporexia/anorexia, lethargy, dehydration, or weight loss in cats receiving Bexacat should prompt immediate discontinuation of Bexacat and assessment for diabetic ketoacidosis, regardless of blood glucose level.
- During treatment with Bexacat, blood glucose, fructosamine, serum β-hydroxybutyrate (BHBA), serum feline pancreas-specific lipase (fPL), liver parameters, serum cholesterol and triglycerides; and body weight and clinical signs should be routinely monitored.
  - Increasing or persistently elevated feline pancreas-specific lipase or liver parameters should prompt further evaluation for pancreatitis and/or hepatic disease and consideration for discontinuing Bexacat.
  - BHBA is the predominate ketoacid in diabetic ketoacidosis. Bexacat should be discontinued if a notable reduction in BHBA is not observed after initiation of Bexacat, or if BHBA persistently rises after an initial reduction.
  - Cats with increasing or persistently elevated cholesterol and triglyceride levels may be at an increased risk for developing diabetic ketoacidosis or euglycemic diabetic ketoacidosis.
  - Bexacat should be discontinued if poor glycemic control, as described below, develops.
- During the first 8 weeks after initiation of Bexacat, assessment of glycemic control and clinical improvement should be evaluated.
  - A physical examination, an 8-hour blood glucose curve, serum fructosamine and body weight should be assessed at 2, 4 and 8 weeks.
  - Cats demonstrating poor glycemic control, including weight loss, an average blood glucose concentration from an 8-hour blood glucose curve ≥ 250 mg/dL, and/or a fructosamine indicating poor glycemic control should be closely monitored.
  - Bexacat should be discontinued, and initiation of insulin considered in cats demonstrating poor glycemic control, as described above, at 8 weeks.
- Cats may present with diabetic ketoacidosis and a normal blood glucose concentration (euglycemic diabetic ketoacidosis). Delay in recognition and treatment of diabetic ketoacidosis and euglycemic diabetic ketoacidosis may result in increased morbidity and mortality.
- Development of diabetic ketoacidosis and euglycemic diabetic ketoacidosis requires the following actions:
  - Discontinuation of Bexacat
  - Prompt initiation of insulin therapy
  - Administration of dextrose or other carbohydrate source, regardless of blood glucose concentration
  - Appropriate nutritional support should be promptly initiated to prevent or treat hepatic lipidosis.

For more information refer to **CONTRAINDICATIONS** and **WARNINGS.**

CONTRAINDICATIONS
- Do not use Bexacat in cats with diabetes mellitus who have previously been treated with insulin, who are receiving insulin, or in cats with insulin-dependent diabetes mellitus. The use of Bexacat in cats with insulin-dependent diabetes mellitus, or the withdrawal of insulin and initiation of Bexacat, is associated with an increased risk of diabetic ketoacidosis or euglycemic diabetic ketoacidosis and death.
- Due to risk of severe adverse reactions, do not use Bexacat in cats with evidence of hepatic disease or reduced renal function.

WARNINGS
User Safety Warnings
Not for use in humans. Keep out of reach of children. Consult a physician in case of accidental ingestion by humans.

Animal Safety Warnings
- Bexacat should not be initiated in cats with:
  - Anorexia, dehydration, or lethargy at the time of diagnosis of diabetes mellitus, as it may indicate the presence of other concurrent disease and increase the risk of diabetic ketoacidosis.
  - An fPL level > 5.3 mcg/L, diagnostic imaging consistent with pancreatitis, a history of pancreatitis, or current clinical signs suggestive of pancreatitis.
  - Laboratory values consistent with diabetic ketoacidosis, including elevated urine or serum ketones, and metabolic acidosis (high anion gap, or decreased bicarbonate, pH, or partial pressure carbon dioxide [$PaCO_2$] levels).
  - A BHBA > 37 mg/dL, or if BHBA is > 25 mg/dL and the cat has a history of renal disease or metabolic acidosis.
- Persistent plasma bexagliflozin concentrations and reduced clearance of Bexacat, represented as the presence of plasma half-lives in excess of 24 hours, may result in prolonged clinical effects such as glucosuria and/or euglycemia despite discontinuation of Bexacat in some cats with hepatic disease and/or reduced renal function, including cats with clinically undetectable disease at the time of Bexacat initiation. Reduced clearance of Bexacat may contribute to persistent glucosuria, resulting in an osmotic diuresis and dehydration that requires appropriate hydration support. These cats may require hospitalization, which may be protracted, for sequalae such as diabetic ketoacidosis, euglycemic diabetic ketoacidosis, or hepatic lipidosis.
- Cats should be screened for urinary tract infections and treated, if indicated, when initiating Bexacat. Treatment with Bexacat may increase the risk for urinary tract infections (see **Adverse Reactions**). Cats treated with Bexacat should be monitored for urinary tract infections and treated promptly. Consider discontinuation of Bexacat in cats with recurrent urinary tract infections.
- Bexacat may cause increased serum calcium concentrations. Bexacat should be discontinued in cats with persistent increases in serum total calcium or ionized calcium because of increased risk of forming calcium containing uroliths (see **Adverse Reactions**).
- Long term use of Bexacat may increase the risk of urothelial carcinoma (see **Adverse Reactions**).
- Keep Bexacat in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

PRECAUTIONS
- Bexacat should be discontinued in cats who develop diarrhea unresponsive to conventional therapy.
- Consider temporary discontinuation of Bexacat in cats during times of decreased caloric intake, such as surgery or decreased appetite, as administration of Bexacat in these cats may increase the risk of diabetic ketoacidosis or hepatic lipidosis.
- The osmotic diuretic effects of Bexacat may contribute to inappropriate urination in some cats (see **Adverse Reactions**).
- Polyphagia as a compensatory response to caloric wasting from glucosuria may persist in up to 80% of cats, despite evidence of adequate glycemic control, and may lead to progressive weight gain.
- Approximately 20-30% of cats may have persistent polyuria and/or polydipsia secondary to Bexacat-induced osmotic diuresis and may be a risk factor for dehydration-associated diabetic ketoacidosis.
- The concurrent use of volume depleting drugs in cats treated with Bexacat has not been evaluated.
- The safety of Bexacat in breeding, pregnant, and lactating cats has not been evaluated.

ADVERSE REACTIONS
Field Study
Eighty-four cats with newly diagnosed diabetes mellitus were enrolled in a 180-day multicenter field effectiveness and safety study. Safety data were evaluated in 84 cats treated with at least one dose of Bexacat. All cats received one tablet, once daily, regardless of body weight or blood glucose level. Seventy-two of the 84 enrolled cats completed the study. The most common adverse reactions included elevated blood urea nitrogen (BUN), vomiting, elevated urine specific gravity (USG), elevated serum fPL, diarrhea, anorexia, lethargy, and dehydration. The adverse reactions seen during the field study are summarized in Table 1 below.

Table 1. Adverse Reactions (n=84)

Adverse Reaction	Number (%)
Elevated BUN*	46 (54.8)
Vomiting	42 (50.0)
Elevated USG†	33 (39.3)
Elevated fPL‡	33 (39.3)
Diarrhea	32 (38.1)
Anorexia	31 (37.0)
Lethargy	17 (20.2)
Dehydration	16 (19.0)
Elevated symmetrical dimethylarginine (SDMA)	13 (15.5)
Weight loss	13 (15.5)
Urinary tract infection	12 (14.3)

Adverse Reaction	Number (%)
Elevated ALT and/or AST§	11 (13.1)
Hypercalcemia	8 (9.5)
Behavioral changes**	6 (7.1)
Proteinuria	5 (6.0)
Elevated creatinine	4 (4.8)
Elevated creatine kinase	4 (4.8)
Inappropriate urination	4 (4.8)
Death	3 (3.6)
Diabetic ketoacidosis	3 (3.6)
Pancreatitis	3 (3.6)
Euglycemic diabetic ketoacidosis	2 (2.4)
Hepatic lipidosis	2 (2.4)
Elevated alkaline phosphatase	2 (2.4)
Elevated total bilirubin	2 (2.4)
Constipation	2 (2.4)

* Most cats had elevations < 1.5 times the upper limit of normal (ULN).
† Elevations were predominantly attributable to dehydration and/or glucosuria.
‡ Most cats had one or more isolated elevations, followed by a return to previous values.
§ Of nine cats with elevations ≥ 1.5X ULN, 2 cats developed diabetic ketoacidosis and were transitioned to insulin. One cat developed diabetic ketoacidosis and hepatic lipidosis resulting in death (euthanasia). One cat developed anemia, progressive weight loss and fPL elevations resulting in death.
** Observations included hiding, agitation, aggression, vocalization, and anxious behavior.

Nine serious adverse reactions associated with Bexacat administration occurred during the study, including three cats who died or were euthanized. Of the three cats who died or were euthanized, two cats became clinically ill within 5 doses of Bexacat administration (range 3 to 5 doses). One cat with euglycemic diabetic ketoacidosis and hepatic lipidosis was euthanized due to further deterioration of its clinical condition, despite supportive treatment. One cat demonstrating anorexia, lethargy, dehydration, azotemia, and hypokalemia was euthanized without supportive treatment. One cat, who demonstrated a lack of effectiveness, anemia and hepatic lipidosis died on Day 77 despite supportive treatment and additional diagnostics. Six of the nine cats had serious adverse reactions that did not result in death or euthanasia. Five cats were treated for their clinical conditions and transitioned to insulin. Serious adverse reactions in these cats were associated with the following conditions (number of cats): euglycemic diabetic ketoacidosis (1); lack of effectiveness, diabetic ketoacidosis, elevated liver parameters (1); diabetic ketoacidosis (1); diabetic ketoacidosis and pyelonephritis (1); and lack of effectiveness, weight loss, dehydration (1). One cat with constipation and pancreatitis received supportive treatment and remained on Bexacat (bexagliflozin tablets).

Pilot Field Study

Eighty-nine cats with newly diagnosed diabetes mellitus were enrolled in a 56-day multicenter pilot field effectiveness and safety study, with continued use for up to 180 days. All cats received one tablet, once daily, regardless of body weight or blood glucose level. Safety data were evaluated for all 89 cats treated with at least one dose of bexagliflozin. The most common adverse reactions included elevated blood urea nitrogen (BUN), elevated urine specific gravity (USG), elevated serum feline pancreas-specific lipase, vomiting, diarrhea/loose stool, hyporexia/anorexia, lethargy, elevated serum alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST), and urinary tract infections. The adverse reactions seen in the pilot study are summarized in Table 2 below.

Table 2. Adverse Reactions (n=89)

Adverse Reaction	Number (%)
Elevated BUN*	51 (57.3)
Elevated USG†	43 (48.3)
Elevated fPL‡	39 (43.8)
Vomiting	39 (43.8)
Diarrhea/Loose Stool	29 (32.6)
Hyporexia/Anorexia	28 (31.4)
Lethargy	16 (18.0)
Elevated ALT and/or AST§	13 (14.6)
Urinary tract infection	13 (14.6)
Dehydration	10 (11.2)
Elevated symmetrical dimethylarginine (SDMA)	10 (11.2)
Behavioral changes**	9 (10.1)
Ketosis/Ketonuria	8 (9.0)
Weight loss	8 (9.0)
Proteinuria	8 (9.0)
Pancreatitis	7 (7.9)
Death	6 (6.7)
Anemia	6 (6.7)
Hepatopathy	6 (6.7)
Hypercalcemia	4 (4.5)
Elevated creatine kinase	4 (4.5)
Inappropriate urination	4 (4.5)
Peritonitis	3 (3.4)
Constipation	3 (3.4)
Elevated creatinine	2 (2.2)
Euglycemic diabetic ketoacidosis	2 (2.2)
Diabetic ketoacidosis	2 (2.2)
Hemolytic anemia	2 (2.2)
Elevated total bilirubin	2 (2.2)

* Most cats had elevations ≤ 1.5X upper limit of normal (ULN).
† Elevations were predominantly attributable to dehydration and/or glucosuria.
‡ Most cats had one or more isolated elevations, followed by a return to previous values.
§ Most elevations were ≤ 2X ULN. One cat had marked ALT and AST (9X and 6X upper limit of normal, respectively) elevations on Day 28. Following discontinuation of bexagliflozin, the liver enzymes decreased within 24 hours and returned to within reference range in 10 days.
** Observations included hiding, hyperactivity, vocalization, and abnormal behavior.

Twenty cats (22%) had at least one blood glucose value < 65 mg/dL recorded during 8-hour blood glucose curves. No clinical signs of hypoglycemia were observed and bexagliflozin dosing was not adjusted in any cat due to documented hypoglycemia. Nine serious adverse reactions associated with bexagliflozin administration occurred during the study, including six cats who died or were euthanized. Of the six cats who died or were euthanized, five became clinically ill within receiving 5 doses of bexagliflozin (range 1 to 5 doses). Four of the cats were euthanized due to further deterioration of their clinical condition despite supportive treatment. One cat died despite supportive treatment. Deaths were associated with the following conditions (number of cats): necrotizing pancreatitis and pancreatic abscess (1), pancreatitis and hepatic lipidosis (1), euglycemic diabetic ketoacidosis and severe hepatic lipidosis (1), pancreatitis and hepatic abscesses (1), diabetic ketoacidosis (1), and persistent polyuria and polydipsia and quality of life concerns (1).

Three of nine serious adverse reactions that did not result in death or euthanasia included the following (number of cats): acute hepatocellular injury (1), immune-mediated hemolytic anemia (1), and euglycemic diabetic ketoacidosis with concurrent pancreatitis and hepatopathy (1). Two cats with serious adverse reactions demonstrated persistent bexagliflozin blood plasma levels and elimination half-lives after discontinuation of bexagliflozin. One cat with renal and liver values within the reference range at screening was euthanized due to a continued decline in clinical condition despite treatment for euglycemic diabetic ketoacidosis and severe hepatic lipidosis. The second cat, noted to have IRIS (International Renal Interest Society) stage II renal disease and liver values within the reference range at screening, recovered following treatment for marked liver enzyme elevations above the reference range on Day 28.

Extended Use Field Study

One hundred twenty-five cats with diabetes mellitus that had previously completed a bexagliflozin field study were enrolled in a multicenter extended use field study. Cats were enrolled in the study for a range of 7 to 1064 days, with a mean of 329 days. Safety data were evaluated for all 125 cats treated with at least one dose of Bexacat (bexagliflozin tablets). All cats received one tablet, once daily, regardless of body weight or blood glucose level. Forty-nine of the 125 enrolled cats were withdrawn from the study due to adverse reactions, serious adverse reactions, death/euthanasia, lack of effectiveness, suspected diabetic remission, withdrawal of owner consent, or lost to follow up. The most common adverse reactions were similar to those noted in the previous field studies and included elevated USG (35.2%), vomiting (27.2%), elevated fPL (26.4%), anorexia (24.0%), diarrhea (22.4%), urinary tract infections (17.6%), lethargy (16.8%), and death (16.0%).

Twenty serious adverse reactions associated with Bexacat administration occurred during the study, all resulting in death or euthanasia. Clinical signs of hypoglycemia were observed in two of these cats. Deaths were associated with the following conditions (number of cats), with some cats experiencing multiple comorbidities (necropsy was not granted in all cases): euglycemic diabetic ketoacidosis (8); diabetic ketoacidosis (4); hepatic lipidosis (5); pancreatic necrosis/peripancreatic fat saponification (3); urothelial carcinoma (2); hypercalcemia, recurrent calcium containing cystic calculi (1); lack of effectiveness, weight loss, anorexia (1); lethargy, weight loss, pallor (1); chronic renal disease, glomerulonephritis (1); chronic enteropathy (1); hypoglycemia, possible pancreatitis (1).

CONTACT INFORMATION

To report suspected adverse events, for technical assistance, or to obtain a copy of the Safety Data Sheet (SDS), contact Elanco US Inc at 1-888-545-5973.

For additional information about reporting adverse drug experiences for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae.

INFORMATION FOR CAT OWNERS

Owners should be given the Client Information Sheet to read before Bexacat is administered. Owners should be advised to discontinue Bexacat and contact a veterinarian immediately if their cat develops anorexia, lethargy, vomiting, diarrhea, or weakness.

CLINICAL PHARMACOLOGY

Mechanism of Action

Bexagliflozin is an inhibitor of sodium-glucose cotransporter 2 (SGLT2), the renal transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation. By inhibiting SGLT2, bexagliflozin reduces renal reabsorption of filtered glucose and lowers the renal threshold for glucose, thereby increasing urinary glucose excretion.

Pharmacokinetics

In a laboratory pilot study conducted to determine the prandial state of maximum exposure, systemic exposure for bexagliflozin was greater in the fasted state than in the fed state by 82% for the mean maximum observed plasma concentration (C_{max}), and by 54% for the mean area under the plasma concentration versus time curve (AUC) from dosing (time 0) to the last quantifiable concentration ($AUC_{0\text{-last}}$), respectively.

In a well-controlled margin of safety study (see **Target Animal Safety**), mean C_{max} was approximately dose-proportional over a dosage range of 5 mg/kg (1X) to 25 mg/kg (5X). Mean AUC from time 0 to 24 hours exposure was approximately dose-proportional over a dosage range of 5 to 15 mg/kg, but more than dose-proportional at 15 to 25 mg/kg. An increase in exposure (AUC_{0-24} and C_{max}), was observed in female cats compared to male cats on all evaluation days. Median time to reach peak plasma concentration (T_{max}) was approximately 0.5 hours (range 0.5 to 2 hours) and mean half-life ($T_{1/2}$) was approximately 5 hours across all dose groups. There was no accumulation of bexagliflozin following daily dosing of 5, 15, and 25 mg/kg in healthy non-diabetic cats. However, field studies showed that some diabetic cats had persistent bexagliflozin blood levels after discontinuation of the drug, which may be related to a decrease in liver function in some cats (see **Animal Safety Warnings**).

EFFECTIVENESS

Field Study

Eighty-four cats diagnosed with diabetes mellitus were enrolled in a 180-day multicenter field effectiveness and safety study. Enrolled cats included purebreds and mixed breeds, ranging in age from 3 to 19 years, and weighing between 7.3 to 24.3 lbs (3.3 to 11.3 kg). Cats received one tablet, once daily, regardless of body weight or blood glucose level. Treatment success was defined as improvement in at least one blood glucose variable (blood glucose curve mean or fructosamine) and improvement in at least one clinical sign of diabetes mellitus (polyuria, polydipsia, polyphagia, or body weight [weight gain or no weight loss]).

Of 77 cats included in the effectiveness-evaluable population:

- 64 cats (83.1%) were considered a treatment success on Day 56.
- The lower bound two-sided 90% confidence interval was 74.5%. Effectiveness was demonstrated if the lower bound of the confidence interval was > 66%.
- Mean blood glucose curve mean decreased from 284 mg/dL on Day 0 to 143 mg/dL on Day 56.
- Mean fructosamine levels decreased from 544 µmol/L prior to Day 0 to 295 µmol/L on Day 56.
- Improvements in the clinical signs of polyuria, polydipsia, polyphagia, and body weight on Day 56 were observed in 53 (68.8%), 57 (74.0%), 44 (57.1%), and 42 (54.6%) cats, respectively.
- 66 cats (85.7%) completed the 180-day study.

Pilot Field Study

Eighty-nine cats diagnosed with diabetes mellitus were enrolled in a 56-day, multicenter pilot field effectiveness and safety study with continued use for up to 180 days. Enrolled cats included purebreds and mixed breeds, ranging in age from 3 to 17 years and weighing 6.4 to 22.9 lbs (2.9 to 10.4 kg). Cats received one tablet, once daily, regardless of weight. Treatment success was defined as improvement in at least one blood glucose variable (blood glucose curve mean or fructosamine) and improvement in at least one clinical sign of diabetes mellitus (polyuria, polydipsia, polyphagia, or body weight [weight gain or no weight loss]). Of the 72 cats included in the effectiveness-evaluable population, 58 (80.6%) were considered treatment successes on Day 56.

TARGET ANIMAL SAFETY

In a well-controlled laboratory margin of safety study, Bexacat was administered orally to 28 fasted, healthy, lean, intact adult cats at doses of at least 1X (8 cats), 3X (8 cats), and 5X (12 cats) the maximum exposure dose (5 mg/kg) once daily for 26 weeks. The control group (8 cats) was sham dosed. The maximum exposure dose (5 mg/kg) was based on the assessment that the minimum weight of an eligible cat with diabetes mellitus is approximately 3 kg. Polyuria, glucosuria (with a corresponding increase in food consumption), loose stools and diarrhea, and ketonuria were reported more frequently in cats that received Bexacat than in control cats. There were drug-related clinically insignificant increases in calcium, magnesium, and cholesterol levels, and decreases in creatinine and amylase levels, and blood pressure and heart rate values. Gross necropsy demonstrated treatment-related observations of mild, diffuse zonal patterns in the liver. One cat with the observed zonal pattern had mild elevations of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), and a histopathological observation of minimal, multifocal necrosis in the liver. The histopathological finding did not correspond to the zonal patterns observed grossly. There were no clinically relevant, drug-related effects on hematology and coagulation parameters and organ weight values.

STORAGE CONDITIONS Bexacat should be stored at room temperature 68 to 77 °F (20 to 25 °C).

HOW SUPPLIED

Flavored tablet each containing 15 mg bexagliflozin; 30 or 90 tablets per bottle.

Approved by FDA under NADA # 141-566
Manufactured for: Elanco US Inc, Greenfield, IN 46140

September 2022

FRIDAY, OCTOBER 13, 2023 continued

11:55 – 12:45 pm

A Use of Assisted Enteral Nutrition, *Dr. Valerie Parker* LS
We will review timing and implementation of assisted enteral nutritional support. We will discuss feeding tube and diet selection, determining caloric needs, and how to troubleshoot common complications associated with feeding tubes.

B Do Nutrients & Ingredients Matter for Weight Loss? How to Select a Diet, *Dr. Adronie Verbrugghe* LS
Feline obesity is common and achieving weight loss is a challenge. In this session we will explore key nutritional factors to maximize weight loss success. Evaluation of dietary nutrients and ingredients is the basis to select a diet and design an individualized weight loss plan.

1:00 – 2:00 pm

L Velagliflozin: An Oral Solution for the Diabetic Cat, *Diabetes Masterclass Speakers* IPO
A brief overview of the SGLT-2 inhibitors and the role of velagliflozin in the management of feline diabetes mellitus will be presented. A panel of experts will then answer questions and share their perspectives on how to introduce this exciting new product into our practices.

L Evolving the Feline MDB: Purrfect Balance for Your Patient Assessment, *Drs. Elizabeth Schooley & Kelly St. Denis* IPO
The minimum database is a concept that many veterinarians are familiar with but should the MDB be the same for all patients? Recent data studies looking at the diagnostic findings of cats across age ranges and diagnostic use cases will be discussed. Additionally, the unique diagnostic behaviors of Cat Friendly Practices® will be shared. This information will help pave the way to create the purrfect diagnostic plan for the feline patients in your care.

L Calming Cats: The Impact of Transport & Anxiety on Our Cats, Cat Caregivers, & Practices, *Dr. Tracey Deiss* IPO
This session will look at feline transport and vet visit fear, anxiety, and stress from the lens of the cat, cat caregiver, and practice. By examining what we know about feline behavior, routines, and comfort, we can better understand why transport and vet visit is a rate limiting factor in transport and exam success. Recognizing that FAS manifests in a gambit of clinical behaviors, we can help our cat caregivers and teams promote treatment for the spectrum and touch on current pharmacologic and non-pharmacologic treatment modalities.

2:10 – 3:00 pm

A Nutritional Management of Chronic Enteropathies, *Dr. Valerie Parker* LS
We will review various methods by which to manage chronic enteropathies (e.g., inflammatory bowel disease) with diet and other nutritional modifications.

B Feeding Comorbidities: Obese Cats with Other Diseases, *Dr. Adronie Verbrugghe* LS
Feline obesity is highly prevalent. Weight loss is recommended, but often complicated by other diseases. This session will use a case-based approach to explore diet selection and weight loss in cats with multiple diseases.

3:05 – 3:55 pm

A Harnessing the Power of Fiber to Manage GI Disease, *Dr. Valerie Parker* LS
We will begin the discussion reviewing how we can describe different fiber sources. Then we will discuss how to quantify fiber and different situations in which fiber supplementation may prove useful in controlling stool quality. Cases will be used to illustrate points.

B Navigating Alternative Cat Foods: Intersection Between Cat Needs & Client Preferences, *Dr. Adronie Verbrugghe* LS
The pet food market continues to evolve with more and more cat food choices available. Moreover, humanization of pets leads to cat caregivers looking for diets that resemble their own. Alternative diets can be commercial or homemade, heat-processed or raw, meat- or plant-based. This session will explore how to navigate alternative diet discussions in the consult room.

4:40 – 5:30 pm

A Nutritional Management of Hypercalcemia, *Dr. Valerie Parker* LS
We will briefly review the pathophysiology and etiologies of hypercalcemia in cats. We will review various nutritional approaches that have been suggested in the past and then discuss a potential new paradigm shift to manage hypercalcemia in cats.

B Feeding the Allergic Cat, *Dr. Sara Ramos* LS
A primary goal of this lecture is to provide a new sense of confidence to attendees on how to design an appropriate diagnostic plan for the pruritic feline patient. This seminar will focus heavily on the dietary and nutritional aspects of feeding allergic patients with a review of food allergies in feline patients. Performing an excellent diagnostic work-up for the pruritic feline patient will allow quicker identification of the primary disease. Subsequently, once the primary disease is identified, appropriate and effective treatment can be prescribed to increase patient comfort and client satisfaction.

American Association of FELINE PRACTITIONERS

Meow Hear This: Exciting Announcements from the AAFP

2023 AAFP/IAAHPC Feline Hospice and Palliative Care Guidelines

These Guidelines were developed by experts from the AAFP and the International Association for Animal Hospice and Palliative Care. Key features include:

- A comprehensive, five-step care plan that allows for tailoring the approach to both the cat and the family involved in the care.
- Discussion about communication and caregiver preferences, relationship-centered care, and guiding the caregiver through the consultation.
- Establishing 'budgets of care,' a concept that greatly influences what can be done for the individual cat by establishing what is reasonable, practical, and ethical.
- A further concept of the 'care unit' is introduced, which is extrapolated from human hospice and palliative care, and encourages and empowers the caregiver to become a part of the cat's care every step of the way.
- Ethical considerations include a decision-making framework.
- The importance of comfort care is emphasized, and the latest information available about how to assess the quality of a cat's life is reviewed.
- Review of the cat's emotional health, meeting the individual cat's essential needs, and environmental modification is detailed.
- Nutrition and hydration management is discussed.

These Guidelines were supported by an educational grant from Royal Canin.

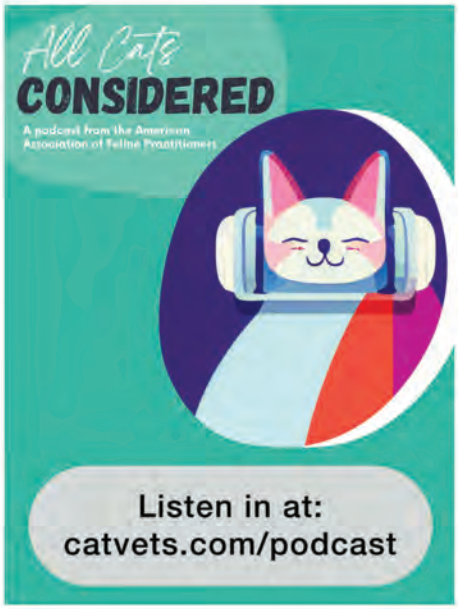
Access the 2023 AAFP/ IAAHPC Feline Hospice and Palliative Care Guidelines at **catvets.com/hospice.**

AAFP eLearning Center

Join us for live and on-demand sessions on a variety of feline topics. Upcoming RACE-approved feline education presentations include:

- November 7, 2023: *The Story of Mayhem Maya and Insane Ida: How to Prioritize Nutrition for Kitties with Comorbidities* | Speaker: Lindsey Bullen, DVM, DACVIM (Nutrition);
- December 2023 (TBA) *A Guide to Diagnosis of FIP, FIV, and FeLV in 2023* | Speaker: Samantha Evans, DVM, Ph.D., DACVP;

AAFP Members have exclusive access to over 65 on-demand presentations. Learn more at **catvets.com/elearning**.



Session Abstracts

Schedule is in Central Daylight Time

KEY: S BREAKFAST SYMPOSIUM LS LIVE STREAMED
A TRACK A
B TRACK B
C TRACK C

SATURDAY, OCTOBER 14, 2023

7:00 – 7:50 am

S **Controlling OA Pain in Cats: Where Do I Start?,** *Drs. Joyce Login & Michelle Meyer* LS
Cats may seem like they're hiding pain, but they're usually telling us plenty if we know their language. Help clients understand the signs of chronic feline osteoarthritis (OA) pain, get familiar with the ways OA affects more than just the joints of older cats—and find out all about how an anti-nerve growth factor (Anti-NGF) monoclonal antibody can control that pain. There will be real-world case studies shared that show before/after videos and give practical ways to get started treating more cats. It's easier than you think!

8:00 – 8:50 am

A **Nutritional Management of Diabetes Mellitus,** *Dr. Audrey Cook* LS
There is still substantial controversy regarding feeding protocols for cats with diabetes mellitus, along with new concerns about the impact of highly processed foods on pancreatic function. In this session, we will review the evidence behind current recommendations, and discuss the physiological responses of cats to various macronutrient profiles. The role of the incretins in glucose homeostasis and food intake will be summarized, along with the potential impact of advanced glycation end products on islet cell health.

B **The Feline Philosophy Behind Diagnosing GI Disease,** *Dr. Craig Webb* LS
This discussion will use cases to highlight fundamental principles–often best expressed by non-veterinarians–that are critical to the successful practice of veterinary medicine. Attendees will learn to recognize and appreciate the critical role that "philosophy" plays in their approach to everyday feline cases.

C **Sippin' Through Straws: Taking the Stress Out of Feline Neonate Tube Feeding,** *Ellen Carozza* LS
In this lecture we will go over this necessary and essential skill for technicians and practitioners, and we will troubleshoot common problems and nutrition goals encountered with tube feeding. You'll leave feeling confident and bring back a skill you can use immediately in practice. As a bonus, the speaker will discuss how to properly meet their nutritional needs during a crisis.

8:55 – 9:45 am

A **Nuanced Nutrition: Calcium Oxalate Urolithiasis,** *Dr. Audrey Cook* LS
Calcium oxalate stones are routinely identified in feline patients and cause considerable morbidity. Dietary modification may reduce stone formation, but the impact of electrolytes such as sodium must be carefully considered. As calcium oxalate urolithiasis is associated with chronic kidney disease, strategies to address both issues will be outlined.

B **The Feline Pyramid of Poop,** *Dr. Craig Webb* LS
This discussion will build a pyramid of differentials for feline diarrhea where each layer represents a unique category. The structure emphasizes the steps required to successfully travel from one layer to the next, guided by standard script recognition as well as key features of each level.

C **Chew With Your Mouth Closed! Preventing Food Phobias & Fighting at the Dinner Table in the Multi-cat Household,** *Ellen Carozza* LS
Feeding the multi-cat household can be quite the challenge for a family. In this discussion we will go over creating safe, friendly meal environments as well as preventing food aversion from fearful interactions. You will also learn how to deal with common problems with age difference feedings and prescription diets in the home.

11:00 – 11:25 am

A **Cobalamin: Diagnostic & Therapeutic Implications,** *Dr. Audrey Cook* LS
Vitamin B12 plays a key role in numerous metabolic processes, and deficiency can impact appetite, gastrointestinal tract function, and hematopoiesis. Although hypocobalaminemia is routinely reported in cats with inflammatory or infiltrative bowel disease, various other conditions can also impact serum cobalamin concentrations. In this lecture, the indications for measuring B12 and the implications of subnormal levels will be discussed.

11:00 – 12:15 pm

B **No Way Out! Constipation, Obstipation, Megacolon: Panel Discussion,** *Drs. Adam Rudinsky, Betsy Swanson, & Craig Webb* LS
This panel discussion will cover all aspects of this serious and stubborn feline condition.

C **RECOVER CPR Guideline Updates: Feline Focus,** *Ken Yagi* LS
When patients experience cardiopulmonary arrest (CPA), seconds count. A well-trained and prepared veterinary health care team can mean the difference between life and death when a patient experiences CPA. Once CPA occurs, high quality Basic Life Support (BLS) including chest compressions and ventilation are arguably the most important part of resuscitating the patient. Once chest compressions and ventilation have been started in cats that experience CPA, Advanced Life Support (ALS) interventions can help maximize the chance of achieving return of spontaneous circulation. This lecture will explain key concepts from the newly updated RECOVER 2.0 guidelines and BLS and ALS with a focus on updates related to felines.

11:25 – 12:15 pm

A **Modifying the Microbiome: The Role of Probiotics in Feline Practice,** *Dr. Audrey Cook* LS
Numerous probiotics products are routinely advocated for a range of diseases and conditions in cats. In this lecture, we will review the evidence to support the use of probiotics and discuss the limitations of our current understanding. We will also establish some 'best practices' when reaching for a probiotic, and provide the attendee with solid guidelines regarding when to consider this approach and how to select an appropriate product.

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Session Abstracts

Schedule is in Central Daylight Time

KEY: L LUNCH & LEARN | A TRACK A | B TRACK B | C TRACK C | LS LIVE STREAMED | IPO IN-PERSON ONLY

SATURDAY, OCTOBER 14, 2023

12:30 – 1:30 pm

L Feline GI Immunity's Inextricable Links to Dietary & Microbiome Components, *Dr. Alison Manchester* IPO

The gastrointestinal tract is home to the largest number of immune cells in the body. This organ system is tasked with excluding pathogens while assimilating nutrients. During this hour, we'll take a case-based approach to delve into function and dysfunction within the feline gastrointestinal immune system. Special attention will be devoted to the gut's most influential environmental triggers: the mucosal microbiome and dietary components. Attendees will be presented with data clarifying how and why microbial counterparts and food constituents impact the feline GI tract, as well as with existing evidence for the role of nutritional interventions in cats with chronic enteropathy. The lecture will incorporate basic and clinical research with the goal of providing actionable recommendations to improve management of clinical cases.

L Why is This Kitty Skinny? What Should I Do About It?, *Dr. Jessica Pritchard* IPO

Participants will learn to differentiate sarcopenia from cachexia and interventions to help cats losing weight. We'll discuss the most common disease processes leading to weight loss in cats, how to diagnose them, and how to help cats gain weight back. Pharmacologic interventions will be the main focus, with a brief discussion of assisted feeding techniques as well.

L Let's Get Digital: How Smart Pet Tech Can Make a Big Impact on Cat Care, *Dr. Sheryl Gamble* IPO

Millennial and Gen Z clients are now the largest segment of pet caregivers. A recent study shows that this new generation of caregivers view their pet as a part of the family and are willing to spend more money on them than previous generations. As digital natives, this segment of pet caregivers seek out technology to solve common issues, including for their health and pets. The Sure Petcare feline line of microchip and app connected technologies seeks to bridge the gap between pet caregivers, pet health, and best medical practice in the veterinary clinic while also solving for common issues in multi-cat households.

1:40 – 2:30 pm

A Management of Liver Disease, *Dr. Adam Rudinsky* LS

What tools are available for management of liver disease? Are we using them correctly? In this lecture, we will review the most common medications, dietary approaches, and other supplements used for liver disease management and treatment in cats. This discussion will include evidence-based analysis of the management strategies we reach for in our hospital pharmacies. We will also discuss how these therapies apply to the most prevalent differentials in feline chronic liver disease.

B Diagnostic Testing in Feline Chronic Enteropathy Demonstrates Evolution from Inflammatory Bowel Disease to Intestinal Lymphoma, *Dr. Anne Avery* LS

The most common form of feline inflammatory bowel disease is characterized by epitheliotropic T lymphocytes. A diagnosis of lymphoma is made when these cells are present in high concentrations or cause disruption of mucosal architecture, or both. Although not formally demonstrated by a longitudinal study, these two diseases are almost certainly a continuum. The point at which the disease transitions from inflammation to neoplasia is difficult to detect by histology alone. Other testing, including clonality assessment with the PARR assay and detection of the STAT5B mutation, may be useful for clarifying histology, but ultimately the utility of these diagnostics will be determined by their ability to predict outcome. In this talk, data from multiple types of diagnostic testing will be presented to support the hypothesis that inflammatory bowel disease and lymphoma are a continuum. The principles behind different tests, their relationship to one another, and their ability to predict outcomes will also be discussed.

C Nursing & Nutrition for the Critical Feline Patient Who Just Won't Eat!, *Dr. Ashlie Saffire* LS

Nutritional support for the critically ill is an important part of nursing hospitalized patients and prompt intervention is crucial to recovery. In this discussion we will review helpful nursing techniques for anorexic hospitalized patients. Improving the hospitalization environment to reduce stress, recognizing signs of pain and nausea, in addition to placement and use of enteral feeding tubes will be discussed.

3:15 – 4:05 pm

A Liver & Biliary System: Peri-Operative Care, Surgical Evaluation, & Diagnostic Sampling, *Dr. Betsy Swanson* LS

This presentation will discuss presurgical workup, perioperative considerations, common surgical liver diseases, and indications and techniques for obtaining liver biopsies in cats. We will also review normal feline biliary tract anatomy and biliary diseases, how to evaluate the biliary system during surgery, how to collect a bile sample, and when to refer for surgery.

B The Role of Microbiome: Supporting, Immune Modulating, & Stress Lessening Probiotics in GI Diseases, *Dr. Michael Lappin* LS

Research evaluating the clinical effects of probiotics and synbiotics used in cats is ongoing. In this session, data supporting the use of certain probiotics to lessen stress, stabilize the GI microbiome, and modulate the immune system in cats will be presented. Emphasis will be placed on commercially available probiotics and clinical uses.

C Discussing Diabetes Mellitus: Empowering Technicians, *Ken Yagi* LS

Become the diabetes Tech Champion of your clinic. From the first interaction you have with a pet caregivers to the diabetes conversation after diagnosis and throughout the long-term care of a diabetic pet, this presentation will empower you to support pet caregivers as they embark on the diabetes journey.

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MERCK Animal Health

SATURDAY, OCTOBER 14, 2023 continued

4:10 – 5:00 pm

A Interpreting Liver Biopsies, *Dr. Adam Rudinsky* LS

The liver biopsy is the elusive, holy grail of hepatic diagnostics. But as clinicians, what are we looking for and when? In this lecture, we will review when a liver biopsy is most useful and worth the investment of time and patient involvement. We will discuss the most useful findings and differentials obtained from liver biopsies related to feline chronic liver disease. And more importantly, how to effectively translate this information into an action plan for our patients. In a world where convincing caregivers to biopsy the liver is a challenge, we will emphasize evidence-based justification for this procedure so that we can utilize it appropriately, confidently, safely, and judiciously.

B Update on the Diagnosis & Management of Infectious GI Diseases, *Dr. Michael Lappin* LS

There are multiple bacterial, parasitic, and viral agents associated with vomiting or diarrhea in cats. In this session, updates on many of the most common infections will be presented. Emphasis will be placed on newer diagnostic tests and newer treatments. Prevention will also be discussed for most agents.

C Practical Application of Feline Emergency Transfusions, *Ken Yagi* LS

The ability to perform transfusions in an emergency is a lifesaving form of treatment today. When it comes to feline patients, the story becomes complicated and faces practical challenges. Having enough of the correct type of blood can be a practical limitation in providing care. Application of transfusion medicine involves determining when transfusions are truly needed, compatibility testing, and careful administration. The option of transfusing dog blood into cats has been an emergency maneuver more veterinary practitioners are depending on to provide the needed red blood cells. We will explore the facts surroundings feline transfusions including the most recent evidence.

5:00 – 5:30 pm

Cat Friendly Practice®: Because You're Worth It

If you are looking for a proven way to improve cat caregiver satisfaction, bring more cats into your practice for healthcare, and improve your team dynamic when handling and caring for cats, the Cat Friendly Practice Program is for you! Please join us to learn how to improve your practices' bottom line, your teams' safety and happiness at work while we discuss the Cat Friendly Practice Program and the small changes you can make to achieve this designation.

SUNDAY, OCTOBER 15, 2023

7:00 – 7:50 am

S Feline Constipation: Updates on Acute & Chronic Treatment Modalities, *Dr. Ashlie Saffire* LS

Join us for a comprehensive discussion on acute and chronic management strategies for feline constipation. Techniques including the use of polyethylene glycol (PEG 3350) administered at a constant rate infusion via nasoesophageal tube in the acutely obstipated patient will be shared. Additionally, we will discuss how the use of fiber and diet therapy can help with chronic management and prevention.

7:30 – 10:00 am

W Cat Friendly Interactions & Handling Workshop, *Dr. Ilona Rodan* IPO

Cat Friendly veterinary interactions and handling increase human safety, team and client satisfaction, appointment efficiency, feline veterinary visits, and patient welfare. The goal is to understand the cat, both as a species and individual, and tailor the exam to each cat by appropriately responding to their emotional state and behavioral responses. As the stress of veterinary visits starts and ends at home, an important component of our care is cooperative care, partnering with caregivers to create feline positive emotional associations with the carrier and veterinary care. Working cooperatively with cats to increase physical and emotional health makes cats safer and easier to work with, resulting in appointments being completed more quickly and reducing the numbers of personnel needed. This hands-on workshop will begin with an updated summary presentation to help understand cats and why certain handling techniques work best. This will be followed by a breakout into small groups with demonstration of multiple techniques by Dr. Rodan; each attendee will then have the opportunity to apply those techniques utilizing live cats. This session requires separate registration. Read more on page 23.

8:00 – 8:50 am

A Approach to the Vomiting Cat: Causes, Treatment, & Management, *Dr. Adam Rudinsky* LS

Do all cats vomit? That is the common misconception amongst many caregivers, as well as some veterinarians. We will start the discussion of this topic with a review of the scope of the problem and how prevalent vomiting is for cats. Following that, we will discuss the more frequently overlooked causes of vomiting, how they are diagnosed, and how they are treated. This is a large world of differentials well beyond chronic inflammatory enteropathies and small cell lymphoma!

B Stem Cells in Feline GI Disease, *Dr. Craig Webb* LS

The basic but fascinating biology of feline adipose-derived mesenchymal stem cells will be discussed as it relates to cats: where they come from, what they can do, what has been done with them so far, what might we do with them, and what might you do with them.

8:55 – 9:45 am

A Approach to Diarrhea in Kittens, *Dr. Adam Rudinsky* LS

In this seminar, we will review pediatric feline diarrhea management and major roadblocks in addressing this frustrating clinical scenario. This lecture will prioritize fundamental diagnostics and empirical treatments which can be utilized based on current literature and new findings from recent research. A special focus will be made on the vast array of infectious diseases and associated diagnostics targeted in early life gastrointestinal disease.

B Diagnostic Dilemmas: The History, Mystery, & Bemoaning of Feline Triaditis, *Dr. Craig Webb* LS

Although the education of veterinarians is designed in 50-minute blocks as if diseases occur one-at-a-time and are clearly labelled, nothing could be further from the truth. Cats are the poster child for comorbidities, with Feline Triaditis being a classic representation of this phenomenon.

SUNDAY, OCTOBER 15, 2023 continued

10:45 – 11:35 am

A Feline Pancreatic Disease: Familiar Friends & Missed Connections, *Dr. Adam Rudinsky* LS

In this lecture, we will review inflammatory pancreatic disease (e.g., pancreatitis) in cats as well as underrecognized disease of the pancreas (e.g., feline exocrine pancreatic insufficiency) with an emphasis on achieving a diagnosis and proper case management. We are all familiar with pancreatitis and in the first half of this lecture we will review current updates in diagnosis and management of this syndrome. In the second half of the lecture, we will focus on the often overlooked exocrine disorder of the pancreas and how it deviates from many clinician's 'classic' view of the disorder.

B Feline Chronic Enteropathy, *Dr. Craig Webb* LS

This discussion will focus on a few of the more rare and more recent entries into the recognized group of Feline Chronic Enteropathies, but most of our focus will be on inflammatory bowel disease versus low-grade alimentary lymphoma. Attendees will learn what we know about diagnosis, prognosis, and treatment, as well as what we don't know.

11:40 – 12:30 pm

A Approach to the Yellow Cat, *Dr. Adam Rudinsky* LS

In this lecture, we will review the most common causes of chronic liver disease in cats with an evidence-based emphasis on empirical management strategies. We will discuss the most prevalent, concerning, and important differentials related to feline chronic liver disease and how to effectively translate this information into empirical management plans for chronic liver patients. In a world where convincing caregivers to biopsy the liver is a challenge, we will demystify the empirical 'without biopsy' approach to liver patients in a practical patient-centered approach.

B FMT: What's Coming Down the Pipeline, *Dr. Craig Webb* LS

The "Microbiome" is all the rage, seemingly responsible for most every ailment known to the veterinary profession. So it is no surprise that Fecal Microbiota Transplantation (FMT) is rising out of the litter box and into our practice at a rapid rate. This discussion will help attendees appreciate the potential, put together a recipe, and critically consider the paucity of evidence behind the magic that is FMT.

12:40 – 1:40 pm

L Elevate Your Practice's Feline Wellness at Every Life Stage, *Dr. Matt McGlasson* IPO

Today's feline caregivers want the absolute best for their cats. Is your practicing doing enough? In this lecture, we will discuss important touch points and messaging for every life stage of our feline patients. Cats make our lives so much better—let's elevate the care that we provide!

L Cats Don't Read Textbooks: The Conundrums of Diagnosing Feline Hyperthyroidism, *Dr. Kelly St. Denis* IPO

We all know *that* cat. The total T4 is a little bit high, but there are no clinical signs. Or maybe the T4 is normal, but the clinical picture fits with feline hyperthyroidism. Perhaps there are comorbidities which are complicating the diagnosis. Sometimes a diagnosis of feline hyperthyroidism can be straight forward, but at times we are left with 'that cat,' trying to sort out what to do next. In this seminar, we will explore diagnostic dilemmas with feline hyperthyroidism including how to use additional testing to navigate our way through the diagnostic maze. We will also look at case management, with or without comorbidities.

L Don't Sugar Coat It: Treatment Options for the Diabetic Cat, *Dr. Cynthia Ward* IPO

Treatment of the diabetic cat can be a challenge to caregivers and veterinarians. This talk will focus on options available for successful diabetic management in the cat. Different approaches to treatment will be discussed and appropriate clinical cases will be highlighted.

1:45 – 2:35 pm

A Emerging or Just Ignored: Ductal Plate Malformations, *Dr. Adam Rudinsky* LS

In this lecture, we will discuss one of the emerging diseases in feline liver disease, ductal plate malformations. Are they really new? Or are we just now understanding the scope of what they are? Here we will discuss what types of ductal plate malformations are recognized and how they may be impacting some of our most challenging and refractory liver patients.

B The Vomiting Cat: Probing for Answers in the Older Cat, *Dr. Jennifer Babineaux* LS

This session will cover using ultrasound to diagnose the underlying causes of vomiting in the older cat, focusing on chronic enteropathies and neoplasia. The session will review the ultrasound appearance of the normal feline gastrointestinal system and contrast normal with changes observed on ultrasound in cats with chronic enteropathies and gastrointestinal neoplasia. Attendees will feel more confident in utilizing ultrasound to assist in the diagnosis of chronic enteropathies and gastrointestinal neoplasia.

2:40 – 3:30 pm

A Feline Gastrointestinal Eosinophilic Sclerosing Fibroplasia, *Dr. Petra Cerna* LS

Feline gastrointestinal eosinophilic sclerosing fibroplasia (FGESF) is a recently described disease in cats that presents as eosinophilic mass(es) that are associated with the gastrointestinal tract and abdominal lymph nodes, most commonly near the pylorus or ileocolic junction. This disease is most commonly seen in middle-aged cats of all breeds with Ragdolls being overrepresented. This lecture will focus on presenting the most common clinicopathological findings in cats with FGESF as well as well as diagnosis of this disease. Last but not least, it will cover possible treatments and outcome of cats with FGESF.

B The Vomiting Cat: Probing for Answers in the Younger Cat, *Dr. Jennifer Babineaux* LS

This session will cover using ultrasound to diagnose the underlying causes of vomiting in the younger cat, focusing on acute causes of vomiting. Attendees will develop a solid understanding of when to choose radiographs vs. ultrasound as an imaging modality in cases of acute vomiting. Attendees will feel more confident in utilizing ultrasound to assist in the diagnosis of gastric or intestinal foreign bodies, acute gastroenteritis, intussusception, and acute pancreatitis.

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American Association of FELINE PRACTITIONERS®
STUDENT CHAPTER

The AAFP Cat Friendly Certificate Program: Take Your Cat Care Skills to the Next Level

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- Understanding of cats.
- Commitment to feline health.
- Increased confidence when working with cats.
- Enhanced ability to fulfill client and patient needs.

Plus, you can take the certificate wherever your career takes you!

The Cat Friendly Practice® Program

The Cat Friendly Practice® (CFP) Program is designed to help you elevate care for cats. You will learn how to enhance the veterinary experience and reduce stress for the cat, their caregiver, and your team.

The Program consists of an online self-assessment checklist covering 10 topic areas to ensure that your practice is optimized for feline care, and is available exclusively to AAFP Members...so why not join today?

The Cat Friendly Practice® Program can result in*:

- A less stressful environment for the patients, caregivers, and staff.
- A team that is passionate for their feline patients and unique needs.
- Higher satisfaction rates among current clients.
- Increased feline healthcare expertise among your team members.
- A positive change in team dynamics.
- Better veterinary diagnostic care for feline patients.
- Cost reduction in workers' compensation claims.

*As reported on the 2022 CFP Survey

Cat Friendly Veterinarian®
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The **award-winning** Cat Friendly Certificate Program consists of up to nine modules that explore feline-specific topics. Join the more than **10,000 veterinary professionals** who have invested in their careers by completing the Certificate appropriate for your role at the practice!

Get started at **catvets.com/certificate.**

Cat Friendly Guidelines

The Cat Friendly Interactions and Environment Guidelines offer tips and techniques for:

- Implementing Cat Friendly interactions and minimal handling that allows the cat to have a sense of control and choice (and training every team member on how to do this).
- Educating cat caregivers about how to reduce distress when traveling to the veterinary practice (including carrier training). Stressor stacking can affect the entire veterinary experience, so starting a positive experience at home is key.
- Creating an experience that considers the cat's natural behaviors and altering an approach to each individual cat.
- Creating an environment that considers and implements ways to reduce fear-anxiety, and promotes positive emotions and behaviors that cats find comforting.
- Ensuring the entire veterinary team understands species-specific behavior and individual differences (and how this affects the entire veterinary visit/experience).
- Understanding how to identify the cat's emotional state and the subsequent behavioral response (and what to do in each situation).

Download the Guidelines at:

catvets.com/interaction

catvets.com/environment

Read AAFP Members' Newest Favorite Magazine

Check out *The Feline Practitioner*, the AAFP's quarterly print and digital publication created with veterinary professionals in mind.

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This popular publication is ONLY available to AAFP Members. Join today so you don't miss an issue. Plus, you can catch up on all the back issues online.

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[1]Khenifar E. et al, 2018

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THURSDAY, OCTOBER 12, 2023

Pre-conference Day*

Schedule is in Central Daylight Time

TIME	SESSION TITLE		SPEAKER	ROOM	SPONSOR/ PARTNER
7:45 - 11:45 am	Hands-on Feline Orthopedic Evaluation Workshop**	IPO	Drs. Duncan Lascelles & Margaret Gruen	110 & 111	zoetis
	PRE-CONFERENCE DAY*				
10:00 - 11:45 am	**Early Morning Learning Sessions**				
10:00 - 10:50 am	The Allergic Patient: New Insights in Skin Barrier Science	LS	Dr. Melissa Hall	Ballroom B	Ceva
10:55 - 11:45 am	Serenity Now! A Deeper Dive into the Peaceful Practice	LS	Dr. Natalie Marks	Ballroom B	Ceva
11:45 - 1:15 pm	**Food for Thought Luncheon**				
12:15 - 1:15 pm	Nutritional Counselor Program: Get Inspired to Run your Own Nutritional Consultations	LS	Vicky Ograin	Ballroom B	Hill's Transforming Lives
1:30 - 5:30 pm	**Seminar & Social**				ABVP
1:30 - 2:00 pm	Diabetes Masterclass: Oral Hypoglycemics - An Overview	LS	Dr. Audrey Cook	Ballroom B	Boehringer Ingelheim
2:00 - 3:15 pm	Diabetes Masterclass: SGLT-2 Inhibitors - Safety & Efficacy Data	LS	Drs. Ellen Behrend & Patty Lathan	Ballroom B	Boehringer Ingelheim
3:15 - 3:45 pm	**Refreshment Break**			Ballroom C	
3:45 - 4:10 pm	Diabetes Masterclass: Getting Started & Monitoring	LS	Dr. Cynthia Ward	Ballroom B	Boehringer Ingelheim
4:10 - 5:00 pm	Diabetes Masterclass: Troubleshooting & Complications	LS	Drs. Thomas Schermerhorn & Catharine Scott-Moncrieff	Ballroom B	Boehringer Ingelheim
5:00 - 5:30 pm	Diabetes Masterclass: Panel Discussion		Diabetes Masterclass Speakers	Ballroom B	Boehringer Ingelheim
5:30 - 7:00 pm	Welcome Reception *All attendees invited*			Riverview Lobby	Boehringer Ingelheim

LS Live Streamed

IPO In-person Only

Sessions and speakers are subject to change.

*In-person attendees need to register for Pre-conference Day if they would like to attend. Additional fees apply.

**Separate Registration Required from Pre-conference Day. Additional fees apply.

Hands-on Feline Orthopedic Evaluation Workshop

Duncan Lascelles, BSc, BVSc, CVA, PhD, FRCVS, DSAS(ST), DECVS, DACVS
Margaret Gruen, DVM, MVPH, PhD, DACVB

The approach to a clinically meaningful, and efficient orthopedic evaluation of the cat will be discussed. The components of capturing a relevant history, observation of the cat and the hands-on examination will be presented and discussed. Delegates will gain hands-on (and expert guided) experience in techniques for successful orthopedic / osteoarthritis examinations. Feline-friendly and staff friendly approaches will be emphasized.

The following notes complement this practical session, and participants will receive extended notes.

Keys to a Successful OA Examination in Cats

The important keys to performing this successfully are:

- SCREENING FOR FELINE OA PAIN:
  Use of a checklist in the practice to screen for cats that may have OA pain
- OWNER ASSESSMENT
  Capturing owner-observed information and history through video and questionnaires
- FELINE FRIENDLY HANDLING FOR OA PATIENTS
  Facilitating and optimizing the visit to the practice, and employing feline-friendly handling techniques
- IN CLINIC OBSERVATIONS
  Observing and interpreting movement and observations in the clinic
- ORTHOPEDIC EVALUATION/EXAM
  Hands-on orthopedic examination including assessing sensitivity, muscle mass and joint pain
- OVERALL ASSESSMENT OF PAIN AND DISABILITY
  Capturing an overall assessment of the status of pain and disability
- MONITORING FELINE OA
  Monitoring therapeutic efficacy through the use of owner-completed questionnaires

SCREENING FOR FELINE OA PAIN

Owners play a critical role in helping veterinarians diagnose feline OA pain. To that end, using a simple checklist that is easy and quick to complete can help owners understand signs of OA pain in their cats and relay that information to their veterinarian.

Such a checklist helps bridge the gap between how owners perceive pain in their cats and how veterinarians assess pain. The Zoetis Petcare Cat Osteoarthritis Pain Checklist (https://www.zoetispetcare.com/checklist/osteoarthritis-checklist-cat) is based on a published checklist (the Musculoskeletal Pain Screening Checklist – MiPSC) developed using sound scientific approaches. (1) The checklist provides a clinically expedient communication tool, both educating and empowering owners about OA and increasing the ability of veterinarians to screen for OA pain in cats.

The checklist works as an important educational tool by helping owners recognize the behaviors that can signal OA pain in cats, as these can differ from those in dogs. It also serves as a collaborative communication method between owners and veterinarians, providing an effective way to start this discussion with the owner. In addition, it gives veterinarians a clinically useful tool to identify cats likely to be suffering from OA pain, prompting further evaluation. The first checklist an owner completes becomes the cat's baseline before treatment.

Having an effective strategy to gain insight into a cat's behavior and activity at home is invaluable to help the veterinarian diagnose feline OA. Ideally, the checklist will be incorporated into the clinic routine and used for every feline patient.

Before implementing the use of the Zoetis Petcare Cat Osteoarthritis Pain Checklist, the entire practice team needs to be onboard. This first means understanding the value of the checklist.

- For the cat: When OA is caught early and appropriate management is started promptly, it can help improve the cat's quality of life.
- For the owner: Increased awareness and understanding of OA and potential signs of pain can empower the owner.

- For the veterinary technician: The easy-to-use tool provides a bridge for communication between the technician and the owner, making history taking more efficient.
- For the veterinarian: The checklist provides an accurate method to proactively screen feline patients for OA, potentially facilitating an earlier diagnosis and intervention.
- For the practice: Not only can the checklist make owner education easier, but when OA is identified early and managed appropriately, this can provide the cat with better mobility and comfort, supporting good quality of care and strengthening client trust in the veterinarian and the practice.

OWNER ASSESSMENTS

Building on the information gathered by the Zoetis Petcare Cat Osteoarthritis Pain Checklist, owners can provide critical information aiding in OA pain assessment in 2 ways:

- Taking video - Owners record video of their cat moving around in their home environment and performing specific activities of daily living. The veterinarian then reviews the video, gaining insight into the cat's movements.
- Completing Clinical Metrology Instruments—Owners answer questions about their cat's ability to perform activities of daily living, as well as the cat's general mobility and well-being, using a clinical metrology instrument (CMI). CMIs are questionnaires specifically designed for evaluating clinical conditions, including those designed for evaluating feline OA pain.

These owner assessments can provide insight that is nearly impossible to get in an exam room.

Video: Prior to their visit, owners can be asked to take video of their cat performing the activities of daily living described in the Zoetis Petcare Cat Osteoarthritis Pain Checklist: walking, running, jumping up, jumping down, and (if applicable) going up and down the stairs. These videos can be reviewed in the office, even prior to handling the cat.

Clinical Metrology Instruments: Feline Musculoskeletal Pain Index (FMPI) (2)
This validated clinical metrology instrument was developed at the North Carolina State University Translational Research in Pain program (https://cvm.ncsu.edu/research/labs/clinical-sciences/comparative-pain-research/clinical-metrology-instruments/). Based on the results of the Zoetis Petcare Cat Osteoarthritis Pain Checklist, veterinary team members can ask owners to fill out this questionnaire to assess the severity of pain associated with OA in their individual cat.

The FMPI (2) is intended for use in both *diagnosis* and *monitoring* of cats with OA pain; another helpful tool for long-term monitoring of feline OA pain is described later in this guide

FELINE FRIENDLY HANDLING FOR OA PATIENTS

The American Association of Feline Practitioners (AAFP) and the International Society of Feline Medicine (ISFM), created the Feline-Friendly Handling Guidelines. These guidelines were developed to address the importance of providing the best possible care for cats and can be found at this link:
https://catvets.com/guidelines/practice-guidelines/handling-guidelines

Feline Friendly Handling Tips

- Foster calm by using low voices in both the waiting and exam rooms
- Read the cat's behavioral cues
- Use gentle handling
- Apply minimal restraint
- Do not scruff
- Take it slow
- Strive to complete exam in the room
- For cats with OA, increased stress will make it more difficult to assess pain

Feline Friendly Visits for OA Cats

Many cat owners don't understand the need for regular veterinary care for a healthy cat. When asked why pet owners don't bring their cats in for veterinary care, the primary reason was the stress of the clinic visit; which includes all of the smells, sounds, strange people, and other pets at the clinic. Together, these can increase the cat's negative experience and stress associated with the visit.

Veterinary teams can change client and cat clinic experiences by:

- Providing tips for getting cats into the clinic in a less stressful way
- Creating calm and comfort in the waiting area and exam room
- Clearly explaining what they are doing with the cat and why
- Establishing feline friendly handling techniques that minimize restraint and are responsive to cues from the cats

Keep the Cat Comfortable During the Examination

Use these tips to keep the exam feline friendly:

- *Use tools:* Provide non-slip surfaces, towels, turkey or chicken baby food or other food treats, and pheromones to increase cat comfort. Use towel wraps to help facilitate examination and avoid scruffing which increases stress and discomfort. Pre-appointment medication such as gabapentin may be used even when conducting an OA evaluation.
- *Meet them where they are*: Perform the exam (including joint evaluation) in a position the cat is most comfortable in, whether that's sitting on the exam table, lying in the owner's arms, or lying in its carrier.
- *Remember that cats don't like "point contact"* Keep your hands or body in contact with the cat at all times while manipulating parts of their body (including the joints). Gently move a hand down to the point you want to manipulate and then start the manipulation, rather than touching the area abruptly and starting the manipulation. This technique helps avoid the cat's immediate withdrawal, which could be interpreted as an aversive reaction rather than simply a dislike of that immediate point contact.

IN-CLINIC OBSERVATIONS

Important information may be gathered by observation and the exam room provides a useful setting for practitioners to observe cats. Rather than keeping the cat in the carrier until it's time for the examination:

- Open the cat's carrier, and allow the cat to come out at its own pace, and walk around the exam room.
- While taking the history from the owner, watch the cat move around the room and observe the cat's mobility.
- Consider encouraging the cat to jump up onto chairs or down from the exam table to get a broader picture of the cat's mobility.

This observation can provide great clues about how impaired a cat is, as well as where the impairment is centered. Remember, owner history, review of video, and careful in-clinic observation are crucial to a successful evaluation for OA in cats.

IN CLINIC ORTHOPEDIC EVALUATION/EXAM

Because of the high prevalence of feline OA, orthopedic examinations are warranted for all cats suspected of having chronic pain. The following notes provide practitioners with key information on the hands-on part of the orthopedic examination for an assessment of pain associated with degenerative joint disease (DJD) in cats.

The orthopedic examination is an important part of putting the pieces of the puzzle together. During this evaluation, you'll focus on:

- Assessing sensitivity and identifying any hypersensitivities
- Assessing muscle mass, looking for muscle atrophy that may indicate individual joint issues
- Assessing joints by performing a joint examination. This requires manipulating major joints with the cat in different positions, either with an assistant or without

All components of the orthopedic examination is explained in a series of videos that can be found at:
https://www.zoetisus.com/oa-pain/feline-exam-videos.aspx

Tip: Limiting your touch to two fingers—your thumb and forefinger—as you perform these assessments tends to increase the sensitivity (how well you can feel the muscles).

Assess Sensitivity

The hands-on part of the feline evaluation begins with assessing excessive sensitivity. Ongoing OA pain can result in excessive activity of the sensory system, and this is manifested as 'sensitivity'. These hypersensitivities can be associated with flea allergy and other dermatologic skin conditions, but they can also be indicative of maladaptive pain. Excessive sensitivities may develop much more readily in association with long-standing joint pain in cats than in dogs.

Assess Muscle Mass

Assessing the muscle mass in major muscle groups can help you determine which specific limbs or joints to focus on further during the joint examination. Again, using feline friendly handling techniques, begin observing and palpating the cat's muscles:

- Start with the upper forelimbs, and move down the limbs. Then move to the gluteal area and the hindlimbs. For each muscle, assess (1) whether the muscle mass is appropriate bilaterally and (2) whether either side is showing signs of muscle atrophy.

Assess the Joints

Next, make an assessment of each joint for pain, crepitus, effusion, and thickening. We suggest focusing on the main joints you suspect are affected first. Not all joints are equally affected.

Techniques to use during the evaluation of major joints are described below, and described in a series of educational videos: https://www.zoetisus.com/oa-pain/feline-exam-videos.aspx

OVERALL ASSESSMENT OF PAIN AND DISABILITY

Assessment of disability

The Feline Musculoskeletal Pain Index (FMPI), or the Client Specific Outcome Measures (CSOM-feline) (both available at: https://cvm.ncsu.edu/research/labs/clinical-sciences/comparative-pain-research/clinical-metrology-instruments/) can provide a good overall evaluation of the impact of pain and disability on the cat, coupled with a written record of the orthopedic evaluation. The FMPI is easy to complete as it is a set of questions the owner answers, and this gives an immediate overall score of 'pain and disability' associated with musculoskeletal pain. It was designed to capture the overall impact of musculoskeletal pain, and is often completed at the start of the assessment (and so can form part of the history). The CSOMf can also be used, but is less of an overall assessment, rather it is an assessment of the ability to perform specific activities.

MONITORING FELINE OA

As with screening and diagnosis, management and monitoring of feline OA benefits from a partnership between the owner and veterinary team. By using monitoring tools, veterinarians can keep owners invested in their cat's care and actively involved in monitoring their cat's OA pain. This allows owners to also see their cat's progress on specific activities individualized for their cat.

We recommend considering use of one of two monitoring tools: the feline Musculoskeletal Pain Index (FMPI) or the Client Specific Outcome Measures-Feline.

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NOTES:

The Allergic Patient: New Insights in Skin Barrier Science

Melissa Hall, DVM, DACVD

Introduction

Feline dermatologic diseases often present therapeutic challenges in part due to the limited treatment options available and patient compliance. During this lecture, we will review three recent studies utilizing the DOUXO® S3 with OPHYTRIUM™ for the management of various feline skin conditions.

DOUXO® S3 CALM:

Performance of a protocol combining applications of Ophytrium-containing Shampoo and/or Mousse in cats with non-flea induced hypersensitivity dermatitis: a multicentric prospective field trial.

- A Cózar, X DeJaeger, M Gatellet, T Tuyeras, C Noli, H Dropsy, V Deschamps, M Debraine, A Puozzo-Barichard, A Briand, A Bressolin.

Objectives: Feline hypersensitivity disorders lead to pruritus and skin irritation that negatively impacts the cat's wellbeing and strains the human-animal bond. Appropriate treatment is mandatory to bring quick relief but systemic therapies including glucocorticoids may come with unwanted side effects. Often topical therapy is often not utilized in feline patients due to limited studies and concern for patient tolerance. A multicentric prospective field study aimed at evaluating the performance of a protocol applying topical productions containing Ophritum in cats with non-flea induced hypersensitivity disorders was recently presented.

Methods: Cats were shampooed or moussed on Day 0, then received by the owner eight applications of the mousse every 48 to 72 hours for three weeks. On Day 0, Day 7 and Day 21, a veterinarian assessed each patient using the Scoring Feline Allergic Dermatitis (SCORFAD). At each time point, pruritus was assessed by the owner using the feline Pruritus Visual Analog Scale (PVAS, VAScat). On the final day of the study, Day 21, overall assessment questionnaires were completed by both the veterinarian and the pet owners.

Results: Nineteen cats completed the study. There was a significant improvement in the mean SCOFAD scores from Day 0 compared to Day 21, with a mean reduction of 55%. The VAScat score also decreased from a mean of 7.5 to 4.3. Veterinarians assessed the improvement in clinical disease as satisfactory, good or excellent in 94% of cases. The owners reported the protocol to be efficient and practical in 94% of cases.

Conclusions: The topical protocol with Ophytrium-containing Shampoo and/or Mousse quickly and significantly improved the severity of clinical lesions and pruritus in cats with non-flea induced hypersensitivity dermatitis, resulting in high satisfaction levels in for both veterinarians and owners.

DOUXO® S3 SEB:

Performance pf a protocol combining applications of Ophytrium® and Seboliance®-containing mousse +/- shampoo in cats with keratinization disorders: a multicentric prospective field trial.

- A Cózar, M Gatellet, X DeJaeger, T Tuyeras, H Dropsy, F Leymarios, R Cristante, C Moura, A Puozzo-Barichard, M Debraine, C Noli

Objectives: Feline keratinization disorders may appear to many different triggers including impaired grooming behaviors due to obesity or pain, secondary to various triggers including parasitic and infectious conditions, as well as primary conditions including cutaneous lymphoma. While many of these conditions require specific management, topical therapy can be used in conjunction to restore cutaneous balance and improve the patient's well-being. A multicentric, prospective, open field study aimed at evaluating the performance of a protocol applying topical products containing Ophytrium® and Seboliance®(DOUXO® S3 SEB shampoo and mousse) in cats with scaling disorders was recently presented.

Methods: Cats were shampooed or moussed on Day 0, then received by the owner eight applications of the mousse every 48 to 72 hours for three weeks. On Day 0, Day 7 and Day 21, a veterinarian assessed each patient using the skin seborrheic score (SSS) as well as evaluating the extent, the scaling, the greasiness, and the secondary dermatological features. On the final day of the study, Day 21, overall assessment questionnaires were completed by both the veterinarian and the pet owners.

Results: Seventeen cats completed the study. There was a significant improvement in the mean SSS at Day 21 compared to Day 0 with a 72% mean improvement and 82% of cats decreasing greater than 50% in SSS. The extend of scaling and greasiness decreased on average by 92% and 70%, respectively. Secondary dermatological features improved by 68%.

Veterinarians considered improvement as satisfactory, good or excellent in all cats. Owners considered the protocol practical and efficient, with 94% of owners emphasizing a resultant nice skin and coat.

Conclusions: The topical protocol of Ophytrium® and Seboliance® containing shampoo and/or mousse quickly and significantly improved cats' skin with keratinization disturbances, resulting in high satisfaction levels for both veterinarians and owners.

DOUXO® S3 PYO:

Performance pf a protocol combining applications of Ophytrium® and chlorhexidine-containing pads +/- shampoo in cats with bacterial and/or Malassezia disturbances: a multicentric prospective field trial.

- A Cózar, M Gatellet, X DeJaeger, T Tuyeras, C. Noli, H Dropsy, F Leymarios, R Cristante, V Deschamps

Objectives: Cats may suffer from cutaneous microbial imbalance or dysbiosis, often most commonly caused by skin pathogens such as *Staphylococcus pseudintermedius* and *Malassezia pachydermatitis*. Topical products carry the active ingredients directly where needed, often avoiding systemic antimicrobial administration, and therefore decreasing the risks of developing microbial resistance. A multicentric, prospective, open field study aimed at evaluating the performance of a protocol applying topical products containing Ophytrium® and chlorhexidine digluconate (DOUXO® S3 PYO shampoo and pads) in cats with bacterial and/or Malassezia overgrowth was recently presented.

Methods: Cats were shampooed or received pads on Day 0, then received daily pads applications for 14 or 21 days according to cytological resolution (end of follow up (EOF)). Weekly cytological examinations (mean count on 6 oil immersion fields (OIF)) were performed by veterinarians. Pruritus was assessed by the owner weekly using the feline Pruritus Visual Analog Scale (PVAS, VAScat). At the end of follow-up (either Day 14 or 21 depending on cytological resolution), overall assessment questionnaires were completed by both the veterinarian and the pet owners.

Results: Ten cats were included in the study; three with bacteria, four with Malassezia and three with both. Mean microbial count decreased significantly between Day 0 and EOF, from 30.8 to 8.2 for bacteria and from 5.7 to 0.1 for Malassezia. 90% of cats achieved a normal count (less than or equal to two bacteria and less than or equal to one Malassezia per OIF). The VAScat score also decreased from a mean of 4.7 to 2.7. At the conclusion of the study, veterinarians considered improvement as satisfactory, good or excellent in 90% of cases. Owners considered the protocol efficient and practical in 100% and 90% of cases, respectively. 80% of owners emphasized the resultant nice skin and coat.

Conclusions: The protocol with Ophytrium® and chlorhexidine-containing pads +/- shampoo quickly and significantly improved microbial overgrowth and pruritus in cats, yielding high satisfaction levels for both veterinarians and owners.

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Serenity Now! A Deeper Dive into the Peaceful Practice

Natalie Marks, DVM, MS, CVJ

Introduction

There is a universal acceptance among the veterinary community that we must all work on improving feline medicalization. With over 80 million cats in the United States and less than 2 in 5 ever seeing a veterinarian, and the 2011 Executive Summary of the Bayer Veterinary Care Usage study revealed that 28% of cat caregivers reported that they would consult their veterinarian more often if the visit was not associated with so much stress for their cat, there's tremendous opportunity to improve.[1.] In a similar survey in from a 2013 JAVMA article, 44.9% of cat caregivers did not take their cat to a veterinarian, despite the recommendation of an annual exam visit.[2.] It's crucial that we take a deeper dive into some of the more specific factors influencing this reluctancy. One starting point is identifying stress and its consequences, both in our patients and our veterinary team, how it manifests, and what we can do to make a difference.

The Pathophysiology of Fear and Anxiety

Fear has had a necessary protective nature stemming back to the most primitive of mammalian species, and the amygdala remains a central component. When a fearful memory is experienced, it's permanently stored, waiting to be triggered, activated, and escalated to a more intense and longer lasting experience for the patient. From a biochemical perspective, the release of glutamate and monoamine neurotransmitters are the culprits and targets for anxiolytic therapy. But, of more practical importance is how these patients manifest anxiety and fear clinically at home and in the hospital, and why.

Fearful Body Postures

A vital part to success working with feline patients and families is the concept of shared decision making – working together as home and hospital advocates towards the caregiver's goals for the cat. In order for a caregiver to be the best advocate, they also must become educated on what 'abnormal' behaviors look like. Providing resources around specific body part changes can help empower cat caregivers at home and encourage veterinary visit early.

In general, fearful cats try to make themselves smaller than normal. From head to tail, there are several changes in body part shape and position[3]:

- Ears – direct backwards, sideways, or flattened
- Eyes – pupil enlargement
- Tail – close to body when sitting or lying

The tail can also sway back and forth, indicating agitation, annoyance, or even high arousal.[4] Cats can also hold their tail stiffly up or down, on their tiptoes to show defensive behavior. But escalated even beyond this, we know that a cat will quickly be demonstrating aggressive behavior when their ears are sideways exposing their inner pinna and their pupils are oblong.

The Physical Exam

Body language assessment is also important for veterinarians as well as veterinary professionals. But, in addition to that, there are two vital components to every feline physical exam we must prepare for as well: proactive anticipation of anxious and fearful body language and fluid adaptation of handling, restraint, and diagnostic plan. Let's start with alignment around some statistically significant associations that may help us better understand cat behavior in the exam room.

A 2021 Italian study looked at the behavior of 95 cats in the exam room looking at associations between behavior and age, gender, temperament, clinical parameters, and familiarity with the veterinary clinic.[5] Here are a few interesting findings:

- A large majority of cats (85%) had a higher-than-normal heart rate and mydriasis.
- Males were more vocal than females and had a higher anxiety score.
- Younger cats were more anxious and tended to try to escape.
- Elderly cats were more frightened and irritated, and tended to show scratching, tail lashing, and piloerection.

It's helpful to keep these top of mind to help anticipate certain behavioral trends.

The reality is that we don't often have control over how our patients arrive at the veterinary hospital and know that even in the most proactive clinics who prepare cat caregivers for reduction of stress during travel, there are situations out of our control. We must always be ready to adapt, pause, postpone, and potentially change plans based on the emotional needs of our patients. Cats tend to demonstrate freezing and fleeing behavior when stressed, and only upon significant escalation do they

reach the point of aggression or fighting.[6] If, as teams, we are waiting until the point of seeing a feline patient hiss, grow, swat, or bite until we change our behavior, restraint, and plan, we are missing several signs of anxiety and escalating fear along the way.

Consequences of Stress

Stress, and its long-term consequences, have been studied for decades in humans, and similar findings have been found in cats. Stress can be a contributing factor to many different disease states, including upper respiratory infection, dysrexia, and several types of gastrointestinal disease.[7] Let's take a closer look at other ways anxiety, stress, and fear can negatively impact our patients.

Physiologic Abnormalities

The objective data obtained at the beginning of every feline physical exam is foundational in assessing patient health. Inaccuracies in these values can confound our clarity in what steps to take and what diagnostics are needed. It can cause us to potentially misdiagnose or even miss disease altogether. A 2017 study by Quimby et al. looked at if these parameters are significantly different from readings at home as compared to in the hospital.[8] The study found that blood pressure was on average 6mmHg higher in the hospital, temperature increased 0.3 degrees F, heart rate increased 33 beats/min more in the hospital, and respiratory rate increased 12 breaths/min more away from home, with all findings except temperature to be statistically significant.

Lab work Abnormalities

Stress can also have a significant impact on clinical pathology results, making interpretation challenging. One common place to find these changes is in the stress leukogram. Endogenous corticosteroids create findings of neutrophilia and lymphocytosis; however, monocytosis and eosinopenia are variable and not frequently present in cats as they are in dogs.[9] Lymphocytosis is particularly specific to felines and can be present in both kittens and young cats and can be up to twice the upper reference range.[10] The most well-known of all of the stress-induced bloodwork changes is physiologic hyperglycemia, and it can make differentiation from true diabetes mellitus challenging. Interestingly, acute or transient stress hyperglycemia is typically due to catecholamine release like norepinephrine and epinephrine, but in patients with chronic stress, endogenous corticosteroids are more likely the cause.[11] For completeness, there is no increase in corticosteroid-induced ALP activity as cats do not have C-ALP.

Long-term Behavioral Changes

Finally, many studies have looked at the impact stress has on long-term behavioral changes in cats. There is a myriad of factors that can trigger anxiety, stress, and fear, including loud or unfamiliar noises, sudden movements, strangers in the home, noxious odors, lack of enrichment, unfamiliar objects, and places, including travel to the veterinary hospital. When these factors become frequent or chronic, we end up seeing initiation and potentiation of the more common behavioral problems like house-soiling and aggression.[12] These are in addition to the stress-associated multifactorial disease of FIC, or feline interstitial cystitis. Cats are typically surrendered to shelters because of these stress-induced diseases or continue to erode the human-animal bond.

The Impact of Stress on the Hospital Team

One aspect of stress, anxiety and fear that is infrequently discussed but deserves attention is the impact stressed patients and their associated cat caregivers have on the veterinary hospital team.

Work Culture

While occupational stress has been studied frequently in human medicine, it is only as of late that we are seeing investigation on its effects in the animal health space. And, as we battle tremendous challenges in wellbeing, mental health, and healthy work cultures, understanding the causes of occupational stress will help develop helpful interventions to create healthier veterinary clinic environments. Did you know that chronic stress in the workplace has not only been shown to be the cause of acute and chronic illnesses, but even a culprit in decreased fertility in women?[13]

A big part of work culture is feeling safe and supported by the management team or owners. A pivotal 2014 study sought to investigate this further, specifically as source of cumulative stress.[14] One crucial finding was that amongst veterinary support staff, a common feeling was that illness and injury were accepted as a commonplace risk in the veterinary setting. These injuries, typically due to lack of training on low-stress handling, lack of pharmaceutical intervention, lack of body language assessment, or all of the above, lead to bites, scratches, and other significant injuries. Many are underreported as so many of the respondents disclosed self-treatment due to employers guiding them not to seek treatment or not allowing them to use workers' compensation insurance. In fact, many veterinarians will pay medical bills out of pocket to avoid claims and escalating

rates. In 2009, the US Bureau of Labor Statistics (BLS) reported 1400 injuries per 10,000 workers for sprains, strains, and fractures. But there is no entity currently aggregating bites and scratches, which lead to infection and even zoonotic disease.

Staff Retention

One of the other stresses within the veterinary hospital related to staffing. This takes two forms, both from a retaining current staff and recruiting new team members. A select group of veterinary professionals with focused training in the areas of low-stress handling and other solutions for reduction of fear and anxiety are just like many of you, Cat Friendly Practitioners. In a 2022 Cat Friendly Practice program survey, 88% felt that the training had a positive team dynamic impact when handling, treating, and caring for their patients. And 84% of these team members reported that they had received positive feedback from clients for being a Cat Friendly Practitioner. Finally, 90% of those surveyed reported improved knowledge and feline care among staff. When a veterinary team feels educated, empowered, valued, validated, and safe, staff retention and recruitment is more effective and successful long-term.

Change Through a Multi-Modal Approach

Change is never easy, but a goal of a peaceful and calmer clinic for all of the reasons mentioned above is desirable enough to start the process! There are seven steps to consider on this journey:

- Assign a "Calming Advocate"
- Create a calm environment
- Create a prepared exam room
- Use treats & toy through the visit at the clinic
- Use low stress handling techniques
- Use calming agents throughout the clinic
- Communicate expectations with pet owners

First and foremost, find a champion, a calming advocate (or "catvocate"!) to lead your team. There doesn't need to be any initial training for this team member except the willingness to work on this goal and have an interest in veterinary behavior medicine. This leader will focus on three goals: reducing fear, anxiety and stress in patients, clients, and team members, coordinating continuing education and reviewing cases with opportunity to improve with management.

Next, think about what immediate challenges in the clinic environment are. While we know pastel paint colors and landscape portraits are best, they might not be initially able to be modified. However, eliminating white coats, patterns, and strong perfumes can be immediately changed.

Treats and toys should be utilized throughout the visit at the clinic. There are many suggested treats that will act as high rewards for our feline patients, including:

- Tuna/salmon
- Anchovy paste
- Baby shrimp
- Bonita fish flakes
- Easy Cheese cheddar and bacon
- Fancy Feast foil packs
- Green olive
- Marshmallows
- Vegemite
- Whipped cream

Low stress handling techniques should be implemented in every exam room and treatment area.

Calming agents throughout the clinic are an imperative piece of this puzzle. Diffusers, specifically Feliway Optimum, can be placed in waiting areas, exam rooms, treatment, and boarding areas. Team members can have a checklist to ensure that refills are changed monthly, and diffuser heads are replaced every 6 months. In addition, 8 pumps of pheromone sprays can be used on towels, bedding, and even scrubs every 5 hours, and exam room equipment wiped down with similar compounds to eliminate the presence of fear pheromones.

Finally, the last but very important piece of peace, especially for the veterinary team, is effective communication with cat caregivers. They have expectations that the reason for the visit will be addressed and resolved in a timely manner and that

they will return home with their patient without undue stress, anxiety, and fear. A team that conveys clinical empathy, uses nonjudgmental statements, relates personal experiences, demonstrates neutral to positive nonverbal body language, and uses reflective listening will be the most successful communicators.

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Nutritional Counselor Program: Get Inspired to Run your Own Nutritional Consultations

Vicky Ograin, MBA, RVT, VTS (Nutrition)

Introduction

Proper nutritional management is one of the most important factors in the health and disease management of cats. As cat owners become more aware of the importance of nutrition in their own health, they will expect a higher standard of nutritional care for their cats. The nutritional counselor should be the preferred, expert source of the best nutritional information for cats. Nutritional counselors that understand and embrace clinical nutrition and demonstrate in-clinic behaviors consistent with that conviction will benefit their patients, their clients, their practice and the profession.

What is a Nutritional Counselor?

Nutritional counselors work with the veterinarian to reinforce, implement and follow up the food recommended for the cat. They accomplish this by working with the cat owner, explaining what and why the food is being recommended and to answer any questions the cat owner may have. A nutritional counselor follows up with the cat owner to assure compliance, but more importantly to be the cheerleader for the owner and more importantly the cat. Cat owners need to know someone is there for them to help with questions or concerns even after the initial visit.

Nutritional Counselors Reinforce the Veterinarian's Recommendation.

The consultation will start after the veterinarian (or technician) has made a food recommendation for the cat. If the veterinarian gave the recommendation, they will advise what the recommended food is and if the cat can have dry, canned or both. The veterinarian should mention if only specific treats can be fed. If the cat needs to lose weight, the veterinarian will also advise what the goal weight should be.

Nutritional Counselors Implement the Recommendation

The second part of the consultation is very important. This is where you will help the owner accept the recommendation by communicating everything they need to know about the new food: how much to feed, how to transition and answer questions they may have. This insures they accept the recommendation. The technician plays a pivotal role in helping the cat owner. Switching to a new food can be a stressful time for the cat owner, especially if the cat is switching to a therapeutic food. We are there to be the cat owners' cheerleader and let them know we are there for support.

Follow up

The last part of the consultation is to follow up with the cat owner. This helps with compliance. Technicians are instrumental in helping the cat owner when a new food is being recommended.

How to perform a Nutritional Consultation

To begin the consultation, ask two very important questions: what are you currently feeding and why? When asking what they are currently feeding, this includes everything they are feeding, including cat food, treats, table food, and supplements. Have cat owners tell you everything that passes their cat's lips, be it solid or liquid food (it is common for cat owners to give milk). This will give you a lot of important information and will help guide you in your discussion to make sure transitioning to the new food is successful.

After gaining an understanding of what they are feeding and why, you will know what you need to discuss to make the transition to the new food successful. Discuss with the cat owner what the new food is, and why the veterinarian is recommending it. For example, the veterinarian is recommending a renal food for your cat; it has controlled protein, phosphorous and sodium, to take the work load of your cat's kidneys and will improve and extend the quality and length of your cat's life.

If available, use a brochure that discusses the new food. If the pet food company does not provide brochures, make your own with basic information about how the food will benefit the cat and feeding amounts. Many cat owners are stressed and not completely taking in what you tell them at the clinic, so it is important to give them something to read at home. The cat owner can share the information with family members that were not present at the veterinary clinic during the exam and recommendation. It is important to give the cat owner full instructions on how much to feed and any additional instructions,

such as how many treats, along with information on how to transition, and a measuring cup (if the pet food companies supply them), or instruction to purchase the correct 8 oz. (250 g) measuring cup.

How Much to Feed?
It is important to discuss how much to feed. It is best if you calculate exactly what the cat should be eating; do not leave it up to the cat owner to decide how much to feed. This is especially important when a cat needs to lose weight. Based on your initial questions and what the veterinarian has recommended, you will know if the cat will be getting canned, dry or both and treats.

To calculate feeding amounts first calculate resting energy requirement. There are a few calculations recommended, such as RER= (70x kg BW0.75) or RER= 70 + (30xkg BW). To get the daily requirements multiplied the RER by a factor that takes into account the age, activity, or physiological condition of the animal.1 The factors for cats is kitten times 2.5, intact adult cat times 1.4, neutered adult times 1.2, obese prone times 1.0 and weight loss times 0.8 2. For example if calculating the feeding amount for a 10 lbs. (4.5kg) average neutered cat, the calculation would be (70 x 4.5kg 0.75) times 1.2 (factor of a neutered cat) = 216. This is the total amount of calories neutered cat needs to maintain their weight.

When calculating for weight loss, use the goal weight to calculate the feeding amount.2 Make sure you advise the owner that the amount you are recommending is a starting point. The amount may need to be adjusted based the how the cat responds to the feeding amount. This is especially important for weight loss.

Transition
It is important to recommend a transition. There are two reasons to do a transition: 1) occasionally a cat will have a GI upset when switched to a new diet. There is more of a chance with a hydrolyzed protein or different (high or low) fiber level food to cause a GI upset. 2) A cat will accept a new food better when a transition is done to allow the cat to get use to the new texture and flavor.

Transition recommendation- 1) Recommend ¾ old diet – ¼ new diet, 2) Do this for a few days; if no GI upset, go to the next step, 3) ½ old diet- ½ new diet, 4) Do this for a few days; if no GI upset, go to the next step, 5) ¼ old diet- ¾ new diet, 6) Do this for a few days; if no GI upset, go to the next step, 7) End with 100% of the new food. Sometimes a transition should be longer, especially for cats. Use the same recommendation, but instead of a few days, recommend doing each step for a week or more. Some cats have texture issues and there needs to be more time given for the cat to get used to the new texture. For example, offering a canned food when the cat has never eaten can food. Since this is a different texture than the dry food they are used to eating, it could take longer for the cat to accept the new food. It is important to help the cat owner understand the importance of having patience as the cat gets used to the new texture.

Common Questions/ Discussion with the Cat Owner
Based on what food has been recommended and what you have learned from your discussion with the cat owner, you will customize the consult with information needed for the cat.

Treats
Giving treats can be a very emotional experience for cat owners; it is often how cat owners bond with their cat and show love. If the cat owner likes giving treats, it is important to try to incorporate treats into the food plan. Treats should never be more than 10% of the total calories.3 The veterinarian will let you know if treats can be allowed. There are alternative ways to show love without giving food, like petting, play activities or praise.

Palatability Tips
Cat owners may want something to add to the food to help with the transition to the new food. Some suggested palatability tips include: warm the food (make sure the food is not too hot, or it could burn their mouth). Feed in separate bowls; some cats do not like different foods in the same bowl. If allowed, try a different texture; if a cat does not like the dry form, try the canned form; add low- salt flavored broth; add a small amount of oregano, not recommended for hyperthyroid foods.

Nutritional Counselors Follow up
After the consultation is finished and the owner has gone home, it is important to follow up with the cat owner to make sure everything is going well. The nutritional counselor should call in 2 -3 days, 2 weeks, and 2 months to see how the cat is doing. The first follow up is the most important; call in 2-3 days. This will be during the transition and this is when most people will give up on the new food. It is an opportunity to be the owner's support and cheerleader and help with any issues that have

come up. It is also an opportunity for the cat owner to ask any questions that have come up since they went home, especially from family members.

Check in at 2 weeks to see how the cat is doing; by now the cat may be on the new food or still transitioning, so it is a good time to check in and see how everything is going.

At 2 months, check to see how the cat is doing. By now the cat should be on the new food, and you are calling to offer any support they may need. Call as you think necessary after the 2-month check in. If cat needs to lose weight, call monthly until the cat reaches its goal weight. Encourage weighing every 2-4 weeks until the cat reaches its goal weight, then every 6 months.

Summary

Every cat deserves and should receive a nutritional recommendation on every visit. Nutrition is one area of veterinary medicine that affects every cat that comes into the hospital. Working as a nutritional counselor is very rewarding and is an asset to the practice as well as the cat owner and most importantly the cat. You can be instrumental in guiding a cat owner, answering questions and determining feeding amounts. Follow up is imperative for success of a new food. Technicians can pay an integral role in helping cat owners successfully switch to a new food.

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Diabetes Masterclass: Oral Hypoglycemics - An Overview

Audrey Cook, BVM&S, FRCVS, MScVetEd, DACVIM (SAIM), DECVIM, DABVP (Feline)

Introduction

Feline diabetes mellitus (DM) is estimated to affect 1 in 250 cats, which means that hundreds of thousands of cats (and their owners) in the US battle this disease. This condition is generally the end-stage of a chronic process, in which lifestyle, diet, body condition, exercise and genetics likely play a role.

Feline DM is a very treatable disease and is generally addressed with a combination of exogenous insulin and dietary modifications. A substantial percentage of cats will also undergo 'diabetic remission'; this is characterized by euglycemia without the need for insulin administration. However, the outcome for many cats with DM is uncertain, and a substantial number are euthanized soon after diagnosis. The reasons for this are complex, and every cat and owner face their own unique challenges, but for many caregivers, the requirement for twice daily insulin injections, coupled with a fear of hypoglycemia, becomes unduly burdensome. Based on some recent data, about 10% of cats with this treatable disease are euthanized immediately, and over 40% are dead within 3 months.[1,2]

As a general guideline, more than 50% of cats with DM fit the model for human type 2 DM.[3] This is driven by sustained insulin resistance; numerous processes can negatively impact insulin responsiveness, but obesity and inflammatory conditions are well-recognized triggers. Like people with type 2 disease, many cats have viable pancreatic β-cells at the time of diagnosis and may even have some residual insulin production. However, surviving β-cell function is limited in the face of sustained hyperglycemia; this reflects 'glucose toxicity' in which -cells undergo apoptosis or simply shut down if blood glucose stays over 200 mg/dL.[4] If we can mitigate insulin resistance and bring BG below the threshold for glucose toxicity, these -cells can regain function and make enough insulin to achieve euglycemia.

Knowing that feline DM is similar to type 2 DM in people, one would expect that affected cats can also be managed with oral hypoglycemic agents. There is an extensive range of such drugs for use in people, either as sole agents or in combination with other therapies. Consequently, many efforts have been made over the last few decades to identify a suitable and effective oral therapy for feline diabetics.[5]

Sulfonylureas

This drug class is the oldest of the oral hypoglycemic agents and exerts its effects by blocking ATP-sensitive potassium channels on -cell membranes. This causes depolarization, which triggers the influx of calcium ions through voltage dependent channels, and the subsequent secretion of insulin. Unlike the other oral hypoglycemic drugs routinely used in people, the sulfonylureas can cause hypoglycemia. This is usually dose dependent or triggered by fasting.[6] Agents in this class includes glyburide, glibenclamide, tozalamide and glipizide (Glucotrol®).

Glipizide

This is regarded as a second-generation sulfonylurea and has been evaluated in diabetic cats. In a study looking at 20 newly diagnosed patients, just 5 (25%) responded; of these, 2 went into remission but 1 needed insulin therapy after 6 months. Side effects included vomiting and a reversible hepatopathy.[7]

Biguanides

This drug class was developed from extracts from *Galega officinalis*, a flowering plant native to northern Africa, western Asia, and Europe. Its common name is French lilac or goat's rue, and it was historically used to mitigate diabetic hyperglycemia prior to the discovery of insulin. The mechanism of action of the biguanides is still unclear, but these drugs improve hepatic and peripheral responses to insulin (either exogenous or endogenous), with a decrease in hepatic gluconeogenesis and glycogenolysis, and increased uptake of glucose by muscle cells. Two members of this class have been withdrawn from the market due to toxicity.[8]

Metformin

The effect of metformin was evaluated in 5 newly diagnosed diabetic cats. One cat, which had measurably insulin at the time of enrollment, had a positive response to this drug. One cat died unexpectedly after 11 days of administration, and the three other cats remained hyperglycemic.[9]

Alpha-glucosidase inhibitors
These agents inhibit the digestion of disaccharides within the intestinal lumen by brush border enzymes. Only monosaccharides can be absorbed, so preventing this final stage of carbohydrate digestion will decrease the amount of sugars such as glucose that enter the blood stream.

Acarbose
This drug has been looked at in a small group of cats with relatively new (2 weeks) or established but poorly controlled DM. The acarbose was given in conjunction with a switch to a low carbohydrate diet (<10% on a dry matter basis) along with insulin or glipizide.[10] Overall, the cats demonstrated improved glycemic parameters, and some went into remission. However, it seems unlikely that the acarbose had much effect in light of the low carb diet, and it is not possible to tease out the impact of this particular intervention. In healthy cats, administering acarbose had the same effect on post-prandial BG as feeding a low carbohydrate diet.[11] Although it has been proposed that acarbose may be useful in diabetic cats with chronic kidney disease consuming high carbohydrate diets, the drug must be given with a meal (which may be problematic in cats with poor appetite) and can cause an osmotic diarrhea.

Dipeptidyl-peptidase (DPP-4) inhibitors
This enzyme is responsible for the clearance of the incretin glucagon-like peptide 1 (GLP-1). GLP-1 plays a key role in the body's responses to ingested calories and maintains β-cell function and viability. It also suppressed appetite through its action within the hypothalamus. Inhibiting clearance prolongs the half-life of GLP-1, and thereby increases its positive effects.[12]

Sitagliptin
This DDP-4 inhibitor has been evaluated in non-diabetic cats and has been shown to potentiate GLP-1 responses to food or orally administered glucose. Insulin secretion also increased by 50%.[13,14] However, the injectable incretin analogues such as exenatide have a significantly more impact on glycemic control in this species.[14,15]

Sodium-glucose linked transporter-2 (SGLT-2) inhibitors
This drug class (referred to as the 'gliflozins') is widely used in human medicine, primarily in the management of patients with type 2 DM, but also in combination with insulin in type 1 diabetics. These drugs are also being investigated for their cardiovascular and reno-protective effects in non-diabetic people.

The sodium-glucose linked transporters (aka sodium-dependent glucose transporters or sodium-glucose cotransporters) are a family of proteins that move glucose into cells. The two most important are SGLT-1 and SGLT-2, which are found primarily in the gastrointestinal tract and kidney. SGLT-1 is responsible for the update of glucose from the intestinal lumen but is also expressed in the kidney where it contributes modestly (<10%) to the reuptake of glucose from the tubular filtrate. SGLT-2 is found in the SI segment of the renal tubules and is responsible for >90% of glucose reclamation from the filtrate. Blocking SGLT-2 therefore results in the loss of glucose in urine. In non-diabetic individuals, BG is maintained by the mobilization of energy stores, mediated by glucagon. In diabetics, BG is significantly lowered.

Lowering BG by this route reduces the workload on the pancreas, and reverses glucose toxicity. So, the struggling pancreas can recover enough function to achieve a euglycemic state. Successful long-term management of a diabetic patient with an SGLT-2 inhibitor is therefore dependent on the presence of viable β-cells. Although many diabetic cats have zero to minimal insulin secretion at the time of diagnosis, we know that a large number do in fact have viable β-cells; they may be 'turned off' by glucose toxicity, but they are still there and can regain function if BG can be kept below 200 mg/dL.

Clinical hypoglycemia is extremely unlikely in patients receiving an SGLT-2 inhibitor alone, as glucagon is available to trigger hepatic gluconeogenesis, if necessary. This is a significant difference to cats on insulin, as glucagon secretion is inhibited by insulin, and the body's natural counter-responses to hypoglycemia are therefore curtailed. In addition, the uptake of glucose within the renal tubules by SGLT-1 receptors appears to be upregulated; this provides additional protection against hypoglycemia.

Feline diabetics are therefore likely to respond to treatment with an SGLT-2 inhibitor, particularly if this approach is supported by appropriate dietary modifications and mitigation of concurrent insulin resistant conditions.[16,17,18]

Velagliflozin
Preliminary findings from a trial comparing insulin to velagliflozin were presented at the 2022 ECVIM meeting.[19] In a study of both newly diagnosed and insulin-treated diabetic cats, patients were treated with lente insulin, SQ twice daily (dose adjusted as appropriate by attending veterinarian), or velagliflozin, 1 mg/kg PO daily. This medication was routinely mixed with the food

or placed directly in the cat's mouth. Thirteen cats were assigned to each group and monitored for 60 days. The cats on the velagliflozin outperformed the cats on insulin, with a decrease in mean BG from 388 to 194 mg/dL by Day 7, and a drop in fructosamine from 604 to 401 µmol/L by Day 30. After just one month of treatment with velagliflozin, the BG for all cats remained below the renal threshold all day.

Because of its mechanism of action, velagliflozin will cause polyuria and polydipsia when given to a euglycemic cat. In a diabetic patient, polyuria and polydipsia are often improved from baseline, as a lower BG reduces the amount of glucose that ends up in the filtrate. Other markers of diabetic control such as polyphagia and undesirable weight loss are expected to improve as euglycemia is established.

More data from a large US-based clinical field trial will be shared in the following session.

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Diabetes Masterclass: SGLT-2 Inhibitors - Safety & Efficacy Data

Ellen Behrend, VMD, PhD, DACVIM (SAIM) & Patty Lathan, VMD, MS, DACVIM (SAIM)

Introduction

The incidence of feline diabetes mellitus (DM) has been steadily increasing, with a reported prevalence range of 0.12-0.5%.1-3. Most cases of feline DM are similar to human Type 2 DM, which is characterized by a combination of peripheral insulin resistance and inadequate insulin secretion.4,5 With continued exposure to hyperglycemia, insulin-secreting pancreatic beta cells undergo oxidative stress and apoptosis and cease secreting insulin (glucose toxicity). Obesity, inactivity, and inappropriate diet are risk factors for both humans and cats with Type 2 DM.6

The mainstay of treatment for feline DM is insulin therapy, usually twice-daily.[7] Many owners find the injection schedule onerous and are fearful of needles and disruption of the human-animal bond.[8] Additionally, insulin requires exact dosing; miscalculation can result in life-threatening hypoglycemia. Insulin therapy requires close monitoring to ensure appropriate glycemic control, demanding time and financial resources from owners. Not surprisingly, owners elect euthanasia in up to 20% of cats at or within the first year after a diagnosis of DM.[8]

Sodium glucose co-transporters (SGLT) are responsible for reabsorption of glucose in the proximal tubule of the kidneys. Under normal physiologic conditions, SGLT2 reabsorbs approximately 90% of glucose in the early proximal tubule, and SGLT1 reabsorbs approximately 10% of glucose in the late proximal tubule. SGLT1 also reabsorbs glucose in the intestinal epithelium.

Sodium-glucose co-transporter 2 inhibitors (SGLT2i) were initially FDA approved for people in 2013 and are a mainstay in therapy for human type 2 DM.[9] They inhibit glucose reabsorption in the renal proximal tubule, causing increased urinary glucose excretion. In human diabetics, SGLT2i administration results in euglycemia and reduction of clinical signs. Additionally, with resolution of hyperglycemia, some pancreatic beta cells may regain insulin-secreting ability.[10]

SGLT2i have been explored as a treatment for feline DM. The SGLT2i velagliflozin increased insulin sensitivity in a small number of non-diabetic obese cats.[11] In a clinical trial of diabetic cats, velagliflozin improved clinical signs and hyperglycemia.[12] Bexagliflozin, another SGLT2i, reduced insulin dose and glycemic control in a small number of insulin-treated diabetic cats[13] and controlled hyperglycemia and clinical signs as sole therapy in 68 of 84 cats (84.0%) with newly diagnosed DM.[14]

US Clinical Trial—Velagliflozin[16]

Velagliflozin is an oral solution intended for once daily stand-alone therapy for cats with DM. Naïve diabetics and cats previously treated with insulin ($\geq$ 5 days) were included. Exclusion criteria for the clinical trial included recent or chronic history of decreased appetite, vomiting, diarrhea, or suspicion of pancreatitis. Additionally, cats with a history of ketonuria or ketoacidosis prior to or at the time of screening were excluded. Cats receiving oral or dietary therapy for hyperthyroidism were excluded, but cats that had received surgical or radioiodine therapy and had a total T4 concentration within reference range for over 3 months could be included. Removal for hypersomatotropism was left to the discretion of the attending veterinarian.

Physical examinations, blood collections and screening of urine for ketones were performed on days 0, 3, 7, 30, 60, 120, and 180. Data are median (range).

Our hypotheses were that >70% of diabetic cats would have improvement in at least one glycemic and one clinical parameter, velagliflozin would not cause clinical hypoglycemia, and that <15% of cats would be removed due to an adverse event related to velagliflozin administration.

Results

For the study, 252 client-owned diabetic cats were enrolled; 214 (85%) were naïve diabetics (ND) and 38 (15%) were previously insulin-treated (IT). Treatment with velagliflozin was started on day 0. On days 30, 60, 120, and 180, a single BG after velagliflozin administration was 153 (62-480), 134 (64-414), 128 (55-461), and 125 (77-384), respectively. Fructosamine at screening was 538 µmol/l (375-794; reference range, 191-347 umol/L). On the same recheck days, fructosamine was 310 (204 - 609), 286 (175 - 531), 269 (189 - 575), and 263 (203 - 620).

Adverse Events
Eighteen cats (7.1%) developed ketoacidosis, and 17 cats (6.7%) developed ketosis without acidosis. Sixteen of the cats with ketosis were clinically well. Ketoacidosis was less common in ND (11/214; 5.1%) compared to IT cats (7/38; 18.4%). At ketoacidosis diagnosis, 14 cats (77.8%) had euglycemic ketoacidosis, i.e. BG $\leq$ 250 mg/dL. Most ketoacidotic events (14/18; 78%) occurred within the first 14 days of treatment.

By day 180, polyuria, polydipsia and or polyphagia resolved in the majority of cats. The most common adverse event was diarrhea. In most cats, it was mild and self-limiting.

No clinical hypoglycemia occurred during the study.

Conclusions and clinical importance
Velagliflozin is effective as a stand-alone oral solution therapy in feline diabetics with a low overall incidence of ketoacidosis and no clinical hypoglycemia during the clinical trial.[16]

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Diabetes Masterclass: Getting Started & Monitoring

Cynthia Ward, VMD, PhD, DACVIM

Introduction

Sodium-glucose cotransporter 2 inhibitors (SGLT2i) represent a class of drugs that have emerged as a significant breakthrough in the management of feline diabetes mellitus (FDM). These agents act by selectively inhibiting the sodium-glucose cotransporter 2 (SGLT2) located predominantly in the proximal tubules of the kidneys. By modulating the renal glucose reabsorption, SGLT2i promote urinary glucose excretion, resulting in improved glycemic control. They have been shown to be safe and effective when used in diabetic cats with a low risk of hypoglycemia.

What are SGLT2i and how do they work?

Sodium-glucose cotransporter 2 (SGLT2) is a protein primarily expressed in the proximal tubules of the kidneys. Its role in glucose reabsorption from the renal tubules makes it an attractive target for the treatment of FDM, where impaired glucose homeostasis is a hallmark feature. SGLT2 inhibitors (SGLT2i) are a class of oral antidiabetic drugs that selectively inhibit the function of SGLT2, thereby reducing renal glucose reabsorption and increasing urinary glucose excretion.

The mechanism of action of SGLT2i involves blocking the active transport of glucose from the renal tubules back into the bloodstream. Normally, the majority of filtered glucose is reabsorbed from the tubules via SGLT2, leading to its recycling. By inhibiting SGLT2, these drugs prevent glucose from being reabsorbed and increase its excretion in the urine, resulting in lower blood glucose levels. This unique mechanism allows SGLT2i to work independently of insulin, making them suitable for use in cats with FDM who have varying degrees of insulin resistance and pancreatic beta-cell dysfunction.

When SGLT2i are inhibited, increase glucose is reabsorbed in the distal tubule of the kidney by SGLT1 transport proteins. These proteins cause reabsorption of approximately 30-50% of the glucose load in the kidney when SGLT2 are blocked. This allows for glucose loss through the urine; however, hypoglycemia is prevented.

Screening of cats for SGLT2i

Screening diabetic cats for the appropriate use of SGLT2 inhibitors (SGLT2i) involves a comprehensive evaluation to ensure patient safety and optimal therapeutic outcomes. The first step in screening is confirming the diagnosis of diabetes mellitus through clinical signs, such as polyuria, polydipsia, and weight loss, along with elevated blood glucose and fructosamine levels. The ALIVE criteria set forth by the ESVE and endorsed by the SCE provides standard criteria by which FDM may be diagnosed. It is crucial to rule out other concurrent diseases that may contribute to similar clinical signs. Additionally, a thorough physical examination and baseline laboratory testing, including a complete blood count, serum biochemistry profile, TT4, urinalysis, and urine culture, are essential to assess the overall health status of the cat and identify any comorbidities. Further diagnostic procedures, such as serum IGF-1, fPL, and abdominal ultrasound, may be warranted to evaluate the pancreas and rule out concurrent diseases, such as acromegaly and pancreatitis.

Before initiating an SGLT2i, concurrent diseases must be addressed and resolved as much as possible. Because SGLT2i primarily act on the kidneys, cats with IRIS stage CKD > 3 should not be started on an SGLT2i. If that is the only treatment option for such a cat, they should be monitored closely, and owners warned of worsening of CKD.

The oral SGLT2i can be started. It is optimal to give it every 24 hours, but if the owner's schedule does not permit that, the dosing schedule does not have to be that exact. The SGLT2i does not have to be given with a meal and if the dose is spit out, another dose may be given as soon as the missed dose is recognized.

Initial Monitoring of cats on SGLT2i

When initiating SGLT2i therapy in cats with FDM, careful monitoring is crucial to assess the response to treatment, ensure safety, and optimize therapeutic outcomes. SGLT2i have a low risk of hypoglycemia and hyperglycemia is rapidly controlled and stable over the day. In this respect, they do not function like insulin that can rapidly lower blood glucose. However, using SGLT2i may result in unexpected ketosis, especially early in treatment. Therefore, a shift in monitoring paradigms for the veterinarian is recommended. Blood glucose curves are probably less useful, and ketone monitoring is more crucial, especially when beginning therapy.

It is recommended that cats that have been started on an SGLT2i be checked at 2-3 days, 7 day, 14 days and 30 days. This is to closely monitor for ketosis that most often develops in the first 2-3 weeks of therapy. At each visit the owner should be asked about resolution of clinical signs or if there are concerning clinical signs that have emerged. The cat should have a thorough PE and a blood glucose and ketone should be checked. Ketones may be monitored by urine dipstick using urine or plasma/serum, by sending out to a reference laboratory, or by an in-clinic handheld whole blood ketone meter (Abbott Precison^{R}). The Abbott Precison meters have been validated for use in the cat. Each method measures different ketones. Most endocrinologists prefer the use of the whole blood ketone meter. It measures beta hydroxybutyrate (BHB) ketone (urine dipsticks measure aceto acetate) which is the predominate ketone in people. An advantage of the handheld meter is that you can get numerical readings that are easy to trend over time. And you can get the readings on the spot. If the Abbott meter in unavailable, ketones can be measured by urine dipstick usine urine or plasma/serum on the ketone pad. Alternately, serum can be sent to a reference laboratory which will measure BHB; this can be expensive, and results may not be available for days.

If ketones are detected or clinical signs of FDM do not resolve or glycemic parameters do not improve, cats should be taken off the SGLT2i and insulin therapy initiated.

Additional Reading

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NOTES:

Diabetes Masterclass: Troubleshooting & Complications

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INTRODUCTION

Until recently, treatment of feline diabetes mellitus has relied upon treatment with insulin and feeding of a low carbohydrate diet. A new class of drugs, known as sodium glucose co-transporter 2 (SGLT2) inhibitors have now become available for treatment of diabetes in cats.

SGLT2 INHIBITORS

Active reuptake of glucose by the kidney is principally performed by SGLT2, a multi-spanning integral membrane protein expressed in the pars convoluta of the proximal tubule. This protein is responsible for the resorption of more than 90% of the glucose from the glomerular filtrate of healthy animals. Inhibitors of the SGLT2 protein increase urinary glucose excretion by inhibiting glucose uptake in the proximal renal tubule. Mice and humans genetically deficient for SGLT2 activity do not experience hypoglycemia despite profound glucosuria. Pharmacological inhibitors of SGLT2 improve glycemic control in humans with type 2 diabetes mellitus by lowering the blood glucose concentration and decreasing glycosylated hemoglobin without the risk of hypoglycemia. Additional benefits of SGLT2 inhibitor therapy reported in many human studies include improvement in insulin resistance, weight loss, a reduction in systolic blood pressure, decreased susceptibility to major adverse cardiovascular events and a reduction in the rate of progression of chronic kidney disease. Inhibition of SGLT2 does not usually result in hypoglycemia, although episodes of hypoglycemia have been observed in the context of co-administration with other antidiabetic agents, such as insulin and sulfonylureas.

SGLT2 INHIBITORS IN CATS

There are two FDA approved SGLT2 inhibitors available for use in cats. Bexagliflozin is a 15 mg oral tablet and Velagliflozin is an oral solution. Both drugs are administered once a day. SGLT2 inhibitors act in the renal proximal tubules to prevent absorption of glucose from the glomerular filtrate., SGLT-2 inhibitors enhance glucose loss in urine which results in a rapid decrease in the blood glucose, decreased fructosamine and improvement of clinical signs of diabetes such as polyuria, polydipsia, polyphagia, and weight loss. It is believed that the rapid and sustained decrease in blood glucose caused by SGLT2 inhibitors helps resolve glucose toxicity and allows the beta cells of the pancreas to increase secretion of some endogenous insulin, which prevents development of ketoacidosis. SGLT2 inhibitors are not indicated for treatment of diabetic cats with an absolute insulin requirement. The drugs are indicated for treatment of cats with newly diagnosed diabetes mellitus that do not have underlying systemic illness. Cats with underlying diseases such as hepatic disease, renal disease (IRIS stage 3 or higher), pancreatitis and other serious systemic illness should not be treated with SGLT2 inhibitors.

ADVERSE EFFECTS OF SGLT2 INHIBITORS IN CATS

The most common side effect of SGLT2 inhibitors is gastrointestinal upset, with clinical signs such as diarrhea, vomiting, anorexia, and dehydration. The most serious adverse effects reported in cats treated with SGLT2 inhibitors are diabetic ketoacidosis (which may be euglycemic), pancreatitis, and hepatic lipidosis. Other less common side effects are hypercalcemia, hyperlipidemia, and urinary tract infection.

Gastrointestinal upset

Diarrhea, likely due to inhibition of the SGLT1 protein in the gastrointestinal tract, is the most common side effect seen with SGLT2 inhibitors in cats. Diarrhea is usually self-limiting, rarely requires cessation of treatment, and usually improves with supportive care. Similarly, transient vomiting, hyporexia or anorexia can occur. SGLT2 inhibitors should be discontinued in cats that become anorexic, depressed or dehydrated.

Diabetic ketoacidosis

Diabetic ketoacidosis is the most serious complication associated with SGLT2 inhibitors, and likely occurs due to a lack of endogenous insulin secretion from the pancreatic beta cells. Diabetic ketoacidosis can occur shortly after initiation of SGLT2 inhibitors or at any time during treatment, if beta cell loss is progressive or if concurrent illness develops. Cats treated with SGLT2 inhibitors that develop DKAmay be euglycemic because of the effect of ongoing SGLT2 inhibition to promote urine glucose loss prevents the development of hyperglycemia, despite insulin insufficiency. This makes this particular complication a challenge for veterinarians to recognize and treat. Careful monitoring of cats for any early clinical signs of ketosis (lethargy, anorexia, vomiting and weight loss) and frequent measurement of urine ketones, and serum ketone beta-hydroxybutyrate is

very important. Treatment of DKA requires cessation of treatment with the SGLT2 inhibitor and initiation of regular insulin. Insulin may be administered by IV infusion or intermittent IM insulin. IV dextrose should be administered concurrently in cats that are euglycemic. Cats with concurrent renal or hepatic disease may have prolongation of metabolism of SGLT2 inhibitors and therefore euglycemia can persist for 5-7 days after cessation of treatment.

Pancreatitis
Risk of pancreatitis can be decreased by screening for pancreatitis prior to treatment by measurement of feline pancreatic lipase. If the SNAP fPL test is positive then the SPEC fPL should be performed. Cats with a SPEC fPL >5.3 µg/L should be treated with insulin rather than an SGLT2 inhibitor. In cats that develop clinical signs of pancreatitis during treatment, the SGLT2 inhibitor should be discontinued and the cat should be transitioned to insulin.

Hepatic lipidosis
Hepatic lipidosis is a possible complication of pancreatitis and DKA. Diagnosis relies on documentation of increased liver enzymes and hyperbilirubinemia. Cats with hepatic lipidosis may have prolonged metabolism of SGLT2 inhibitors. Treatment relies on supportive care, nutritional support with a feeding tube, appetite stimulants, and anti-nausea drugs.

The prognosis for cats with severe adverse effects of SGLT2 inhibitors is best if the disorder is identified as soon as possible. Cats treated with SGLT2 inhibitors should therefore be monitored very carefully during the first 8 weeks of treatment (Table 1). After the initial 8 weeks of treatment, cats that continue on SGLT2 inhibitors should be monitored whenever they show signs of systemic illness and at least every 3 months.

Table 1 Monitoring recommendations for cats treated with SGLT2 inhibitors

Time after Tx	**Monitoring**	**Action**
3-5 Days	Physical Exam including weight Urine ketones/blood BHBA	• **Continue SGLT2 inhibitor** unless BHBA is not decreasing, then discontinue drug and transition to insulin. • **Recheck at the two-week timepoint**
2 Weeks	Physical Exam including weight Urine ketones/blood BHBA Glucose Curve & Fructosamine	• **Continue SGLT2 inhibitor** unless cat is losing weight or if BHBA is rising, then discontinue drug and transition to insulin • If average BG from an 8-hour curve ≥ 250mg/dL and/or serum fructosamine above reference range, monitor closely • **Recheck in two weeks**
4 Weeks	Physical Exam including weight Urine ketones/blood BHBA Glucose Curve & Fructosamine	• **Continue SGLT2 inhibitor** unless cat is losing weight or if BHBA is rising, then discontinue drug and transition to insulin • If average BG from an 8-hour curve ≥ 250mg/dL and/or serum fructosamine above reference range, monitor closely • **Recheck in four weeks**

8 Weeks	Physical Exam including weight	• **Continue SGLT2 inhibitor** unless cat is losing weight or if BHBA is rising, then discontinue drug and transition to insulin • If average BG from an 8-hour curve ≥ 250mg/dL and/or serum fructosamine above reference range, transition to insulin • **Recheck every 90 days or as medically indicated**

Cats that develop clinical sighs of systemic illness at any time point during treatment, should be evaluated for ketoacidosis and pancreatitis. The presence of euglycemia does NOT rule out diabetic ketoacidosis. Cats that lack insulin secretion or have been treated with insulin and have become insulin-dependent diabetics should not be treated with SGLT2 inhibitors, however there is no good test for differentiating between cats with inability to secrete endogenous insulin and those that can recover insulin secretion. Therefore, careful screening prior to treatment and careful monitoring for ketosis during treatment is extremely important. A delay in in recognition and treatment of DKA and euglycemic DKA, may result in increased morbidity and mortality. In contrast to treatment with insulin, hypoglycemia is rare in cats treated with SGLT2 inhibitors.

SUMMARY

The SGLT2 inhibitors are an exciting new class of drugs in veterinary medicine. Studies suggest that bexagliflozin and velagliflozin are effective for management of diabetes mellitus in cats. Other roles for these drugs in veterinary medicine still need to be investigated. Issues that still need further study include the role of diet in the response to SGLT2 inhibitors, whether diabetic remission occurs in cats treated with SGLT2 inhibitors, and development of an accurate test to determine the endogenous secretory capacity of the feline pancreas that will predict a positive response to SGLT2 inhibitor treatment.

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Diabetes Masterclass: Panel Discussion
Diabetes Masterclass Speakers

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2023 CONFERENCE

The Ins and Outs of Feline Nutrition and Gastroenterology

7th WORLD FELINE VETERINARY CONFERENCE

October 12 – 15, 2023 Renasant Convention Center, Memphis, TN & Virtual

FRIDAY, OCTOBER 13, 2023

Schedule is in Central Daylight Time

TIME	SESSION TITLE		SPEAKER	ROOM	SPONSOR/ PARTNER
6:00 - 7:00 am	Early Riser Yoga Class*	IPO		Sheraton Hotel - Heritage Ballroom	
7:15 - 8:00 am	Continental Breakfast			Ballroom Foyer	TRIVIUM VET
8:00 - 8:15 am	President's Address	LS	Dr. Kira Ramdas	Ballroom A & B	
8:15 - 9:30 am	Critical Nutritional Foundations for Every Cat	LS	Dr. Valerie Parker	Ballroom A & B	Hills
9:30 - 11:00 am	Networking Refreshment Break			Exhibit Hall	Boehringer Ingelheim
11:00 - 11:50 am	Nutritional Management of the Comorbid CKD Patient	LS	Dr. Valerie Parker	Ballroom A	ROYAL CANIN
	Nutritional Idiosyncrasies & the Role in Obesity, Diabetes Mellitus, & Hepatic Lipidosis	LS	Dr. Adronie Verbrugghe	Ballroom B	EveryCAT
11:55 - 12:45 pm	Use of Assisted Enteral Nutrition	LS	Dr. Valerie Parker	Ballroom A	Hills
	Do Nutrients & Ingredients Matter for Weight Loss? How to Select a Diet	LS	Dr. Adronie Verbrugghe	Ballroom B	EveryCAT
12:45 - 2:10 pm	Lunch			Exhibit Hall	
1:00 - 2:00 pm	*Lunch & Learn #1:** Velagliflozin: An Oral Solution for the Diabetic Cat	IPO	Diabetes Masterclass Speakers	102 - 104	Boehringer Ingelheim
1:00 - 2:00 pm	*Lunch & Learn #2:** Evolving the Feline MDB: Purrfect Balance for Your Patient Assessment	IPO	Drs. Elizabeth Schooley & Kelly St. Denis	105 - 107	IDEXX
1:00 - 2:00 pm	*Lunch & Learn #3:** Calming Cats: The Impact of Transport & Anxiety on Our Cats, Cat Caregivers, & Practices	IPO	Dr. Tracey Deiss	113 - 115	zoetis
2:10 - 3:00 pm	Nutritional Management of Chronic Enteropathies	LS	Dr. Valerie Parker	Ballroom A	PRO PLAN VETERINARY DIETS
	Feeding Comorbidities: Obese Cats with Other Diseases	LS	Dr. Adronie Verbrugghe	Ballroom B	
3:05 - 3:55 pm	Harnessing the Power of Fiber to Manage GI Disease	LS	Dr. Valerie Parker	Ballroom A	ROYAL CANIN
	Navigating Alternative Cat Foods: Intersection Between Cat Needs & Client Preferences	LS	Dr. Adronie Verbrugghe	Ballroom B	
3:55 - 4:40 pm	Networking Refreshment Break			Exhibit Hall	Boehringer Ingelheim
3:55 - 4:40 pm	Student Social **All Students Invited to Attend*			Memphis Board Room	
4:40 - 5:30 pm	Nutritional Management of Hypercalcemia	LS	Dr. Valerie Parker	Ballroom A	Dechra
	Feeding the Allergic Cat	LS	Dr. Sara Ramos	Ballroom B	Hills
5:30 - 6:45 pm	Happy Hour Reception			Exhibit Hall	Elanco

LS Live Streamed

IPO In-person Only

*Separate registration required. No fees associated.

Critical Nutritional Foundations for Every Cat

Valerie Parker, DVM, DACVIM (SAIM, Nutrition)

Key Components of a Nutritional Assessment

Nutritional screening evaluations should be performed as standard at every veterinary visit. This should include the cat's body weight, body condition score (BCS), and muscle condition score (MCS). While BCS primarily assesses fat stores, MCS is intended to evaluate muscle specifically. Muscle condition is determined by visual examination and palpation over the temporal bones, scapulae, thoracic and lumbar vertebrae, and pelvic bones. Rather than using a numerical scoring system, muscle condition should be described as either normal or exhibiting some degree of atrophy (e.g., mild, moderate, marked). Since ill or injured cats preferentially lose lean body mass (i.e., muscle), it is important to simultaneously assess both fat and muscle stores, especially since BCS and MCS may not be analogous.[1,2]

A complete diet history should be obtained and the cat's medical conditions and medications should be documented. The diet history should include the brand of food fed, flavor(s), and amount fed daily. It should also include information about treats given and how medications are administered. To make this easier for veterinarians to accomplish, a short diet history form is available in the World Small Animal Veterinary Association (WSAVA) Nutrition Toolkit: https://wsava.org/wp-content/uploads/2020/01/Diet-History-Form.pdf. Clients can fill this out prior to their scheduled appointments or while they are waiting to be seen. If the short diet history or initial body composition assessment prompts any cause for concern (e.g., underweight or overweight, muscle loss, unbalanced home-prepared diet), a more thorough nutritional evaluation should be performed. If a home-prepared diet is being fed, this should prompt additional analysis by a board-certified veterinary nutritionist in order to ensure nutritional adequacy, especially as most recipes that people can find online or in books do not provide complete and balanced nutrition.[3]

Cat Food Choices and Conversations

It can be daunting navigating conversations about nutrition with pet caregivers as there is so much information available to clients via a variety of sources (e.g., pet food stores, media advertisements, online blogs, and videos). The volume of information can easily overwhelm pet caregivers and veterinarians alike. It can be challenging keeping up with the ever-changing landscape of veterinary nutrition, especially since diet formulations can change as frequently as every 6-12 months.

Choosing a pet food is an important decision for pet caregivers, especially if they are first-time pet caregivers and/or if their pet(s) have recently been diagnosed with a new medical condition. It helps to have open, honest conversations with pet caregivers about why a certain diet/brand is recommended. Providing specific reasons why a diet is recommended will increase the likelihood of client compliance. For a cat with newly diagnosed chronic kidney disease (CKD), feeding a diet lower in phosphorus will likely be discussed. Highlighting the differences in the recommended diet(s), and especially how that diet compares with the cat's current diet, may be quite eye-opening for a client.

For information on choosing a pet food company, the WSAVA Guidelines on Selecting Pet Foods is a great resource. This, as well as many other superb client handouts and tools for veterinary clinics, is available on the WSAVA Nutrition Toolkit website. Criteria that may influence a veterinarian's ability to recommend a certain company (or not) include: 1) whether or not the company has one (ideally multiple) full-time veterinary nutritionists on staff, meaning someone who is a Board Certified Veterinary Nutritionist® or who has a PhD in small animal nutrition; 2) whether the company can provide complete nutritional profiles of their diets; 3) having some knowledge of the company's quality control standards; and 4) having some knowledge of the company's research and development.

The Pet Food Label

Pet food labels can provide some useful information; however, their limitations must also be recognized. Pet food labels must state the calories (kcal; per cup or can, as well as on a per kg basis). An ingredient list must be provided (ordered by weight of ingredients), and a guaranteed analysis (GA) presents at least the minimum crude protein, minimum crude fat, and maximum crude fiber (on a % as-fed basis), as well as a maximum moisture concentration. Knowing the caloric density of a diet is crucial to be able to make recommendations for how much to feed an individual cat. While the ingredient list may offer some clues about whether a potential allergen is present, it offers no information about the quality of the diet or the ingredients.

The nutritional profile of one diet cannot be reliably compared with another using the % nutrients from the GA for the following reasons: 1) there can be significant variability between the GA and the typical nutrient analysis;[4] and 2) diets of different caloric densities (i.e., kcal/kg) are not comparable. It is more reliable to compare nutrients on a caloric basis (e.g., grams or mg of nutrient per 100 or 1000 calories [kcal]). If you (or a pet caregiver) want to know how to convert the % nutrient to a g/100 kcal basis, you need two pieces of information: first, the % nutrient (ideally on a typical analysis vs. a minimum from GA); second, the caloric density of the diet on a kcal/kg basis. (Box 1)

Box 1: Converting the % Nutrient to a g/100 kcal Basis

The equation to do this is: 1,000 x (nutrient % ÷ kcal/kg) = g/100 kcal

Example: For a dry cat food with minimum protein of 40% (as fed) and a calorie density of 4,000 kcal/kg, what is the protein concentration on an energy basis (i.e., g/100 kcal)?

1,000 x (40 ÷ 4,000) = 10.0 g/100 kcal (compared with an AAFCO minimum of 6.5 g/100 kcal)

*If you prefer to review the nutrient on a mg per 100 kcal basis, you need to multiply this by 1,000 again.

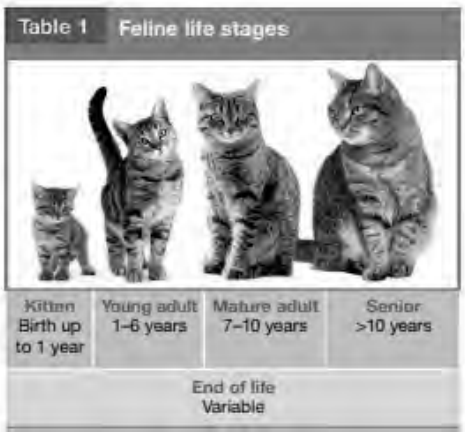
Example: For a canned cat food with a phosphorus level of 0.3% and a caloric density of 1,000 kcal/kg:

1,000 x (0.3 ÷ 1,000) = 0.3 g/100 kcal x 1,000 = 300 mg/100 kcal

Nutritional Considerations by Life Stage

Growth

Once a kitten is weaned from its mother, typically at around 4-6 weeks of age, it should be transitioned to a diet appropriate for growth. This means feeding a diet that has an Association of Feed Control Officials (AAFCO) claim of complete and balanced diet appropriate for growth or "all life stages." Kittens that do not receive complete and balanced nutrition are at risk of several adverse consequences, including nutritional hyperparathyroidism, diffuse osteopenia and bone fractures.[5] While some data suggests that cats develop their preferences for food texture from a young age, other studies have reported that what a kitten is offered from a young age will not influence its acceptance of a different texture of diet at a later stage of life.[6,7]



Besides ensuring that kittens receive diets appropriate for growth, it is imperative to begin discussions with cat caregivers about the importance of maintaining an ideal body weight and BCS. The key factors to ensuring that cats maintain an ideal BCS include feeding a diet of appropriate caloric density, and having some control over how many calories (kcal) per day the cat is eating. This will require providing a specific amount of food daily to the cat which can then be distributed as meal-feeding, multiple small meals, or grazing depending on preference. In a survey of 738 cat caregivers, 65% reported that they free-feed their cats.[8] Meal time can be a source of enrichment via the use of food dispensing toys/puzzles or by distributing food in different parts of the home for cats to "forage."[9]

Veterinarians should introduce caregivers to the concept of BCS early in a cat's life and should teach caregivers how to perform BCS assessments at home. This becomes especially important after kittens are spayed and neutered, as their energy needs will decrease after this time, and there may be a lag between surgical discharge and the cat's next veterinary visit. If caregivers are taught how to assess BCS at home, they might be better equipped to adjust their cat's intake at home to prevent them becoming overweight or obese. There is a wide range of caloric density in dry kitten foods (282 to 610 kcal/cup); thus, if a kitten is showing a tendency toward being overweight at a young age, it is best to transition to a lower calorie density diet that is still appropriate for growth rather than simply reduce the total volume of food fed daily, as this may lead to undesirable behavior if the kitten is not satiated.

Kittens should be transitioned to an adult maintenance diet at around 1 year of age, paying attention to caloric density of the diet. Treats, if provided, should comprise $\leq$ 10% of a cat's total daily intake to avoid unbalancing the diet.

Resting energy requirement (RER) = 70 x body weight (BW; kg)$^{0.75}$
Maintenance energy requirement (MER) for growth: 2.0-2.5 x RER
Maintenance energy requirement (MER) for adult maintenance: 1.2 x RER
It is imperative to consider each individual cat and to adjust the caloric intake based on the cat's BCS.

Young-to-mature adulthood

In young-to-mature adulthood, the biggest nutritional disorder that cats will likely face is the risk of becoming overweight (i.e., BCS 6-7/9) or obese (i.e., BCS 8-9/9). It is reported that 20-31% of cats in the United States are already overweight or obese by 2 years of age.[10-12] Worldwide, feline obesity is reported in up to 63% of adult cats, with middle-age being a significant risk factor.[13,14] Being overweight or obese is associated with greater risk of a variety of conditions, including dermatologic disease, cardiorespiratory disease, diabetes mellitus, lower urinary tract disease, and orthopedic disease. In one study, cats with a BCS of 9/9 were demonstrated to have a decreased lifespan compared with cats with a BCS of 5-8/9.[15]

Risk factors associated with being overweight or obese in cats include feeding a predominantly dry kibble diet, begging for food, and stealing other cats' food.[14-16] The association with dry kibble is most likely due to the inherently higher caloric density of kibble diets (approximately 4.0 kcal per gram) relative to canned diets, which provide roughly 1.0 kcal per gram. This is not to say that cats cannot maintain a healthy body weight and BCS while eating a kibble diet, but it does require paying close attention to overall caloric intake.

Mature-to-senior adulthood

As cats approach 10-12 years of age, they are at greater risk of losing weight, especially lean muscle mass.[17] Muscle loss can be defined either as sarcopenia or cachexia, and some animals display characteristics of both. Briefly, sarcopenia is described as muscle loss associated with age in the absence of other diseases, whereas cachexia is muscle loss that occurs in the presence of disease, often associated with increased inflammatory cytokines. Diseases commonly associated with muscle loss in cats include CKD, hyperthyroidism, hypertrophic cardiomyopathy, and intestinal disease.[18]

Assessing muscle loss requires visual examination and palpation of the spine, scapulae, skull, and wings of the ilia. It is currently recommended to score MCS either as normal or with variable degree of atrophy (i.e., mild, moderate, severe).[19] There is some subjectivity associated with this method; thus, additional tools have been developed to more objectively score MCS. Ultrasound and CT have been reported to accurately measure muscle mass in cats.[20,21] Recently the term vertebral epaxial muscle score (VEMS) was proposed to represent the ultrasound technique of assessing epaxial muscle mass.[20]

Any cat that is found to have experienced weight loss should have a full physical examination and a nutritional screening evaluation performed. Getting a thorough diet history can help clinicians determine if weight loss is affected by inadequate caloric intake or other diseases that may be associated with weight loss despite a seemingly adequate (or increased) caloric intake. A minimum database (complete blood count, chemistry, total thyroxine, and urinalysis) should be completed, and additional diagnostics may be performed on an individual case basis.

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NOTES:

Nutritional Management of the Comorbid CKD Patient

Valerie Parker, DVM, DACVIM (SAIM, Nutrition)

Veterinarians often struggle with making the best nutritional recommendations for cats with multiple diseases, especially cats with kidney disease. A few common disease combinations will be highlighted below; however, the bottom line is that every patient should be considered as an individual. The first step to managing a pet with comorbid conditions is to identify nutritional goals for each disease. Sometimes it is necessary to prioritize one goal over another. If the animal will not eat the optimal diet, or if an owner prefers to feed a home-prepared diet, consultation with a board-certified veterinary nutritionist may be warranted.

Some nutrient profile comparisons will be shown below; however, these nutrient profiles are updated frequently and these lists should not be used long-term for making nutritional recommendations. Additionally, canned and dry diets, even of the same name or variety, may have different nutrient profiles, so specific recommendations must consider dry vs. canned diets as well as specific flavor(s).

Chronic kidney disease (CKD) & Inflammatory bowel disease (IBD)

CKD: The primary nutrient of concern for CKD is phosphorus.[1] Feline renal diets provide ~80-130 mg/100 kcal. Non-CKD diets can provide upwards of 400-600 mg/100 kcal. It seems reasonable to provide < 200 mg phosphorus/100 kcal whenever possible, ideally < 150 mg phosphorus/100 kcal.

IBD: Nutritional management of inflammatory bowel disease (IBD) depends on the specific clinical signs (e.g., vomit, diarrhea). It may involve limiting dietary antigen exposure (e.g., single protein + single carbohydrate diet vs. hydrolyzed diet). In other cats, increasing dietary fiber concentrations may be beneficial for improving stool quality. Reducing dietary fat intake is rarely a goal in management of IBD in cats.[3] When comparing fiber concentrations between diets, it is important to remember that crude fiber is a poor indicator of total dietary fiber (TDF).[4] Veterinary therapeutic limited antigen diets have a wide variety of nutrient profiles, including variable caloric density, and the animal's body weight & body condition score may influence my recommendations.

Some example diets are listed here (nutrients per 100 kcal).

Feline hydrolyzed diets (dry)	**Kcal/cup**	**Phosphorus** (mg)	**Protein** (g)	**TDF** (g)
Royal Canin Renal Support + Hydrolyzed Protein	402	100	6.3	2.3
Royal Canin Ultamino* (high sodium diet)	335	120	6.3	2.0
Hill's Prescription Diet z/d	408	160	8.8	1.2
Royal Canin Hydrolyzed Protein Adult HP	351	170	6.3	2.0

Feline fiber-enriched diets (dry)	**Kcal/**cup	**Phosphorus** (mg)	**Protein** (g)	**TDF** (g)
Hill's Prescription Diet GI Biome	424	172	9.3	2.8
Royal Canin GI Fiber Response	362	260	8.0	2.9

CKD & Diabetes mellitus

CKD: Reduce dietary phosphorus (see above).

Diabetes mellitus: While it can be difficult to wade through the evidence for nutritional management of feline diabetes mellitus[5], my primary nutritional goals for a diabetic cat include the following:

1. Achieve and maintain ideal body weight and body condition score
2. Reduced carbohydrate diet[6]

The lowest carbohydrate commercially available feline diets provide < 1.0 g/100 kcal, and high carbohydrate diets can provide > 12.0 g/100 kcal. Canned and dry veterinary therapeutic diets specifically marketed for cats with diabetes mellitus provide up to 4.0 and 6.6 g/100 kcal, respectively. Not all diabetic cats need to eat high protein diets, and dietary protein and phosphorus concentrations are not directly linked.[1]

Many cats with diabetes mellitus are obese, and obesity can contribute to insulin resistance.[7] Thus, a weight loss strategy might employ the use of a low-calorie, high-fiber diet to influence satiety. Since there are no dry diets that are truly low in both calories and carbohydrates, it might be preferable to feed a canned diet. However, while generally dry diets provide more carbohydrates than canned diets, not all canned diets are low in carbohydrates. It is worth considering the obesity paradox as well. Cats with CKD should ideally maintain a BCS of 5/9 (possibly higher) for long-term survival benefits.[8]

What then should we do when faced with diabetic cats with CKD? Well, here is where I would consider a few things:

1. What stage of CKD is present? I aim to reduce dietary phosphorus intake in all stages; however, I typically do not specifically aim to reduce protein intake unless the cat's CKD has progressed to the point where it is more likely to be beneficial (e.g., uremia, proteinuria).
2. What is the cat currently eating? Dietary consistency is one of the primary goals when managing a diabetic cat. Especially if the cat has been doing well with his diabetic management for a while, perhaps the current diet may prove to be appropriate upon further nutritional evaluation.
3. Is there realistically a good chance to induce diabetic remission in the cat by focusing so much on carbohydrate intake, or should we more so focus on the CKD and adjust insulin therapy as needed based on potentially altered diabetic control?

Some example diets are listed here (nutrients per 100 kcal):

Diet (canned)	**Kcal** per can	**Phosphorus** (mg)	**Carbs** (g)	**Protein** (g)	**TDF** (g)
Royal Canin Aging 12+ Thin Slices in Gravy (3 oz)	71	120	3.8	11.0	1.4
Royal Canin Renal Support D (3 oz)	98	80	4.6	6.8	1.3
Royal Canin Aging 12+ Loaf in Sauce (5.1 oz)	122	120	4.9	11.0	1.4
Royal Canin Renal Support E (5.1 oz)	151	90	5.9	7.0	1.7

CKD and calcium oxalate urolithiasis

These cases are the worst! Which came first – the stones or the CKD? Should you feed a renal diet or a urinary diet? These cases need to be considered on an individual basis. If diet is to be used effectively to reduce the risk of calcium oxalate (CaOx) urolithiasis, it typically entails feeding a diet that promotes a reduced relative supersaturation (RSS).[9] There is a wide range of phosphorus among feline renal diets, and some of them may be appropriate for a cat with CKD. Additionally, some feline renal diets have been reported to provide a reduced RSS for CaOx. It is slightly controversial how dietary sodium intake affects both renal health as well as risk for urolithiasis. This will be briefly discussed during the lecture. If cats are hypercalcemic, additional attention may be paid to their dietary calcium and calcium:phosphorus ratio intake – see Nutritional Management of Hypercalcemia proceedings & lecture notes.

Some feline urinary diets are listed here (nutrients per 100 kcal):

Diet (canned)	**Kcal** per can	**Phosphorus** (mg)	**Calcium** (mg)	**Protein** (g)	**Sodium** (mg)
Royal Canin Urinary SO Aging 7+ + Calm (5.1 oz)	116	140	150	11.2	120
Hill's Prescription Diet c/d Multicare w/ Ocean Fish (5.5 oz)	178	153	172	9.5	79
Hill's Prescription Diet c/d Multicare Chicken & Vegetable Stew (2.9 oz)	69	159	191	9.8	89
Hill's Prescription Diet c/d Multicare Vegetable, Tuna & Rice (2.9 oz)	67	168	200	10.2	93
Hill's Prescription Diet c/d Multicare w/Chicken (5.5 oz)	174	169	180	9.5	87

CKD and hyperthyroidism

This is nearly every hyperthyroid cat! Nutritional management may play a significant role in maintenance of a euthyroid state if neither radioactive I-131 therapy nor methimazole therapy is an option. In those cases, dietary management may be attempted with Hill's Prescription Diet y/d, a low-iodine veterinary therapeutic diet that has been shown to induce euthyroidism within four weeks of feeding it exclusively.[10]

Some veterinarians may question the utility of this diet with the presence of CKD. The primary nutrient of concern I consider when managing CKD patients is phosphorus. Hill's Prescription Diet y/d provides 115 (canned) to 161 mg (dry) phosphorus per 100 kcal, an amount that just slightly exceeds that in most feline veterinary therapeutic renal diets. It provides just a bit more protein than the average renal diet; however, the jury is still out regarding the optimal amount of protein to feed a CKD cat.

What's one potential downside? The target urine pH for Hill's Prescription Diet y/d is a bit lower than I would expect of a typical "renal" diet. It aims for a target pH of 6.4-6.7, rather than a more neutral pH of 6.6-6.9.
Listed below are phosphorus and protein content for Hill's y/d in comparison to a typical renal diet and the AAFCO minimum guidelines. Nutrients are listed on a per 100 kcal basis.

Diet	**Kcal** per cup or can	**Phosphorus** (mg)	**Protein** (g)
Hill's Prescription Diet y/d (dry)	500	161	8.3
Hill's Prescription Diet y/d (can)	194	115	7.3
Average renal diet	--	100	6.5
AAFCO minimum (feline adult)	--	125	6.5

Supplement use
Many pet owners have the desire to provide additional dietary supplements and nutraceuticals to their pets with CKD. In one study, 38% of pet owners administered vitamins, minerals, or other supplements to their cats with CKD. There are a plethora of supplements marketed for patients with kidney disease. Careful selection of type, dose and brand is important to avoid toxicities or lack of efficacy. This entails consideration of the specific brand (e.g., reputable, tested by an independent company), potential benefits (research-driven vs. hypothetical), risks (known or hypothetical), and interaction with other medications and supplements. Some supplements provide unwanted calories and added nutrients that may be nominal or, alternatively, toxic. Additionally, for an animal that is already wary of taking its necessary medication(s), forcing it to take unnecessary (or even potentially harmful) supplements may add undue stress.

The author routinely recommends omega-3 fatty acid supplementation with eicosopentaenoic acid (EPA) and docosahexaenoic acid (DHA) for their anti-inflammatory properties. In experimental models of dogs, EPA/DHA supplementation reduced proteinuria; however, this has not been demonstrated clearly in naturally-occurring disease. Although an optimal dose of EPA/DHA for animals with kidney disease has not determined, general dose recommendations for dogs include 50-75 mg/kg or up to 140 mg EPA and DHA per kg$(BW)^{0.75}$.[11] Many veterinary therapeutic renal diets have added EPA/DHA, and the amounts provided should be determined based on the pet's caloric intake (i.e., mg EPA/DHA per 100 kcal ingested daily). It can then be decided whether to add to the total dose.

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Use of Assisted Enteral Nutrition

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Many cats will present for evaluation by a veterinarian for hyporexia or anorexia. Hospitalized animals specifically are at risk for receiving suboptimal nutrition for a few reasons, whether because of vaguely written or absent feeding orders, sedation from analgesics, procedures requiring the animal to be fasted, or other factors that impede adequate caloric intake. When animals receive inadequate caloric and nutrient intake, adverse consequences of malnutrition are likely to occur. These consequences may include loss of lean body mass, impaired immune function, reduced wound healing and even decreased survival.

Since hyporexia is a vague clinical sign that may be associated with a myriad of diseases. It is imperative to fully evaluate any animal that presents with a decreased appetite for an underlying cause that may be specifically addressed. This means starting with a full physical examination and nutritional screening evaluation. A minimum database (CBC, chemistry, thyroxine concentration, urinalysis) should be completed, and additional diagnostics may be performed on an individual case basis. Optimal nutritional assessment of each patient will allow the clinician to develop an appropriate nutritional plan. This should address patient selection, timing of nutritional support, route of administration and diet selection.

Pending initial workup, medications to ameliorate nausea may be useful (e.g., maropitant, ondansetron); however, bioavailability and efficacy of these drugs is variable across species.[1,2] There is not much evidence that indiscriminate acid-reducing agents will provide significant benefit for hyporexia. The exception to this would be if there is blatant evidence of gastrointestinal bleeding.[3]

Medications to increase food intake can useful in cats. Capromorelin is a medication that can increase food intake and improve body weight in healthy cats.[4] Mirtazapine can be effective in both oral and transdermal forms to aid in weight gain, reduce vomiting and improve appetite.[5,6]

Animal Assessment

Every animal that presents to the veterinarian should have a nutritional screening evaluation performed.[7,8] This should include the animal's body weight, body condition score (BCS) and muscle condition score (MCS). While BCS primarily assesses fat stores, MCS is meant to evaluate muscle specifically. Muscle condition is determined by visual examination and palpation over the temporal bones, scapulae, thoracic and lumbar vertebrae, and pelvic bones. Rather than use a numerical scoring system, muscle condition should be described as either normal or exhibiting some degree of atrophy (e.g., mild, moderate, marked). Since ill or injured animals preferentially lose lean body mass (i.e., muscle), it is important to simultaneously assess both fat and muscle stores, especially since BCS and MCS may not be analogous. Any animal that is in poor body condition (either underweight or overweight) or has muscle loss may require additional evaluation.

A complete diet history should be obtained and the animal's medical conditions and medications should be documented. The diet history should include the brand of food fed, flavor(s), and amount fed daily. It should also include information about treats given, including rawhides and chew toys, and how medications are administered. If a home-prepared diet is being fed, a board-certified veterinary nutritionist should be contacted to conduct diet analysis in order to ensure nutritional adequacy.

Timing of Nutritional Support

Deleterious effects of anorexia (e.g., enterocyte atrophy, decreased immune function) will occur within just a few days of anorexia.[9] Animals that have been, or are expected to be, anorectic for longer than 3 to 5 days are the ones that should be targeted for assisted enteral nutrition. The length of time an animal is anorectic prior to presentation must also be considered in this timing. Whenever possible, enteral feeding is preferred to parenteral nutritional support, because it supports gastrointestinal structure and function. Planning ahead for route of feeding before other procedures are performed is encouraged. If an animal with confirmed or anticipated anorexia is to be sedated or anesthetized for a diagnostic or therapeutic procedure, prophylactic placement of a feeding tube can provide a safety net to provide nutritional support.

Route of Administration

There are a number of options for feeding tubes. Factors to consider when choosing the most appropriate tube include the animal's nutritional status, ability to tolerate anesthesia, the length of time the animal is expected to require nutritional support, location of any primary GI disease, hospital facilities, cost, and the clinician's comfort level with different techniques for tube placement. Table 1 provides a comparison of various feeding tube options. Detailed information for placement of these feeding tubes is described elsewhere.[10,11]

Table 1. Comparison of feeding tubes.

Tube	Duration of nutritional support	Anesthesia required?	Type of diet required	Other factors to consider
Nasoesophageal (NE)	Short-term (< 7 days)	No	Liquid	May cause epistaxis
Nasogastric (NG)	Short-term (< 7 days)	No	Liquid	May cause epistaxis; allows measurement of gastric residual volume and decompression of stomach
Esophagostomy (E)	Long-term (weeks to months)	Yes	Canned diet slurry	Well-tolerated, not technically difficult to place
Gastrostomy (G)	Long-term (weeks to months)	Yes	Canned diet slurry	Requires surgical or endoscopic placement; early removal may have serious consequences

How Much to Feed?

Since there are risks with both underfeeding and overfeeding, it is recommended to feed a hospitalized ill animal its resting energy requirement (RER). While the exponential equation for calculating RER, 70 x $(BW_{kg})^{0.75}$ is more accurate, the linear equation (30 x BW_{kg} + 70) can also provide a reasonable approximation of caloric needs for cats. For obese animals, further reducing caloric intake may be warranted, but it is not appropriate to put a sick, hyporexic animal on a specific weight loss plan. Depending on the individual animal's activity level and metabolism, maintenance energy requirement (MER) can then be determined. This may range from 0.8 to 2.0 x RER, sometimes higher for patients with intestinal malabsorption or extremely high metabolic needs. The amount fed often needs to be adjusted over time to maintain body weight and optimal body condition.

Diet Selection

Choosing the most appropriate diet depends on several factors, including the animal's medical condition(s) that may impact the desired nutrient profile, and non-patient factors, including the type of tube in place, diet availability, and cost. Animals should be offered the option to eat before each feeding. If an animal does not eat enough of its calculated energy requirements, supplemental nutrition should be provided via feeding tube.

For patients with small-bore tubes, a liquid enteral diet must be used. For most patients, Royal Canin Veterinary Diet Recovery Liquid will be an appropriate choice. However, there is an additional veterinary liquid diet formulated for cats with chronic kidney disease (Royal Canin Veterinary Diet Renal Support Liquid Feline). (Table 2)

Some veterinary therapeutic "critical care" diets are formulated to meet feline nutritional requirements, have a consistency amenable to tube feeding, and are relatively calorie-dense. When mixed with a small amount of water (25 ml per 5.5-5.8 oz can), these diets provide approximately 1.0 kilocalories (kcal) per ml (Table 2). Each diet has a different nutrient profile that can be used to determine the diet most appropriate for an individual animal (e.g., avoiding diets high in sodium for an animal with cardiac disease). When these critical care diets are contraindicated for an individual animal, commercial canned veterinary diets (rarely a dry diet) may be blended with water to provide appropriate nutritional support for enteral feeding. The amount of water that must be added to each diet varies based on the individual diet. Additionally, these diets require at least 2 to 3 minutes of high-speed blending before administration, and tube flushing is required to avoid tube clogging.

Table 2. Nutrient concentrations of commercially available veterinary "critical care" and liquid enteral diets for administration via feeding tubes. All nutrients are listed per 100 kcal.

Canned diet	Kcal per can	Water added (ml per can)	Kcal per ml (with water)	Protein (g)	Fat (g)	Phosphorus (mg)	Sodium (mg)
Purina CN (5.5 oz can)	211	25	1.1	8.0	7.4	250	90
Hill's Prescription Diet a/d (5.5 oz can)	183	25	1.0	9.1	6.9	238	180
Royal Canin Recovery (5.8 oz can)	171	25	1.0	9.7	6.3	230	220
Liquid enteral diet	**Kcal per bottle**		**Kcal per ml**	**Protein (g)**	**Fat (g)**	**Phosphorus (mg)**	**Sodium (mg)**
Royal Canin Recovery Liquid (8 fl oz bottle)	217		0.9	9.1	5.7	180	100
Royal Canin Renal Support Liquid Feline (8 fl oz bottle)	217		0.9	7.5	5.9	80	90

Enteral feedings can be administered either in bolus form or as a continuous rate infusion (CRI). Food should be warmed to room temperature. Depending on how long the animal was anorectic, feedings should provide 25 to 33% of RER on the first day, divided into approximately four feedings, with each feeding administered over at least 10 to 15 minutes. As long as the animal tolerates the feedings, the amount fed can be gradually increased to achieve 100% RER over 3 to 5 days. When sending the animal home, it is best to adjust to three feedings per day if possible to aid in owner compliance. While stomach capacity is 40 to 50 ml/kg and most animals tolerate 20 ml/kg as a bolus, some animals require a smaller volume per feeding. Feeding hospitalized animals by CRI is appropriate for those that do not tolerate bolus feeding (e.g., delayed gastric emptying, ileus).

Monitoring and Potential Complications

Feeding tubes are typically well-tolerated; however, complications can arise. Complications can be characterized as mechanical, metabolic, or gastrointestinal. They are minimized by providing good instructions and careful monitoring.

Mechanical complications include tube clogging, inadvertent removal of tubes, and tube migration. To reduce the risk of tube clogging, a few precautions should be taken. Only liquid enteral diets should be administered via small-bore (NE/NG) tubes. Canned diets should be blended thoroughly (at least 2 to 3 minutes) before administering via E or G tubes. Crushed tablets should not be administered via small-bore tubes, and medication compatibility should be verified before administration via E or G tubes.[12] Tubes should be flushed well before and after food and medication administration. Depending on the size, tubes generally require between 2 to 5 ml of water to adequately flush them. If a tube does clog, a solution of ¼ teaspoon pancrelipase (e.g., Viokase) plus 325 mg sodium bicarbonate in 5 ml warm water should be injected and allowed to sit for 5 minutes, then flushed with water.[13] To prevent inadvertent removal of tubes, E-collars and bandages or stockinettes should be used. Inadvertent aspiration of food can occur due to underlying disease (e.g., esophageal dysmotility), inappropriate tube placement, or migration of tubes. Tube placement should be confirmed radiographically before feeding. Animals at risk for aspiration should be fed in an upright position.

Potential metabolic complications include overhydration, electrolyte disturbances, and refeeding syndrome. Concurrent intravenous fluids must be adjusted when initiating enteral feeding to account for the water volume provided by the food and for multiple flushes, which can contribute significantly to daily water intake. Refeeding syndrome, which results in hypophosphatemia, hypokalemia, and hypomagnesemia, is most likely to occur in animals that have not eaten for significant periods of time. In high-risk patients (i.e., those that have been anorectic for >1 week), feeding should be initiated more slowly (10 to 15% on day 1 and progress over 7 to 10 days) and electrolytes should be closely monitored during the first 12 to 72 hours after initiating feedings.

Gastrointestinal complications may include vomiting, diarrhea and abdominal discomfort. Anti-emetic therapy may have some benefit, but feedings may need to be adjusted (e.g., decreased volume, increased frequency or change of diet). All enteral diets should be refrigerated after opening and should be discarded after 48 hours as contamination can occur.

Once an animal is discharged, monitoring should include body weight, BCS, and MCS every 1 to 2 weeks initially to ensure adequate caloric intake. Amount fed may need to be adjusted to achieve and maintain ideal body weight, BCS, and MCS. Tube monitoring should be continued at home and bandages should be changed once a week (or sooner if needed). Owners should be instructed to bring the animal in for evaluation if they have any concerns about the placement of the tube or difficulty feeding. Superficial skin infections at tube sites are not uncommon and can be treated with either topical or systemic antibiotics.

Discontinuing Assisted Feedings

When the animal is voluntarily consuming at least 60% of its RER orally, enteral feedings can be gradually decreased. It is imperative not to remove enteral feeding tubes too early. Animals should be eating full RER voluntarily and maintaining body weight for at least one week before tubes are removed. If an animal is eating without assistance, the tube should be flushed with 3 to 5 ml water four times daily to maintain patency. Once tubes are removed, E and G tube sites typically heal within 24 to 48 hours by second intention.

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Nutritional Management of Chronic Enteropathies

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Defining chronic enteropathies

An animal that presents with at least a 2-week history of vomiting and/or diarrhea may be diagnosed with a chronic enteropathy. By definition, the disease stems from a primary gastrointestinal disease. Other known primary gastrointestinal disorders as well as secondary causes of vomiting and diarrhea must be excluded (Table 1) prior to making this diagnosis. The diarrhea should be characterized as small bowel, large bowel, or mixed bowel in origin, as this may influence diagnostic and therapeutic options. A minimum database (CBC, biochemistry profile, urinalysis), fecal examination and abdominal imaging (e.g., radiographs, ultrasound) are typically recommended. Depending on these results, additional diagnostics may be warranted [e.g., cobalamin (vitamin B12), folate, trypsin-like immunoreactivity (TLI), resting cortisol +/- ACTH stimulation test]. A review of laboratory tests for diagnosis of chronic enteropathies is described elsewhere.1

Table 1. Primary and secondary causes of vomiting and/or diarrhea.

Primary gastrointestinal disorders	Secondary gastrointestinal disorders
Inflammatory bowel disease	Pancreatitis
Lymphangiectasia (rarely in cats)	Exocrine pancreatic insufficiency
Food intolerance, food allergy	Hypoadrenocorticism (Addison's disease)
Foreign body obstruction	Hyperthyroidism
Dietary indiscretion	Hepatic disease
Infectious diarrhea	Kidney disease
Toxin	Neoplasia
Neoplasia	Neurologic disease

Inflammatory bowel disease

Inflammatory bowel disease (IBD) is a chronic enteropathy characterized by mucosal infiltration of inflammatory cells. It is typically classified by the predominant inflammatory cell(s); lymphocytic-plasmacytic inflammation is most commonly diagnosed. The etiology of IBD is multifactorial with genetic, dietary and immunologic factors potentially playing a role. IBD is an umbrella term that envelops a few chronic enteropathies, including food-responsive disease, antibiotic-responsive disease, and immunomodulatory-responsive disease. A histopathologic diagnosis of IBD does not necessarily dictate how an individual animal will respond to therapy. As such, with stable patients, a step-wise management approach is recommended in order to assess the animal's response to one therapy at a time.

Therapeutic options may include a diet trial, fiber supplementation, modification of the intestinal microbiome, and immunomodulatory medications (e.g., corticosteroids, cyclosporine, etc.). Nutritional management of IBD is discussed below. Fiber supplementation may prove useful, especially for animals that present with a component of large bowel diarrhea.[2] In some cases, only the addition of soluble fiber (e.g., psyllium) is necessary to resolve the diarrhea. Similar to the effects of fermentable fiber in the intestine, prebiotics (e.g., inulin, fructooligosaccharides) may also be of benefit by increasing short chain fatty acid production and influencing intestinal flora. There is likely a role for probiotics in cases of chronic enteropathies; however, veterinary data is limited and we must rely for now upon empirical data. Caution must be exercised when recommending specific brands of probiotics as there is variable quality control among supplements. One study that evaluated labels and bacterial contents of 25 commercial probiotics marketed for use in animals revealed that only 2 of 25 products had acceptable labels that accurately described their contents.[3]

Food intolerance & food allergy

A food allergy is an immune-mediated reaction, whereas food intolerance is a non-immunologic reaction (Figure 1). Food allergy typically presents with dermatologic clinical signs (non-seasonal pruritus), gastrointestinal signs or both. The most commonly reported feline food allergens are beef, fish, and chicken.[6,7,8] Food intolerances may be due to a number of factors (e.g., food additive, Maillard reaction). Oftentimes no single, specific dietary component is identified.

A definitive diagnosis of food intolerance requires 1) feeding an elimination diet (e.g., novel protein diet, hydrolyzed diet) for several weeks (minimum 3 for gastrointestinal signs, longer for predominantly dermatologic signs); 2) seeing good improvement in clinical signs; and 3) rechallenging the animal with its original diet to see if there is a relapse. However, even this does not definitively diagnose food intolerance as the animal may be responding to a variety of dietary factors (e.g., increased digestibility, decreased fat concentration, fiber modification).

Diagnosing a true food allergy is even more challenging. There is no easy test to perform. Despite their appeal, serologic titers are fairly useless. After an elimination diet is fed and a response is noted, the animal should be challenged with one ingredient at a time in order to document the food(s) to which the animal reacts (e.g., intense pruritus). If there is no response to a diet trial, or only a partial response, a few factors must be considered: 1) the animal has atopic dermatitis (or concurrent allergies); 2) lack of owner (or pet) compliance; 3) the diet was not truly novel or it was contaminated.

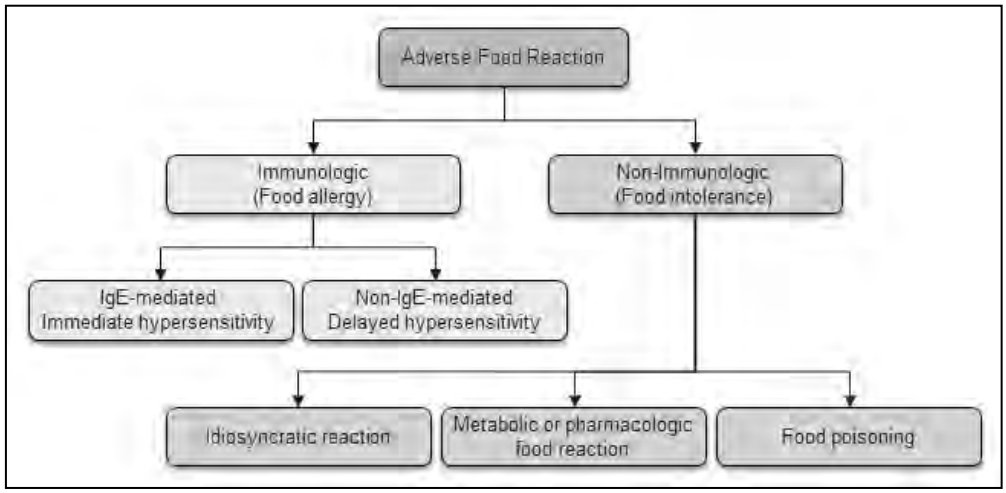

Figure 1. Characterization of adverse food reactions. Adapted from Roudebush, et al.

Nutritional Management

Various nutritional approaches may be taken in the management of chronic enteropathies.[9] The underlying etiology may influence which approach is attempted first. It is important to let clients know that management of chronic enteropathies often entails a bit of trial and error as there is no single diet that will be best for every pet. Additionally, while dietary management may completely resolve the clinical signs, many animals will rely upon some combination of dietary and medical therapy.

Every animal with chronic enteropathy may respond a bit differently to dietary therapy. Various dietary approaches may be considered for pets with FRE including: 1) highly digestible diets; 2) limited antigen diets: either novel protein/limited ingredient diets or hydrolyzed diets; and 4) fiber-enriched diets. In some animals, a home-cooked diet may be recommended. For animals with concurrent hypocobalaminemia, parenteral cobalamin (vitamin B_{12}) supplementation should be provided. Recommendations for cobalamin supplementation can be found elsewhere.[10]

Novel ingredient diet

By definition, a novel ingredient diet should provide both novel protein and novel carbohydrate food sources. These diets may also be known as "limited ingredient" diets, meaning they use only one protein and one carbohydrate source. These diets exist in both veterinary therapeutic and over-the-counter (OTC) forms. Studies have revealed that many limited ingredient canine and feline diets were contaminated with proteins that were not listed in the ingredient list;[11-13] similar studies in cats have not been performed. For this reason, it may be recommended to feed a veterinary therapeutic diet for the initial diet trial. Pending the response to the diet trial, switching to an OTC diet may be attempted. Despite several diets having similar ingredients, their nutrient profiles may be quite variable (e.g., variable caloric, protein, fat concentrations). Thus, in choosing a novel ingredient diet, the veterinarian should consider the whole nutrient profile to determine which diet best suits the individual animal's needs.

Prior to choosing a limited ingredient diet, it is important to get a complete diet history so that it is clear which ingredients (proteins and carbohydrates) the animal has eaten in the past. Given the fact that many OTC diets are now routinely using what were previously considered "novel" ingredients (e.g., potato, venison, fish), there may not be any truly novel ingredient

commercial diets available. In those cases, another diet option may be preferable (e.g., hydrolyzed diet). Alternatively, reducing antigen delivery to the intestinal tract may still provide some benefit even if the diet is not truly novel.

Hydrolyzed diet

Hydrolyzed diets rely upon using proteins that have been broken into small polypeptides (or even amino acids). By disrupting the protein structure, the goal is to prevent immune recognition of proteins by the intestinal tract, thus reducing allergenicity. These diets tend to be highly digestible. Currently hydrolyzed diets are primarily available as veterinary therapeutic diet options. Some of these diets do provide intact carbohydrate sources (e.g., rice, potato); in rare cases, this may incite a reaction. In a study evaluating the efficacy of hydrolyzed diets for cats with chronic enteropathies in primary practice, of 697 cats, 457 (66%) had a favorable response, without requiring the use of antibiotics or corticosteroids, for a median of 818 days (range, 184-3809).[13]

Highly digestible diet

Several veterinary therapeutic diets have been formulated to be specifically highly digestible (~90%). These diets typically use highly digestible ingredients. They provide variable fiber concentrations, usually with mixed soluble & insoluble sources. These diets are not meant to be novel ingredient or hydrolyzed; however they may be a reasonable option for owners who cannot feed one diet exclusively. It is important to remember that dry and canned formulations of the same diet may have different nutrient profiles. Dietary fat concentrations do not appear to be an important factor in management of cats with chronic diarrhea.[14]

Home-prepared diet

While there is no inherent benefit to feeding a home-prepared diet in most cases, some people may prefer to feed a home-prepared diet. Most recipes found online or in books do not provide complete and balanced nutrition;[15] thus, a board-certified veterinary nutritionist should be consulted if an owner wants to feed a home-prepared diet. A home-prepared diet may be formulated to be a novel ingredient diet and most home-prepared diets have excellent digestibility. Clients should be aware that feeding home-cooked diets may not provide financial benefit in most cases.[16]

So Which Diet Should I Choose?

This is the million dollar question! Unfortunately, every animal is different and there is no best diet. Client and pet preferences should be taken into account in order to have the best compliance. Nutrient profiles of the various diets should be compared to see which option seems most appropriate. Good client communication is imperative so that owners do not get frustrated if they do not see immediate results. Animals should be reassessed regularly and therapy should be amended as needed. Most cases require tweaking of both nutritional and medical therapy to achieve the best results.

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Harnessing the Power of Fiber to Manage GI Disease

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Fiber Terminology

Fiber is defined as complex, nondigestible carbohydrates of plant origin. Fiber is resistant to normal enzymatic digestive processes during passage through the gastrointestinal tract. Two main characteristics of fiber sources include solubility and fermentability of the fiber. Solubility of fiber is a measure of its ability to disperse in water. Soluble fiber is typically more readily fermented, which ultimately results in the production of volatile fatty acids that can benefit enterocytes and augment the microbiota ("prebiotic"). Insoluble fiber is typically less fermentable and can increase gastrointestinal tract motility, thus passage of gastrointestinal contents and improve fecal consistency due to water binding ("bulk").[1]

Fiber undergoes various degrees of fermentation by the intestinal microbiota; the degree of fermentation in cats is dependent on the fermentability inherent to that fiber source. Fermentation results in the release of short-chain fatty acids (SCFAs) and organic compounds, subsequently resulting in acidification of the luminal environment. Increasing concentrations of SCFAs contributes to intestinal health in a few ways. Colonocytes use SCFAs as an energy source. By reducing colonic pH and reducing luminal oxygen, there is limited growth of anaerobic pathogens. Short chain fatty acids also help maintain the epithelial cell barrier by stimulating goblet cell differentiation and mucus production.[2] Acidification of the luminal content may reduce ammonia, which is beneficial in other diseases, especially liver disease.

Fiber can also serve as a prebiotic (a nondigestible food ingredient that selectively stimulates bacteria to improve host health).[3] Prebiotics commonly added to pet foods include oligosaccharides and inulin. The by-products of the fermentation of prebiotics serve as nutrients for commensal microorganisms and are not used by the host animal. Investigators have reported beneficial effects of prebiotics in humans and other animals.[4]

A recent consensus statement states that a synbiotic is a "mixture comprising live microorganisms and substrate(s) selectively utilized by host microorganisms that confer a health benefit on the host."[6] Host microorganisms can be defined either as "autochthonous," meaning the bacteria present in the animal, OR as "allochthonous," meaning exogenously provided, such as a probiotic. There are then two subsets for synbiotics: complementary and synergistic. A complementary synbiotic is composed of a probiotic combined with a prebiotic, designed to target the autochthonous microorganisms, whereas a synergistic synbiotic provides a substrate meant to be selectively utilized by the co-administered microorgansisms.[5]

Measuring Fiber

There are many ways to technically measure fiber, which are beyond the scope of these proceedings. When it comes to practical ways for pet food companies to report dietary fiber concentrations, most companies provide only a crude fiber concentration. However, it has been well established that total dietary fiber (TDF) is a more useful descriptor than crude fiber.[6] Total dietary fiber includes all soluble and insoluble sources, whereas crude fiber includes some of the insoluble fiber, but provides no information regarding soluble fiber (Figure 1). Some companies, especially those that formulate fiber-enriched diets, do provide more thorough fiber profiles, including TDF, crude fiber, soluble, and insoluble fiber concentrations. This is one instance where evaluation of the ingredients may offer further insight as to what types of fiber are likely to be present, as specific properties of various ingredients that provide fiber may confer beneficial effects on the animal and its microbiome. Typical fiber-rich ingredients are whole grains, psyllium husks, powdered (ligno)cellulose as examples for water binding "bulk" fiber and beet pulp, chicory root (source of inulin), carob flour, FOS/MOS, vegetable fiber, fruit fiber, or pomaces as examples for fermentable thus primarily "prebiotic" fiber. In most instances of pets with intestinal disease, a mix of soluble and insoluble fiber sources will provide optimal outcomes.

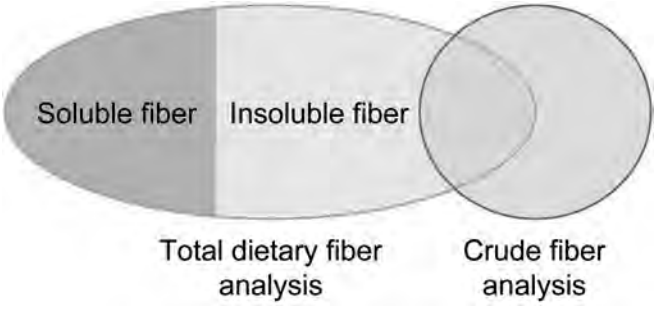

Figure 1. Schematic depiction of the relationship of total dietary fiber, crude fiber, insoluble fiber, and soluble fiber.

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Dietary Fiber Sources		Solubility		
		High	**Moderate**	**Low**
Fermentability	**High**	Fructose, Galactans, Mannans, Mucilages, Apple pectin, Citrus pulp, Guar gum, Gum arabic, Soy fiber, Apple pomace, Carrot pomace, Citrus pectin		
	Moderate	Pectin, Flaxseed	Grape pomace, Tomato pomace, Pea hulls	Hemicellulose, Beet pulp, Corn bran, Pea fiber, Rice bran, Soy hulls, Wheat brans, Wheat middlings
	Low		Pistachio Psyllium	Hemicellulose, Cellulose, Soy hulls, Peanut hulls, Sunflower hulls

Figure 2. Solubility and fermentability of various dietary sources of fiber.

General effects and indications of fiber

Useful general fiber effects in GI patients include changes in viscosity of gastrointestinal contents, thus normalization of intestinal motility and transit, regulation of gastric emptying, buffering of gastric acid, and adsorption of toxins in the digestive tract. Indications for supplementing fiber or feeding fiber-rich diets are as a pure fiber supplement like for diets generally low in fiber (e.g., homemade diets) or hairball prophylaxis in cats. Secondly, fiber plays a vital role in many dietary purposes, especially in obesity, chronic diarrhea, colitis or constipation, dysbiosis, liver and kidney disease, and fat metabolism disorders.

Typical insoluble and soluble fiber used in veterinary nutrition

The two most important "bulk" fibers are cellulose and psyllium husks. Due to their water-binding capacities, they can improve feces consistency (fecal cosmetics) and may also enhance satiety, especially in cats. Cellulose is an insoluble, nonfermentable fiber with high water binding capacity. As it will not lead to SCFA production, no osmotic pressure is raised, and no water is pulled in the lumen and ends up in the feces. Cellulose is tasteless and odorless, ensuring a very high acceptance by cats. The recommended daily dosage for cats is 0.5 – 1 g/kg BW (evenly distributed over meals, slowly increasing amounts at the beginning). Side effects at higher dosage might be larger feces volume.

In contrast to cellulose, psyllium fiber is soluble and has low fermentability, which is somewhat unique. Husks contain mucilage which - in combination with its high water-binding capacity - results in a gel-forming, inert-like mass when added with fluids. The high water binding capacity is remarkable compared to most other soluble fibers. Psyllium is almost odor- and tasteless. This is generally tolerated if added directly to a pet's food. Possible side effects are chain formation of the feces in the first days, higher fecal volume, and flatulence.

The most common soluble and fermentable fibers are pectin, guar, inulin, oligosaccharides like FOS and MOS. They are more likely to be found in fruit or vegetables than insoluble fiber, primarily found in cereals and legumes. They serve as substrates for the gut microbiota, thus representing "prebiotics". Some feed a broad spectrum of microorganisms in the large intestine, and some are more selective substrates, such as *Bifidobacterium* or *Lactobacillus.*

Conclusion

In addition to a basic feeding history focusing on digestibility issues, fibers are indispensable for every GI patient. They should be considered before antibiotics, at least in mild diseases, but especially in chronic cases. Positive effects can be

observed within as few as 2-3 days of administration. Every GI patient might benefit from smaller amounts of fiber, ideally of a mixture or just psyllium. For patients with (stress-induced) colitis, fiber-responsive diarrhea, or constipation, higher amounts of bulking, water binding fiber is more appropriate. An excellent review on the use of fiber to aid in management of GI disease has recently been published.[7]

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Nutritional Management of Hypercalcemia

Valerie Parker, DVM, DACVIM (SAIM, Nutrition)

Etiologies of hypercalcemia in cats

There are several causes of hypercalcemia in cats. The three most commonly identified causes, in no particular order, include: 1) hypercalcemia of malignancy; 2) kidney disease – either acute or chronic; and 3) idiopathic hypercalcemia (IHC).[1,2] Several hypotheses exist regarding the pathophysiology of IHC, which include a possible increased sensitivity to vitamin D metabolites and their interaction with vitamin D receptors, or increased activity of the nonsaturable pathway for intestinal absorption of calcium. In humans with hypercalciuria and calcium oxalate uroliths, there may be intestinal hyperabsorption of calcium.[3]

Nutritional approach to hypercalcemia

A variety of nutritional approaches to address hypercalcemia have been suggested over the last few decades. Dietary factors that have been purported to exert a beneficial effect in lowering circulating calcium in IHC cats include increased concentration of fiber, sodium, and water and decreased concentration of calcium, vitamin D, and vitamin A. Non-acidifying diets and those with moderate magnesium concentrations could be beneficial, but there is no reported evidence to support this. Determining which, if any, of these factors are most influential is challenging because there likely are complex interactions between each diet and the individual animal.[3]

Dietary calcium

Feeding diets reduced in calcium concentration results in restoration of normocalcemia in some cats with IHC. Based on these observations, feeding diets with calcium content of less than 200 mg/100 kilocalories (kcal) has been recommended. The calcium content in commercially available cat foods varies substantially. In order to compare diet content for calcium (and every other nutrient), it is essential to do so using energy density rather than percentage of dry weight for the diet. The grams per megacalorie is not readily available to practitioners from review of product labels, but this information can be obtained in product manuals and directly from the manufacturer of the specific diet of interest.[3]

Recently it has been reported that some cats with chronic kidney disease (CKD) may develop ionized hypercalcemia when fed phosphate-restricted diets, and that the hypercalcemia may resolve when fed a higher phosphate diet.[4] A striking difference between the diets fed when cats developed hypercalcemia vs. when the hypercalcemia resolved was the dietary calcium-to-phosphorus (Ca:P) ratio. The diet that cats were fed when they developed hypercalcemia provided a Ca:P ratio of 1.9:1, whereas the diet that cats were fed to attenuate their hypercalcemia provided a Ca:P ratio of 1.3:1. As such, a newer approach to manage hypercalcemia in cats combines these 2 nutritional goals, namely feeding a diet with both < 200 mg calcium/100 kcal AND a Ca:P ratio < 1.4:1. Results of a recently presented research report will be presented.[5] It is important to remember that nutrient profiles of specific diets evolve frequently, as often as every 6-12 months.

Fiber

Increased dietary fiber was reported to successfully lower circulating total calcium concentrations in 5 cats with ionized hypercalcemia and calcium oxalate urolithiasis. After diagnosis, 4 of 5 (80%) cats were switched to a veterinary therapeutic diet high in insoluble fiber (Hill's Prescription Diet w/d Feline), and one cat was fed a feline maintenance diet with added psyllium, a soluble fiber supplement. In the cats with reported follow-up, total hypercalcemia resolved but none of the cats had iCa concentration monitored.[6] However, in another study, there was no beneficial effect of feeding a diet high in insoluble fiber to cats with IHC.[7] It is theorized that supplemental fiber may lead to increased binding of intestinal calcium, preventing its absorption, and also decreased intestinal transit time through the small intestine, decreasing calcium absorption. It is common practice for most manufacturers to increase the concentration of calcium in high-fiber diets to offset the potential for decreased absorption, so evaluation of the complete nutrient profiles is warranted before reaching for a high fiber diet for management of hypercalcemia.

Chia seeds

In a case series of 3 cats that were unresponsive to dietary management with a variety of different types of diets (e.g., renal diet, urinary diet, high fiber diet), the addition of 2 grams of chia seeds per day resulted in normalization of ionized hypercalcemia, which persisted for at least 10 weeks.[8] This option can be pursued either before or after other dietary modifications depending on the individual cat's and owner's preferences. Interestingly, the nutrient profile of chia seeds

demonstrates that they are a low calcium, moderate phosphorus (thus low Ca:P ratio), and high fiber ingredient. Thus, this nutrient profile may contribute to the effect on decreasing ionized calcium concentrations.

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Nutritional Idiosyncrasies & the Role in Obesity, Diabetes Mellitus, & Hepatic Lipidosis

Adronie Verbrugghe, DVM, PhD, DECVCN

Cats are obligate carnivores. From a nutritional perspective, this means that in their natural habitat cats consume prey and rely on nutrients in animal tissue. Due to evolutionary pressure, cats have developed several physiological and metabolic adaptations, including peculiarities in carbohydrate, protein and fat metabolism that have led to specific and unique nutritional requirements. From these, speculations have arisen around the development of metabolic diseases such as obesity, diabetes mellitus (DM) and feline hepatic lipidosis (FHL).

Feline specific metabolic features

Carbohydrates

Cats possess a limited capacity for starch digestion by endogenous enzymes. Compared to dogs, cats have low levels of salivary amylase which is responsible for initiation of starch digestion. Intestinal amylase activity is also rather low and mainly of pancreatic origin, despite the low level of amylase in the feline pancreas compared to other animals. Further, cats have low maltase and isomaltase activity, and no lactase or sucrase activity in the pancreatic tissue; however, these enzymes are present, though low compared to other species, in the small intestine mucosa. In addition, the sugar transport systems in the feline intestinal brush border are non-adaptive to varying levels of dietary carbohydrates. Yet, D-glucose transport across the intestinal brush border membrane appears to have a considerably higher capacity in cats than in cattle and rabbits, despite similar amounts of glucose reaching the small intestine when fed a natural diet. This relatively high transport capacity, but also the greater mucosal area per unit serosal area in the cat's small intestine compared to rats and dogs, could at least partially compensate for the relative deficit in absorptive surface, due to the limited length of the small intestine. Early research demonstrated that adult cats efficiently digest all carbohydrates added to a meat-based diet, despite the evolutionary adaptations along the feline gastro-intestinal tract. The total apparent digestibility of starch is reported to be between 40 and 100%, depending on source and treatment which proves that cats can digest and absorb carbohydrates, but proper processing and cooking is necessary as in other mammals. Poorly digestible carbohydrates or an overload of highly digestible carbohydrates may induce considerable digestive adverse effects, such as diarrhea, flatulence, and bloating.

Carbohydrate metabolism is also altered by some major evolutionary adaptations in the enzyme activity of the feline liver. In omnivores, two enzymes, hexokinase and glucokinase are responsible for the phosphorylation of glucose to glucose-6-phosphate. Hexokinase is present in the liver in only small amounts and is active at very low concentrations of glucose, whereas glucokinase has a maximal rate of glucose phosphorylation but operates only when the liver receives a large load of glucose from the portal vein and rapid glycogen synthesis is necessary. Feline liver has minimal to absent glucokinase activity and no glucokinase gene expression. Furthermore, D-glucose transport activities in feline hepatocytes are considerably low and activity of hepatic glycogen synthetase have been reported to be minimal. This does not mean that cats are limited in their ability to metabolize glucose. Cats have adapted to moderate carbohydrate intake as the activities of the rate-limiting enzymes involved in glycolysis and glycogenesis are actually greater than those found in dogs, and cats have abundant hexokinase.

Protein and amino acids

Adult cats require more dietary protein than omnivorous species, due to a higher endogenous glucose demand, higher basal nitrogen requirement, as well as a need for specific essential amino acids. As cats have a relatively large brain, a significant proportion of protein must be diverted into gluconeogenesis to supply the brain. Therefore, the high protein requirement in felines is the result of a high metabolic demand for glucose that must be met by amino acid-based gluconeogenesis. Indeed, higher activities of rate limiting enzymes of gluconeogenesis, *i.e.*, pyruvate carboxylase, fructose-1,6-biphosphatase and glucose-6-phosphatase, were observed in feline livers compared to in canine livers. Furthermore, feeding a low protein diet does not downregulate the hepatic gluconeogenic enzyme activities. Unable to adapt urea cycle enzymes, aminotransferases and gluconeogenic enzymes to reduced protein intake, cats possess limited ability to adjust protein metabolic pathways to conserve nitrogen. This means that this species, similar to other carnivores, derives a part of its energy requirement from the breakdown of body proteins. Additionally, cats have an increased need for sulfur-containing amino acids (methionine, cysteine and taurine), as well as for arginine.

B-vitamins

Cats seemingly require higher amounts of several B-vitamins, such as cobalamin, choline, folate and pyridoxine, compared to other species and are therefore predisposed to depletion during prolonged inappetence, maldigestion and malassimilation.

This consequently affects one-carbon metabolism. These vitamins are involved in regeneration of methionine from homocysteine. Subsequently, methionine is converted to *S*-adenosylmethionine (SAMe), a universal methyl donor necessary for formation of nucleic acids, proteins, lipids and secondary metabolites such as L-carnitine, through methylation.

Fatty acids

Early evidence in cats showed a limited capacity to synthetize arachidonic acid from linoleic acid and probably eicosapentaenoic and docosahexaenoic acid from α-linolenic acid. This limited synthetic capacity was attributed to lack of Δ6 and Δ5 desaturases in the feline liver. Detectible amounts of both Δ6 and Δ5 desaturase products have, however, been discovered in the feline liver; yet the activity does not appear to be adequate for maintaining tissue stores of long-chain poly-unsaturated fatty acids.

Health implications

Obesity

Due to the discrepancy in carbohydrate content between a natural prey and currently available traditional commercial cat foods, excess carbohydrate intake is often considered a primary cause of obesity. It has been postulated that excessive amounts of dietary carbohydrates cause an overproduction of insulin resulting in excess fat deposition. Obesity is caused by an intake of calories greater than the animal's needs, irrespective of whether the calories come from protein, fat or carbohydrates. Carbohydrates consumed in excess of energy needs will indeed be converted for storage. Initially glycogen storage will be filled, but the remaining carbohydrates will be converted to fats and stored in adipose tissue resulting in this hypothesis that excessive amounts of dietary carbohydrates are a primary cause of feline obesity. Yet, obesity will also occur with the overconsumption of protein and, especially, fat. Additionally, it has been shown that cats eating a commercial premium dry cat food are more likely to be overweight. Some authors presumed this was due to the higher carbohydrate content in commercial dry foods compared to canned foods, while others thought that these dry diets contained high amounts of fat, predisposing cats to obesity, by increasing energy intake due to high energy density and improved palatability. Though in fact, further research confirmed increased weight gain and expansion of fat mass when fed a high-fat, low-carbohydrate diet in comparison to a low-fat, high-carbohydrate diet. Since fat contains twice as much energy per gram compared to carbohydrates and protein, replacing dietary fat with carbohydrates reduces the caloric density of foods, which may help in reducing the risk for obesity. Additional epidemiological studies also reported a higher risk for obesity in cats consuming dry foods. However, studies did not assess dietary macronutrient content and food intake, so no conclusions can be drawn regarding dietary carbohydrate or fat content and/or intake of these macronutrients. Carbohydrates do not appear to be the biggest concern in the development of obesity. Overfeeding and thereby consumption of excess calories of any macronutrient is a much more important risk factor for obesity and should be the main focus of obesity prevention.

Diabetes Mellitus

It has also been suggested that dietary carbohydrates could increase the risk for DM in cats. It has been postulated that consumption of excessive amounts of highly refined and easily digestible carbohydrates places a large demand on the pancreatic β-cells for excessive insulin secretion, which may eventually result in exhaustion and loss of insulin-producing β-cell and diabetes mellitus. Still, the feline pancreatic β-cells are much less sensitive to glucose than those of omnivores, and amino acids are proven to be important modulators of pancreatic insulin release. Although experimental diets containing up to 40% of simple sugars (sucrose, glucose, etc.) did induce hyperglycemia and glucosuria, this could not be confirmed when complex carbohydrates (starch) were used at similar levels. Also, dietary carbohydrates have even less of an impact on postprandial glucose and insulin responses in healthy cats than in dogs and humans. In healthy non-obese cats, feeding a low-carbohydrate diet with a carbohydrate level reduced below levels for common commercial cat foods, did not result in a better glucose tolerance and insulin response when compared to a low-protein diet and a low-fat diet. The cat's strict carnivorous nature is the most likely explanation for these findings, as cats appear genetically insulin resistant since they evolved and reproduced well on a low-carbohydrate diet. The ability of insulin to inhibit hepatic glucose production as well as to augment tissue glucose disposal is impaired. Therefore, gluconeogenesis is, more or less, permanently switched on. Two other studies also demonstrated impaired glucose tolerance when cats where fed a low-carbohydrate diet but attributed this to increased fat intake. Since the two test diets in both studies differed only by substituting fat for carbohydrates, confounding effects might have occurred. Furthermore, feeding a high-carbohydrate diet to healthy non-obese cats resulted in an increased glucose-induced insulin secretion during a hyperglycemic glucose clamp test, contradicting the hypothesis that high carbohydrate diets lead to β-cell exhaustion. The same researchers could also not produce evidence in an epidemiological study that the proportion of dry food in the cat's diet is a risk factor for the development of feline DM. Many times, it has been suggested that commercially available dry cat foods contain higher amounts of carbohydrates compared to canned foods, however, this assumption is not always valid. Although the research evidence is limited and not always consistent, it does not appear that dietary carbohydrates are a causative factor in feline DM. Even if carbohydrates would be proven to play a role, obesity due to inactive lifestyle and excessive calorie intake, and advancing age would remain the greatest risk factors for DM.

Feline hepatic lipidosis

Although the precise pathogenesis of FHL remains a mystery, most researchers believe that multiple factors associated with the cat's unique pathways of protein and lipid metabolism are involved. Proposed pathophysiologic mechanisms may include metabolic changes associated with starvation, insulin resistance, obesity, protein and amino acid deficiency, L-carnitine deficiency, reduction of antioxidant availability, B-vitamin deficiency, and essential fatty acid deficiency. Overall, the disease is characterized by an accumulation of lipids in the liver, due to an imbalance between peripheral fat stores mobilized to the liver, *de novo* synthesis of fatty acids, hepatic use of fatty acids for energy and redistribution of hepatic TAG, leading to a fatty liver and an impairment of liver function.

During starvation the high rate of protein catabolism becomes a disadvantage and puts cats at risk for protein malnutrition and essential amino acid deficiency. A lack of apolipoprotein B100 may occur with protein malnutrition and was proposed as a reason for the diminished ability of the liver to secrete very low-density lipoproteins (VLDL), leading to lipid accumulation in the liver. This hypothesis is contradicted by reports of hypertriglyceridemia and increased hepatic VLDL secretion. However, this increase may not be sufficient to prevent lipid overload of hepatocytes. Hastened use coupled with an inability for conservation also necessitates a higher dietary intake of essential sulfur amino acids, methionine cysteine and taurine. Decreased plasma methionine concentrations were reported in feline hepatic lipidosis. Methionine is a precursor of S-adenosyl methionine (SAMe), a key methyl donor for phosphatidylcholine synthesis, which is required for the export of VLDL from the liver. However, hypertriglyceridemia and increased serum VLDL concentrations were observed in cats with feline hepatic lipidosis, making this hypothesis unlikely. SAMe is also an essential precursor for L-carnitine, which is required for transport of long-chain fatty acids into hepatic mitochondria where they undergo β-oxidation. Although high circulating, hepatic and skeletal muscle carnitine concentrations and increased urinary elimination of acyl-carnitine occur in cats with feline hepatic lipidosis, it remains unclear whether shifts in dispersal, synthesis and availability are appropriate in magnitude for the metabolic circumstances. If the demand for carnitine exceeds its synthesis, a relative deficiency of carnitine would exist, despite increased concentrations. In cats fed 25% of their energy requirement, hepatic lipid accumulation was minimal when given supplemental carnitine, which implements a much higher carnitine requirement for cats with increased mobilization of fat to the liver and, thus, supports the theory of relative carnitine deficiency in cats with FHL. A protective effect of L-carnitine against fasting was demonstrated as plasma fatty acid concentration rose in fasting cats and during FHL in both control and L-carnitine-supplemented cats, but always to a lesser extent when L-carnitine was administered. Moreover, methionine and cysteine are necessary for hepatocellular GSH production, which is important for hepatocellular protection from oxidant injury. Low hepatic GSH concentrations in the liver of cats with feline hepatic lipidosis compared to healthy control cats are consistent with reduction of tissue antioxidant availability. Taurine-deficiency has been shown to increase total liver lipid content and especially the amount of free fatty acids in the liver in cats, most likely caused by the increased lipolysis in peripheral tissue. Yet, liver lipid accumulation was not affected by taurine supplementation in cats undergoing weight gain and subsequent weight loss. Cats are also predisposed to depletion of B-vitamins during starvation. Because of their role as a methyl donor in one-carbon metabolism, cobalamin, choline and folate insufficiency may evoke metabolic changes that could play an important role in the pathophysiology of FHL. Lastly, development of hepatic steatosis is a well-established manifestation of essential fatty acids deficiency in animal models, including the cat. The essential fatty acid status of the feline may be compromised during food deprivation or rapid weight loss. Since the majority of lipids stored in adipose tissue of healthy felines are saturated and monounsaturated fatty acids and the predominant polyunsaturated fatty acid (PUFA) is linoleic acid, it may be that during food deprivation, the longer chain PUFA (arachidonic and docosahexaenoic acid) are not adequately synthesized, contributing to the pathogenesis of FHL. Not only inadequate desaturation, but also derangement of the *n*-6/*n*-3 PUFA ratio could play a role in regulating both fat accumulation and its elimination by the liver.

Conclusion

This review demonstrates the importance of understanding the peculiarities of feline metabolism to fully understand the impact of diet on the development of feline obesity, DM and FHL. Understanding the underlying pathophysiology is necessary to develop and implement new strategies to prevent and treat these metabolic diseases.

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Do Nutrients & Ingredients Matter for Weight Loss? How to Select a Diet

Adronie Verbrugghe, DVM, PhD, DECVCN

Obesity, the most common nutritional disorder in cats, has become a health and welfare priority, affecting up to 63% of domestic cats. Obesity is characterized as excess adipose tissue accumulation which can result in negative health consequences for the animal. Weight loss is recommended to treat or prevent adverse health consequences and improve quality and quantity of life. The weight management guidelines of the American Animal Hospital Association describe following steps to formulate an individualized weight loss plan: 1) determine ideal body weight, 2) calorie restriction, 3) food selection, 4) treat allowance, 5) feeding management and activity and 6) scheduled follow-up. During this session we will specifically focus on how to navigate food selection through assessment of key nutrients.

Diet selection

Diet selection starts with a thorough nutritional assessment. A first step is a screening evaluation, performed to determine if any nutritional risk factors are present. All cats with a body condition score (BCS) larger than 5/9, will require an extended nutritional assessment to gather further information on the circle of nutrition: the patient, the patient's diet, and the feeding management and environment. Once a detailed diet history, and other data such as body weight trends, appetite and caloric intake has been collected, the veterinary team can develop an individualized weight loss plan. During this process veterinary teams should not forget to inform themselves about client goals, to allow better tailoring of the weight loss plan to align with client preferences. When developing a weight loss plan, it is useful to have access to product guides that provide detailed nutritional information for veterinary therapeutic diets. Wellness diets may also be helpful; for these diets, nutritional information can be obtained from the manufacturers. Diets within the same nutritional management category are variable in nutritional profile, as well as energy density. Select the food which key nutrient content is most similar to the patient's needs. When no commercial diet fits the patient's needs and client's preferences, a homemade diet can be formulated for weight loss with the assistance of a veterinary nutritionist. They can create a truly customized, nutritionally balanced recipe, with additional follow up and support to allow for patient acceptance as well as client adherence and compliance.

Diets formulated for weight loss

Energy restriction is recommended for weight loss however it is important to not restrict essential nutrients, including essential amino acids, essential fatty acids, vitamins and minerals. Assessment of amino acid and vitamin intake in obese cats undergoing a weight loss plan revealed that arginine, choline, crude protein, phenylalanine plus tyrosine and threonine are most at risk. The risk was also larger with over-the-counter diets compared to veterinary therapeutic weight loss diets. Although deficiency of all these nutrients can lead to adverse health effect. Choline draws the attention as this vitamin like nutrient has important bodily functions related to lipid metabolism and deficiency can lead to fat accumulation in the liver. Obese cats already have an increased risk of hepatic lipidosis. The concern is that in obese cats energy restriction may induce fatty acid mobilization, but if choline is not present in enough quantity, there could be impaired transport of fat out of the liver as well as reduced fatty acid oxidation in the liver, leading to an accumulation of fat and subsequent hepatic lipidosis.

Veterinary therapeutic weight loss diets are recommended for patients undergoing significant calorie restriction for weight loss at resting energy requirement (RER) x 0.8 and a weight loss rate of 1-2% of initial body weight per week. These diets are fortified in essential nutrients to avoid potential nutrient deficiencies associated with calorie restriction. Other veterinary therapeutic and wellness diets, when formulated for adult maintenance, can be fed for RER x 1 without further restriction and used for a slower, more modest weight loss plan.

Macronutrients

Energy density and fat

A key feature of veterinary therapeutic diets and over-the-counter weight management diets is a decreased energy density. Regulatory definitions for the terms "light", "lean", "reduced calorie" and "reduced fat" have been implemented by the Association of American Feed Control Officials. However, pet food marketed as restricted in calories can vary widely in energy density including the proportion of nutrients contributing to calories, fiber, and digestibility. Reduced energy density is achieved by reducing fat and simultaneously increasing the fiber content of the food. Fat contains twice as much energy per gram compared to carbohydrates and protein, replacing dietary fat with carbohydrates reduces the caloric density of foods. Other than the effect on energy density, there is no known specific benefit of fat reduction in cats.

Carbohydrates

The carbohydrate group is very diverse including following categories: simple sugars, oligosaccharides, and polysaccharides. Monosaccharides (glucose, fructose, and galactose) are absorbable carbohydrates that do not require enzymatic digestion and can be absorbed directly. Disaccharides (lactose, sucrose, maltose, and trehalose) are readily digested by intestinal enzymes in most mammals, although cats have limited enzyme capacity. Oligosaccharides are resistant to enzymatic digestion and fermented by microbial enzymes in the large intestine. Polysaccharides or complex carbohydrates can be further defined based on the digestibility and the nature of the glycosidic bonds between the sugar units. Starches and glycogen are complex carbohydrates that are enzymatically digested in the mammalian small intestine. Dietary fiber (cellulose, hemicelluloses, pectin, gums, mucilage, lignin) is not digestible in the small intestine. Most dietary fibers are fermentable in the large intestine, although because of the limited length of the feline colon, certain fibers, like cellulose, are not extensively fermented.

Dietary fiber helps produce weight loss by diluting calories, increasing satiety, and limiting food consumption as a result of more bulk being present in the gastro-intestinal tract. Soluble fiber slows gastric emptying and while both soluble and insoluble fiber slow intestinal transit, insoluble fiber produces the greater effect. In cats, conflicting results have been found. One study concluded that compared to dogs, gastric filling appears to limit food intake more effectively in cats. Energy intake was decreased when cats are fed diets supplemented with cellulose, while dry matter intake was maintained. When a challenge meal with a palatable, energy-dense diet was offered after the high fiber diet, dogs doubled their energy intake, while energy intake was only slightly higher in cats, and they did so only after a period during which energy requirements were not met. Another study investigating both cellulose and sugarcane fiber noted that the food intake pattern of cats was not changed, but fiber supplemented cats exhibited greater consumption of a highly palatable challenge meal. Fiber also interferes with the availability of calories by hindering the digestion and absorption of fat, protein, and digestible carbohydrates. Moreover, consumption of different sugars and complex carbohydrate sources alters postprandial glucose levels and insulin secretion. Low glycemic response foods are recommended for weight loss particularly in cats with diminished glucose tolerance. Mono- and disaccharides should be avoided. As for starch sources, rice exhibited the highest postprandial insulin response and higher glucose levels early in the postprandial period, while barley, corn and sorghum seemed better carbohydrate sources for cats with impaired glucose control. In more recent research, cassava was also suggested for improving blood glucose control in cats.

Rather than increasing the dietary fiber level, some veterinary therapeutic weight loss diets for cats, utilize low carbohydrate content. Low carbohydrate diets aim to put the body into a glycogenolytic state in which glycogen stores are depleted and the body moves toward lipolysis and β-oxidation as an alternative energy source. Increased acetyl-CoA production results in increased hepatic ketone body (acetone, acetoacetic acid, β-hydroxybutyric acid) production, providing an alternative energy source for most tissues and reserving glucose for glucose-dependent tissues such as brain and erythrocytes. The shift away from glucose results in decreased fasting and postprandial glucose and circulating insulin. These types of diets may have a metabolic advantage particularly in cats with obesity and insulin resistance that may result in diabetes mellitus, although weight loss regardless of diet selection is most important in controlling or achieving remission of diabetes mellitus in the cat.

Protein and amino acids

Moderate to high protein diets have been shown to spare lean mass with calorie restriction during weight loss in cats. High protein diets may promote weight loss by increasing energy expenditure as well as through a higher thermic effect of feeding, overall aiding in the maintenance of muscle mass during weight loss. Protein can also promote a satiety effect. Not only the amount of protein is important, so is the protein quality and provision of adequate amounts of each essential amino acid.

Moisture

High-moisture diets for cats may increase satiety and help promote weight loss. Energy intake and body weight were significantly decreased in cats consuming a canned diet compared to the same diet with a lower moisture content through freeze-drying, suggesting that higher moisture foods may be of benefit versus dry foods during weight loss in cats. Higher dietary water intake by adding water to dry food or feeding canned food has also been suggested to increase voluntary physical activity, which might increase energy expenditure and potentially aid in weight loss.

In cats, successful weight loss can be achieved by both high fiber and low carbohydrate diets, although there are limited studies comparing these two dietary approaches. Body condition and energy intake, not nutrient composition, influenced body weight during weight loss in one study. Another study evaluating owner-perceived satiety in cats undergoing weight loss was unable to find a difference between high fiber and low carbohydrate diets. If the cat and/or client prefers dry food, the author typically recommends a diet that is high in fiber and low in fat and therefore has a low energy density. Low carbohydrate diets tend to have higher fat levels, therefore have a higher calorie density, which results in a small food volume, which might be less appealing for the cat and the owner. This is less concerning for low carbohydrate wet foods as the moisture content will dilute the energy density and together with the high protein level promote satiation.

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Feeding Comorbidities: Obese Cats with Other Diseases

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Obesity, the most common nutritional disorder in cats, has become a health and welfare priority, affecting up to 63% of domestic cats. Obesity is characterized as excess adipose tissue accumulation which can result in negative health consequences for the animal. For cats, these consequences can include, but are not limited to, insulin resistance, diabetes mellitus, urinary disorders, osteoarthritis, and skin conditions. Weight loss is recommended to treat or prevent adverse health consequences and improve quality and quantity of life. Obesity treatment and management is a process that can include energy restriction, veterinary therapeutic weight loss diets, feeding management, and physical activity. Weight loss is slow and often unsuccessful especially when complicated by concurrent diseases, including obesity-related health consequences, but also other diseases that might develop as cats get older.

Nutritional Assessment

For each and every patient that presents to a veterinary hospital, nutrition should be considered as the fifth vital assessment. The first step of the nutritional assessment is a screening evaluation, performed to determine if any nutritional risk factors are present. All cats with medical conditions, including those with a body condition score (BCS) larger than 5/9, will require an extended nutritional assessment to gather further information on the circle of nutrition: the patient, the patient's diet, and the feeding management and environment. Once a detailed diet history, and other data such as body weight trends, appetite and caloric intake has been collected, the veterinary team can develop an individualized nutrition support plan. During this process veterinary teams should not forget to inform themselves about client goals, to allow better tailoring of the nutrition support plan to align with client preferences.

Prioritization

When dealing with obese cats with complex comorbidities, having a good understanding of the patient's status and the severity and impact of the comorbidities is imperative. This will help to prioritize nutritional strategies. Some concurrent diseases are less or not responsive to specific dietary changes, allowing for straightforward prioritization. Other comorbidities, such as pancreatitis, diabetes mellitus, chronic kidney disease, allergies, urolithiasis, to name a few, can be positively impacted by dietary modifications. When considering two or more nutritionally responsive diseases, it is recommended to make a list of the targeted key nutritional factors, including energy, macro- and micronutrients, diet type as well as feeding management, and look for overlap and conflict between the concurrent diseases. An example of an overlapping nutrient of concern is that a weight loss plan requires a high crude fiber diet to reduce energy density and enhance satiation, while fiber also helps with glucose control in cats with diabetes mellitus. In contrast fiber levels are conflicting for weight loss and pancreatitis, i.e., a low crude fiber level is warranted to ensure high digestibility and high energy density especially for the acute pancreatitis patient. Many of the targeted key nutritional factors may overlap or be neutral. An easy and straightforward combination is weight loss and nutritional treatment or prevention of urolithiasis, as many veterinary therapeutic weight loss diets have a urinary health claim. In other cases, compromise may be needed, which could include less aggressive modifications, such as less severe restriction of phosphorus for kidney disease or sodium for cardiac disease. A key nutritional factor may need to be prioritized lower or abandoned all together.

When prioritizing nutritional management, consider longevity and quality of life, recurrence risk, and expected timeline to see benefits. Aside from key nutritional factors for weight loss and to manage co-morbidities, patient's acceptance and tolerance of specific dietary components, texture and meal volume, owner preferences and needs as well as the route of feeding will also limit available commercial diet options.

Instituting a strict and aggressive weight loss plan may not be feasible in an obese cat with major comorbidities that require dietary modifications. For example, weight loss in an obese cat diagnosed with chronic kidney disease will present challenges and will depend on the current degree and impact of obesity. Cats that have a BCS 6/9 only need to lose a little bit of weight, while a weight loss plan for a 9/9 BCS cat will be a much longer challenge. Keep in mind that veterinary therapeutic weight loss diets should be used when targeting energy restriction at resting energy requirement (RER) x 0.8 and a weight loss rate of 1-2% of initial body weight per week. This is needed to prevent deficiencies of essential nutrients, while targeting energy restriction. Other veterinary therapeutic and wellness diets, when formulated for adult maintenance, can be fed for RER x 1 without further restriction and used for a slower, more modest weight loss plan.

It might also not be possible to strictly feed one very specific veterinary therapeutic diet to a picky cat with a highly selective appetite. Weight loss plans should only be considered when the patient is stable and has a good appetite. In this case the nutrition support plan can consist of multiple phases. For example, a highly digestible diet to ensure the pancreatitis patient starts to eat in hospital, potentially using a feeding tube, and for recovery at home. A strict weight loss plan using a high fiber diet can only be instituted once the cat has recovered from pancreatitis.

Nutrition Support Plan

When developing a nutrition support plan for any complex patient, it is useful to have access to product guides that provide detailed nutritional information for veterinary therapeutic diets. Wellness diets may also be helpful; for these diets, nutritional information can be obtained from the manufacturers. Diets within the same nutritional management category are variable in nutritional profile, as well as energy density and palatability, and selection of options within specific therapeutic categories is appropriate to address specific individual cases. For some cases, there will not be a suitable and appropriate veterinary therapeutic diet or wellness diet, or the patient may not accept or tolerate the few commercial options that are available. In this case a customized balanced homemade diet may be an excellent option for including all key nutritional factors. However, the downside may be cost, time and effort to prepare and cook these diets, and the cat may not accept this type of diet due to the novel taste and texture. If a homemade diet is pursued, consultation with a veterinary nutritionist is highly recommended. They can create a truly customized, nutritionally balanced and palatable recipe, with additional follow up and support to allow for patient acceptance as well as client adherence and compliance.

When making nutritional recommendations, feeding plans should be specific, including feeding amount in grams, feeding management strategies, as well as allowance for treats, snacks, and supplements.

Goals and Monitoring

Clients should understand the goals of the plan in addition to which parameters will be monitored over time. For any patient and any diet type, it is important to stress that the nutritional assessment process is an iterative process that is not finished once the nutrition support plan has been developed. The key to a successful nutritional support plan is monitoring, which involves reassessing the circle of nutrition routinely. Especially, when the goal is weight loss, close monitoring is important to ensure that weight loss is intentional and at an appropriate rate. Although it is ideal, reaching ideal body weight may not be possible for every patient. Expectations and targets should be tailored individually for each patient and client. Yes, there could be a body weight target, but it can also be an action, like being able to jump on the bed, walk the stairs etc. Set up a follow up plan with the client to answer additional questions, troubleshoot obstacles, or revisit the recommendation and expectations. Ensuring that the nutrition support plan is working well for both the patient and the client will help promote better outcomes.

While nutritional management of feline patients with complex comorbidities can be challenging, the successful outcomes can be very rewarding for both the veterinary team, the client, and of course, the patient.

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Navigating Alternative Cat Foods: Intersection Between Cat Needs & Client Preferences

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Pet food selection and feeding practices are more complex than nutritional science and are influenced by the same social and cultural factors that direct the pet owner's personal eating behaviors. Many reasons exist why people seek alternatives to "conventional", commercial heat processed, pet foods. Moreover, it is a daunting task for any veterinary team member to keep up to date with all of the commercial dry and wet options available to pet owners, let alone keeping up with all of the alternative dietary options as well. Once a small niche, products such as fresh, refrigerated, frozen, and dehydrated pet food products are gaining popularity. Also, more pet owners wish to cook for their pet at home or choose to feed plant-based food. These alternative diets may or may not be adequate as the sole source of nutrition.

Prevalence

In the past, conventional, commercial heat-processed, products were the predominant method of feeding. In 2008, 99% cats were reported to be fed conventional pet food, with 85% receiving only conventional food. Homemade food was fed to 13% of cats and raw food to 9.5% of cats, yet exclusive feeding of these diets was not reported. Since then, feeding alternative (raw, homemade, plant-based) diets has risen in popularity. According to a 2018 survey, 90% of cats were fed a diet that comprised at least partially conventional pet foods, but only 32% of cats were fed these diets exclusively. Many cats were offered homemade (46%) and/or raw (53%) foods, but only few cats were fed these diets exclusively; 4% and 6%, respectively. Of the cats receiving raw meat-based diets, more were fed a homemade than a commercial food. Also plant-based diets are becoming more prevalent. The same survey reported that approximately half of cats received plant-based foods as part of their diet, with a small number (15%) fed plant-based exclusively.

Owner motivations

The choice to feed a cat an alternative diet may be symbolic of inclusion of the cat in the owner's family and culture, a desire to pamper the cat similar to a child and may relate to the human-animal bond. Pet owner's motivations may also reflect of the owner's religious beliefs, ethical concerns, ideology and personal identity; for example, pet owner's feeding their cats a plant-based diet are most often vegan themselves. This food choice could also relate to mistrust of conventional pet food manufacturing and negative attitudes toward conventional food processing and products. A major concern among pet owners seeking alternative diet options are the types and sources of ingredients used in conventional pet food manufacturing. Well known examples are meat by-products and grain. When choosing a commercial pet food, owners focus on the ingredient list. Still, the ingredient list is a major marketing tool and can be manipulated in many ways. The quality of the ingredients is also not stated on the ingredient list. Nonetheless, owners want control over the ingredients present in their cat's diet. Another example is concern about the use of artificial preservatives. Preservatives, colorants, and flavors elicit fear about adverse health effects. There have been well-published cases of additives that have been harmful and withdrawn for use. In many instances however, this concern is undeserved. Additives have many positive aspects including organoleptic, technologic, and nutritional benefits. Still, the demand for pet foods free of artificial additives or those prepared with ingredients that are perceived by pet owners to be more wholesome and safer has increased. Misinformation on the internet often also exacerbates these concerns. Lastly, alternative diets may be pursued as the cat owner becomes invested in the cat's health and wellbeing.

Homemade diets

Many reasons for seeking alternative diets apply to owners who desire to prepare food for their pet. Concerns about the wholesomeness and nutritional value of the ingredients in commercial foods are major motivations. Food preparation reinforces the bond they share with their pet and may provide comfort and a sense of purpose when caring for sick or terminal pets. A sick cat may find commercial foods unpalatable and refuse to eat them or a homemade diet could be pursued for therapeutic reasons because a veterinary therapeutic diet is unavailable or unacceptable, or for diagnostic reasons such as food elimination trials. Downsides are that homemade diets are time consuming and expensive to prepare.

When properly formulated and prepared, these diets can provide complete and balanced nutrition. Yet, major concerns with homemade diets that often lead to malnutrition in pets are the use of recipes not or not appropriately designed for pets, failure to follow the recipe, and deviation from the recipe over time. Each of these can lead to many nutritional imbalances and related health problems which have been discussed in many case reports. Less than a third of the owners that feed their pet a homemade diet actually use a recipe designed for pets, putting our pets at an enormous risk for nutritional imbalances.

Formulating a complete and balanced homemade diet requires specialized knowledge and owners should be advised not to try this on their own, but to seek help from a veterinary nutritionist. Many platforms and clinical nutrition service are available online but make sure that recipes are formulate by someone with appropriate credentials. Veterinary nutritionists can create a truly customized, nutritionally balanced and palatable recipe, with additional follow up and support to allow for patient acceptance as well as owner adherence and compliance. Even if the owners use a well-formulated recipe, the overall nutritional adequacy depends on the selected ingredients and how closely the person preparing the food adheres to the recipe. Owners may decide to leaf ingredients out of the recipe or to substitute one item by another or even add new ingredients. It is therefore important to advise owners to follow a properly formulated recipe exactly, and not deviate from the recipe, as any alteration in amount or substitution of ingredients may unbalance the diet and may be detrimental for the pet's health, unless the change is permitted. Also owners should be advised to avoid toxic food items such as onions, garlic, grapes, raisins, chocolate etc. When the owner is provided with a complete and balance recipe and with clear instructions on food preparation, it remains important to follow up with the owner to monitor owner compliance and to examine the patient for signs of nutrient deficiency or excess.

Raw meat-based diets

Raw food can be fed as homemade food, but also commercial raw products are available, ranging from complete frozen foods to grain and supplement mixes which are combined with raw food. Cat owners are attracted to these diets as raw meat-based diets resemble a more natural diet (i.e., minimal processing and less grain content) and typically contain a lower amount of carbohydrates compared to traditional commercial diets. Advocates believe these alternative diets have several health benefits, while those opposed focus on the risks and potential complications. There is a lack of large cohort studies evaluating these purported benefits and risks.

Advocates of raw food also emphasize the importance of ingredients with less emphasis on nutrient balance and claim that nutrients from commercial dry and canned food are less or not available or even absent when compared to feeding raw ingredients. One study showed a better apparent digestibility of dry matter, organic matter, crude protein, and gross energy in kittens fed a raw diet compared to heat-processed diets. However, reservations have also been expressed regarding nutritional adequacy. Many homemade raw foods as well as commercial raw food diets are not complete and balanced and therefore inappropriate for long-term feeding. To date, no scientific evidence exists that demonstrates raw food diets provide additional or exceptionally unique nutrients that cannot be obtained from cooked food.

Evidence also exists that raw meat-based diets can be contaminated with pathogens such as Salmonella, Campylobacter, Listeria, shiga toxigenic Escherichia coli, parasites such as Toxoplasma gondii and exotic agents such as the zoonotic livestock pathogen Brucella suis. Pets exposed to these pathogens can exhibit clinical signs or can be clinically normal and shed the bacteria in feces. Advocates of feeding raw meat, bones and eggs claim that pathogenic organisms in raw meat do not affect cats due to the lower stomach pH and shorter gastro-intestinal transit time. In fact, these are very similar among humans and cats and do not lower the risk to pets. These pathogens not only bear a risk for the pet but also for humans sharing the same environment. It is important to point out that meat and eggs supplied for human consumption are contaminated with microorganisms and feeding raw meat increases the exposure of owners and pets to foodborne bacterial diseases. Another emerging issue concerns the risk of introducing antimicrobial-resistant bacteria. Raw pet food commonly exceeds hygiene thresholds for counts of Enterobacteriaceae. These bacteria often encode resistance to critically important antibiotics such as extended-spectrum cephalosporins, and raw-fed pets create an elevated risk of shedding such resistant bacteria. These types of diets also pose other health risks like increased risk for gastrointestinal obstruction/penetration by bone fragments; and possible exogenous thyrotoxicosis due to contamination with raw thyroid tissue. However, these concerns are often based on isolated case reports.

It is also noteworthy that the pet food industry keeps evolving, with raw pet food manufacturers investing in product formulation, ingredient sourcing, research, pet food safety and technologies to reduce bacterial contamination such as high-pressure pasteurization, organic acidulants, essential oils, and bacteriophages. Nonetheless, safe handling of food, work surfaces and feeding containers is of extreme importance. Extra caution should be emphasized when elderly persons or young children are living in the household or when individuals in the household have immunosuppressive infections, are undergoing chemotherapy or are being treated with anti-inflammatory medications. When cat owners choose to feed commercial or homemade foods containing raw meat or eggs, veterinarians should fully inform pet owners of this increased potential risk for foodborne pathogens, not only to the pet, but to the entire household and provide guidance to minimize the risks. This could mean recommending a heat processed food, either commercial or homemade, or could mean assistance with selection or formulation of a balanced raw meat-based diet and providing tips on how to make a raw meat-based diet as safe as possible for the cat and their family.

Plant-based diets

Pet owners may choose to feed a plant-based diet to their cat because of several reasons; religious beliefs, ethical concerns, health considerations and because conventional commercial diets are perceived as unwholesome. A pet owner survey noted that amongst all pet owners, the concern most reported regarding meat-based pet foods was for the welfare of farm animals. Omnivores pet owners reported fewer concerns with meat-based diets, and vegans had more concerns. Even more so, only vegan respondents reported feeding an entirely plant-based diet to their cat. Many meat-avoiding pet owners have a moral dilemma as they live with animals that rely on animal products for their nutritional sustenance. This conflict can result in feelings of guilt and internal conflict. For some, this may stress the human-animal bond to the point where they do not feel comfortable sharing their home with a carnivorous pet, and abstain from this, despite their desire to do so; others elect to feed a plant-based diet. With regards to health considerations, a recent survey investigating owner-reported health noted that more owners of cats fed plant-based diets reported their cat to be in very good health, with fewer gastro-intestinal and hepatic disorders and more ideal body condition compared to owners of cats fed meat-based diets. Although this was not confirmed by veterinary exams or investigation of medical records.

The most common concern regarding strictly plant-based pet foods is regarding the nutritional completeness of the diet. The domestic cat, is a small mammal of the order Carnivora considered to be an obligate carnivore, based on their evolutionary anatomical, physiological, and metabolic adaptations to a diet exclusively comprised of prey. Consequently, cats have unique nutritional adaptations resulting in specific dietary requirements. Therefore, it is often thought that cats can only consume a meat-based diet, however, all mammals have requirements for nutrients, not ingredients and formulation of a plant-based cat food is not impossible. Few commercial plant-based diets exist in North America, there is poor labeling compliance and concerns have been expressed regarding the nutritional content. For example, none of the vegan diets labeled for feline maintenance and/or growth available on the Canadian market in 2018 met AAFCO recommendations. Nutrients most found insufficient were methionine + cystine, taurine, arachidonic acid, EPA and DHA, calcium, phosphorus, and vitamins A, B12 and D. Though even if diets are formulated to meet industry recommendations, manufactures rarely perform nutritional analyses and feeding trials. Formulating vegetarian and vegan pet food is extremely challenging. Digestibility studies, AAFCO feeding trials and a high level of quality assurance are needed to ensure confidence in the finished product. As very few commercial nutritionally balanced plant-based diets exist, some owners may choose to feed a homemade plant-based diet instead, with increased risk of nutritional imbalances and potential predisposition for diet-associated diseases. Homemade vegetarian diets can be complete if these include eggs and milk products. Vegan diets are a much bigger challenge and should be carefully checked because plant-based diets may be deficient in several essential nutrients unless synthetic additives are added. At home preparation of vegetarian or vegan foods for cats should be discouraged, as without adequate synthetic supplementation, cats are at high risk for many deficiencies. Because selecting this type of feeding is a conscious choice for the pet owner, it should be relatively easy to enter a dialog about the appropriateness and nutritional adequacy of this kind of diet. As with any homemade diet, if a plant-based diet is pursued specialized knowledge is required and owners should be advised not to try this on their own, but to seek help from a veterinary nutritionist.

Diet recommendation and communication

For every patient that presents for a veterinary consult, nutrition should be considered as the fifth vital assessment. The first step of the nutritional assessment is a screening evaluation, performed to determine if any nutritional risk factors are present. All cats that are being fed an alternative diet will require an extended nutritional assessment to gather further information on the circle of nutrition: the patient, the patient's diet, and the feeding management and environment. This all starts with a comprehensive diet history which is the foundation for the diet recommendation. Whether using a diet history form or during an in-person interaction, open-ended questions will allow owners to share information unhindered. Veterinary team members should also recognize and manage their own biases and perceptions associated with pet nutrition in order to enter the conversation with an open mind. When touching on sensitive nutrition topics like feeding alternative diets, focus on discussing nutrition in an open, honest, non-judgmental and approachable manner in which the owner feels comfortable and respected. Validating owner concern is not the same as agreeing with the owner. However, an understanding of the owner's dietary viewpoints will help avoid misunderstandings about the recommendations that you make. When the owner's beliefs, goals, ideas or perceptions are not aligned with our viewpoint, the owner is likely to reject our viewpoint in favor of their own, regardless of the content we communicate.

When communicating nutrition recommendations to owners, use a 2-step approach to teases apart the question of motivation. The first recommendation is a nutrition-related healthcare decision; *a nutrition change is needed to prevent or treat disease*. The second recommendation is a specific diet plan to support the nutrition-related healthcare decision. Before developing a specific diet plan, it is important to first provide the owner with all the options, to involve the owner actively in the decision-making process as well as to educate owners about the benefits or lack of benefits for each option to the health and wellbeing of the pet. Feeding plans should be specific. The selected commercial diet should have an AAFCO nutritional adequacy

statement, indicating that the diet provides all nutrients in appropriate ratios for long-term feeding to the specified life stage. Also homemade diets should provide complete and balanced nutrition. If the patient has specific disorders, consider all nutrients of concern before selecting a target nutrient profile, which could be delivered through a variety of diet types. Overall, when formulating a plan for dietary modification, veterinarians should take into account the pet owner's beliefs, cultural background, lifestyle, and abilities. Once the recommendation is made, we check in with the owner to see how the information was received, this allows further tailoring the recommendation to better align with the owner's goals. Finally, we set up a follow up plan with the owner to answer additional questions, troubleshoot obstacles, or revisit the recommendation. Note that with any diet type, because nutritional adequacy can be questioned, it is advised to follow-up with the cat's owner on a regular basis, i.e. at least two times per year for healthy cats and three times per year for cats with medical conditions.

All in all, when navigating alternative diet conversations, keep in mind both the cat and the owner. If we want to develop diet recommendations that work for the patient and at the same time be successful with owner compliance and adherence, we need to adjust the traditional mindset of "find the problem and fix it" to one that is more client-centered and collaborative.

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Feeding the Allergic Cat

Sara Ramos, DVM, ACVD

Introduction

Pruritus is a symptom of many dermatologic conditions in feline patients. Within feline dermatology there are multiple categories of differentials that can be considered for each patient, however, allergic disease is frequently an underlying cause. Before we can discuss feeding the allergic feline patient, we must first discuss how to properly diagnose the allergic patient. Following a systematic approach can greatly facilitate this work-up and allow the clinician to obtain a diagnosis as quickly as possible. Once a primary disease is identified, appropriate and effective treatment can be prescribed to increase patient comfort and client satisfaction.

Diagnostic Approach

At initial presentation, a thorough medical history is essential. A complete history can help point the clinician towards or away from a certain diagnosis. Following an excellent history, the clinician should then perform both a physical and dermatologic examination. The dermatologic and physical examination will highlight the best areas to take diagnostic samples and allow the clinician to evaluate for the presence of any other systemic disease. A minimum database of cytology, skin scraping, wood's lamp examination and flea comb is going to be recommended for any feline patient presenting for pruritus. Based on your examination and clinical suspicions, a fecal examination and ear cytology may also be considered part of the minimum database.

Differentials and Diagnostics

Pruritus in the feline patient will typically fall in three broad categories: infestation, infectious and allergy. A single condition within a category can be implicated or a patient can have conditions in overlapping categories. There are always exceptions to these categories such as endocrine disease or immune-mediated conditions that can also be primary causes, but these conditions are less common.

Infestation

Depending on the parasite involved and the host's reaction, the reaction from the patient can be mild or severe. Parasites can be classified according to which portion of the skin they affect, such as superficial versus deep dwelling parasites (Miller, Griffin, & Campbell, 2013). Examples of common superficial or surface dwelling parasites include *Demodex gatoi, Notoedres*, *Otodectes* and *Cheyletiella*. An example of a deep dwelling mite is *Demodex cati* (Miller et al., 2013). There are many other categories of parasites that can cause dermatologic disease such as helminthic parasites, and other arthropod parasites, however these are beyond the scope of this lecture. Obtaining a minimum database at the initial visit will help the clinician evaluate for this category of disease.

Infectious

Many primary dermatologic conditions can present with a secondary bacterial or yeast infection. The most common agents associated with these secondary infections include *Staphylococcus* and *Malassezia* species *(Miller et al., 2013)*. Presence of these organisms in high volumes on the skin surface can produce an inflammatory response subsequently releasing inflammatory and pruritogenic mediators (Pucheu-Haston, 2021). If bacterial or yeast overgrowth is present, based on surface cytology results, treating these infectious agents can significantly improve pruritus. It is important for clinicians to remember that these are typically secondary infectious agents, so a primary etiology, such as allergy, may still need investigation depending on the case.

Dermatophytosis is classically a superficial fungal infection that can affect many species. There are more than 30 different species of dermatophytes, however, infection in companion animals is typically due to *Microsporum canis, Microsorum gypseum* and *Trichophyton mentagrophytes* (Moriello, Coyner, Paterson, & Mignon, 2017). Clinical signs of dermatophytosis can vary but can include any of the following: alopecia, scaling, crusting, erythema, and alterations in nail growth/shape/appearance. Less commonly dermtophytes can progress to a deeper dermal or subcutaneous level in some cases producing nodular lesions that can drain and fistulate (Moriello et al., 2017). Various testing options for dermatophytosis exist with no one gold standard test (Moriello et al., 2017). Diagnosis of dermatophytosis is made based on clinical suspicion plus interpretation of complementary diagnostics. Diagnostic testing options include Wood's lamp, direct microscopic examination, dermoscopy, dermatophyte culture and polymerase chain reaction testing (Moriello et al., 2017). Each of these

diagnostic tests has advantages and limitations. Moriello et al. published an open access clinical consensus guideline on the diagnosis and treatment of dermatophytosis in dogs and cats that summarizes the limitations and advantages of each of these diagnostic tests (Moriello et al., 2017). Knowing these limitations and advantages will help the clinician interpret the results and direct future treatment. Treatment of dermatophytosis classically consists of topical and systemic treatment in addition to environmental disinfection.

Flea Allergy

Evidence of fleas or flea dirt may or may not be present on examination or within the minimum database. Given the high prevalence of flea allergy dermatitis (FAD) especially in endemic regions, the first step in the pruritic feline patient is to ensure the patient and all pets in the household are administered excellent flea control (Diesel, 2017; Miller et al., 2013). FAD can be seen as a primary etiology of pruritus or may be present in conjunction with food or environmental allergies.

Food Allergy

Cutaneous adverse food reactions (CAFR) can be subdivided into two types: food allergy and food intolerance. Food intolerance is an abnormal, non-immunologic clinical response to food or a food additive. Food allergy is an immune driven response to food or a food additive. Due to the nature of adverse food reactions within feline medicine, it is not commonly possible to differentiate food allergy from food intolerance, hence the name adverse food reaction. Adverse food reactions can present with cutaneous or non-cutaneous clinical signs. Cutaneous signs include a wide range of clinical signs including, but not limited too: pruritus, alopecia, recurrent bacterial/yeast pyoderma, recurrent otitis externa, hair and coat quality changes etc. Non-cutaneous signs can include vomiting, diarrhea, in-appetence and lethargy (Miller et al., 2013).

CAFR can affect feline patients of all ages, gender and breed (Olivry & Mueller, 2019). Currently there is no clinically significant evidence to support specific feline breed predispositions (Olivry & Mueller, 2019). While CAFR can create generalized pruritus, feline patients are more likely to have head, neck and facial pruritus compared to canine patients (Olivry & Mueller, 2019). Feline hypersensitivity in general can manifest as four classic syndromes: military dermatitis, eosinophilic disease, head (face) and neck dermatitis and symmetric self-induced alopecia (Olivry & Mueller, 2019) (Miller et al., 2013). All of these presentations have been associated with underlying CAFR (Olivry & Mueller, 2019).

Although various serum and saliva based diagnostic tests are available and marketed to diagnose CAFR, these testing options have not been able to produce consistently reliable results in canine or feline patients (Lam, Johnson, & Heinze, 2019; Mueller & Olivry, 2017). The gold standard test to diagnose CAFR remains to perform an elimination diet trial for a minimum of eight weeks (Olivry, Mueller, & Prelaud, 2015). Extending the diet trial to eight weeks led to complete remission in 90% of feline and canine CAFR patients (Olivry et al., 2015) . Frequently, owners will wish to pursue an elimination diet trial with a commercially available non-prescription diet to help conserve expenses, however, this is not recommended due to the discrepancies found when comparing the label ingredients to ingredients found within the diets (Olivry & Mueller, 2018). Dietary options for elimination diet trials are home-cooked dies or prescription based novel protein diets or hydrolyzed diets. Home-cooked diets are work and time intensive. Additionally, it can be difficult to monitor compliance ensuring the diet is balanced for long-term use. For that reason, the author leans towards prescription-based diet trials. Classically, it has been demonstrated that patients tend to have an allergy to protein source within the diet, however, there is evidence that non-protein molecules can also function as allergens (Gianella, 2014). The top three common allergens identified for cats with CAFR are currently beef, fish and chicken (Mueller, Olivry, & Prelaud, 2016). The goal is to use diets that avoid these common allergen sources, however, dietary history will help guide the clinicians selection of protein to use for the diet trial.

In the suspected allergic patient on excellent flea control, dietary therapy is performed first to evaluate for CAFR. If a patient responds well to dietary therapy, CAFR can be confirmed with diet challenge. In the author's experience, most clients do not want to proceed with diet challenge and continue to feed the diet life-long empirically to control the symptoms. In the event the patient fails to respond to the prescribed dietary therapy, the clinician can then consider a second diet trial utilizing a different methodology of diet therapy or discuss the work-up and treatment options for environmental allergies with the client.

Feline atopic syndrome (FAS) is a term proposed to describe allergic disease associated with environmental allergies that encompasses patients with respiratory, gastrointestinal and skin symptoms (Mueller, Nuttall, Prost, Schulz, & Bizikova, 2021). An alternative term for FAS includes "non-flea, non-food hypersensitivity dermatitis" (NFNFHD)(Diesel, 2017). For FAS patients, currently there are no formulated prescription-based skin support diets, such as Hill's DermComplete® for canine patients with atopic disease. In canine atopic dermatitis, there is evidence to support beneficial effects of zinc, vitamin E, vitamin D and EFA supplementation (Klinger et al., 2018; McFadden, Heinrich, Haarstad, & Tomlinson, 2017; Muller et al., 2016;

Plevnik Kapun et al., 2014). In FAS patients there is minimal evidence evaluating supplements, however, there is some evidence to support EFA supplementation(Mueller et al., 2021).

In summary, a thorough systemic work-up is recommended to diagnose the allergic patient. Once an allergic patient is diagnosed, the work-up begins an elimination diet to evaluate for CAFR. Feeding the CAFR feline patient can be simple using the prescription-based diets once the correct diet is selected. In contrast, feeding the FAS patient can be challenging, as more studies regarding FAS are urgently needed to best guide therapy to alleviate these patient's symptoms.

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NOTES:

Velagliflozin: An Oral Solution for the Diabetic Cat

Ellen Behrend, VMD, PhD, DACVIM (SAIM), Audrey Cook, BVM&S, FRCVS, MScVetEd, DACVIM (SAIM), DECVIM, DABVP (Feline), Patricia Lathan, VMD, MS, DACVIM (SAIM), Thomas Schermerhorn, VMD, DACVIM (SAIM), Catharine Scott-Moncrieff, MA, VMB, MS, MRCVS, DACVIM, DECVIM, DSAM, & Cynthia Ward, VMD, PhD, DACVIM

INTRODUCTION

A brief overview of the SGLT-2 inhibitors and the role of velagliflozin in the management of feline diabetes mellitus will be presented. A panel of experts will then answer questions and share their perspectives on how to introduce this exciting new product into our practices. The following QR codes link to further information about each topic.

Patient Selection
Dr. Catherine Scott-Moncrieff
bit.ly/QRselection

Euglycemic DKA
Dr. Patty Lathan
bit.ly/QReDKA

Monitoring
Dr. Audrey Cook
bit.ly/QRmonitoring

Troubleshooting
Dr. Tom Schermerhorn
bit.ly/QRimportant-things

Indications for Insulin
Dr. Cynthia Ward
bit.ly/QRindicators

How It Works
Dr. Ellen Behrend
bit.ly/QRhow-it-works

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Evolving the Feline MDB: Purrfect Balance for Your Patient Assessment

Elizabeth Schooley, DVM, MS, DACVIM (SAIM) & Kelly St. Denis, MSc, DVM, DABVP (Feline)

The minimum data base is a concept that many veterinarians are familiar with but should the MDB the same for all patients? Recent data studies looking at the diagnostic findings of cats across age ranges and diagnostic use case will be discussed. Additionally, the unique diagnostic behaviors of Cat Friendly Practices will be shared. This information will help pave the way to create the Purrfect diagnostic plan for the feline patients in your care.

The minimum data base (MDB) is a concept that many veterinarians are familiar with but there is little consensus about what diagnostics should be part of a MDB. Evidence to support a defined MDB is scarce in veterinary or human medicine and is mostly based on expert opinion. The benefits of a MDB have been described as a framework for diagnostic consistency among veterinarians, a diagnostic approach that will likely provide a diagnosis or presumptive diagnosis in the majority of patients and allows detection of co-morbidities.1 The challenges of a MDB include lack of specificity for the individual patient and the expense involved with a plethora of tests.

A patient-centric approach to diagnostics allows the clinician to consider the needs of the individual based on signalment, reason for the visit and any specific risk factors the patient may have. It also allows us to meet pet parents where they are while providing exceptional care. Considerations for a patient centric approach include various panels of hematology and chemistry parameters, a urinalysis, as well as other tests such as retrovirus testing, NTproBNP, thyroid hormone, blood pressure, fecal and imaging studies.

One of the keys to a patient centric approach is understanding what is normal for your individual patient. Preventative diagnostics throughout life provide an avenue to develop baseline values which can be trended over time to support understanding of what is normal for a specific patient. A significant change may be noted for some analytes before the result is outside of the population-based reference interval. The idea of subject-based reference intervals (individual reference intervals) is emerging in veterinary medicine. Subject-based reference intervals consider both biologic variation and analytic variation to bring a quantitative approach to trending by allowing a better understanding of the significance of a change for the specific animal.2

Several studies support diagnostics in healthy cats.3,4 A recent retrospective study including over fifty thousand cats evaluated the results of wellness diagnostics (CBC, chemistry, UA and T4) in apparently healthy individuals. It was found that 1 in 5 young adult cats, 1 in 3 mature adult cats and 3 in 5 senior cats had clinically relevant findings. Interestingly, inclusion of a urinalysis increased the amount of relevant findings by about 50% across all age groups. The most common findings in young cats were electrolyte disturbances and abnormalities in the red blood cell parameters. As expected, the study found more relevant findings in older cats when compared to young adults which is consistent with the increasing prevalence of chronic disease with age. Evidence of probable endocrine and renal disease were most common in mature adult and senior cats. This study supports the benefit of wellness testing in all age groups. Importantly in young adult cats, obtaining baseline values for future trending is helpful while use of wellness testing in older cats may aid in early detection of disease and earlier intervention.

The Unique Diagnostic Behaviors of CF practices: Putting Cat Friendly to Work

Cat Friendly practice (CFP) is well known to improve business practices,5 reduce injury6 and improve caregiver satisfaction7. In a retrospective analysis comparing the diagnostic testing behavior of CFPs with non CFPs, additional benefits were observed. As with previous studies,5 CFPs were found to have higher average revenue overall, as well as higher average revenue per feline patient. CFPs demonstrated higher average revenue for visits with diagnostic testing (imaging, blood, fecal, or urine tests), performing diagnostic testing at 12% more visits compared to non-CF practices. Cats seen at CFPs had higher odds of having more than one visit that included blood work or urinalysis. Looking specifically at complete blood count (CBC), urinalysis, certain chemistry tests and total thyroid (TT4), CFPs performed more testing at a higher proportion of visits for all analytes. Further, when diagnostics were performed, CFPs were more likely to include testing across the 4 categories, with significantly lower odds of performing tests in only one testing category, and higher odds of performing testing from 2, 3 or 4 categories.

The authors also looked at specific disease categories common in the feline species and found that CFPs identified a higher number of cats with abnormal results associated with endocrine (mainly TT4), kidney, and electrolyte systems. Comparing testing distribution to non-CFPs, CFPS were more likely to have a result within the reference interval for most analytes. The observations made in this study suggest that CFPs have more success receiving consent for and obtaining diagnostic samples for testing. Increased caregiver satisfaction at CFPs has previously been demonstrated, 7 and this combined with the desire to select a CFP for improved care of their cat might lead to better compliance with testing recommendations by the veterinary team. The observation of increased revenue with CFPs during any visit including diagnostic testing supports this. Cat Friendly interactions and the Cat Friendly environment found in CFPS is also likely to increase success with blood and urine sampling in the feline patient.

The increased testing observed appears to have benefits for the patient, with increased identification of certain common feline diseases. Further, with more frequent testing across more categories, and an increased likelihood of having a result that falls within reference intervals, CFPs might be better poised to trend patient data, potentially diagnosing disease earlier. These findings can have increased benefit to the patient with earlier disease management and presumably reduced morbidity.

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NOTES:

Calming Cats: The Impact of Transport & Anxiety on Our Cats, Cat Caregivers, & Practices

Tracey Deiss, DVM

As stated in the 2021 AAHA/AAFP Feline Life Stage Guidelines, cats are the most popular pet in the United States, and although most cat owners revere their feline companions considering them family members, they are substantially underserved in veterinary medicine compared to their canine counterparts[1] with greater than 60% not receiving annual care compared to 18% in dogs.[2]

Perceived to require less frequent veterinary visits due to their self-sufficient and independent nature coupled with their ability to conceal pain and illness, one underlying reason behind cat owners precluding trips to the vet may be based upon unawareness to the need; however, cat owner stress in response to their cat's acute anxiety and fear associated with transport and veterinary visits, may be another barrier preventing care.[3]

In addition to cat owner stress around veterinary visits, veterinarians also identify and empathize with the hardship of loading cats into carriers for transport and the stress of the vet visit experience on cats and their care givers.[4]

Understanding the unique nature of the species and spectrum of signs associated with acute fear and anxiety as it relates to veterinary visits, is essential when cultivating a feline friendly visit. While we may view our examination as a series of unrelated techniques, our procedures can elicit distress, discomfort, or pain that can cause 'trigger stacking.' Trigger stacking, dramatic associations, and learned dislikes occur in response to perceived dangers-like the smells, sights, sounds, and physical exams endured at the clinic.

Mitigating acute anxiety and fear in cats during visits aligns with a holistic approach to their overall well-being. By considering their emotional needs along with their physical health, we can better provide comprehensive care. Leveraging all the techniques in our cat friendly repertoire along with considering pre-visit pharmaceuticals for ***every*** cat on the acute fear, anxiety, and stress manifestation spectrum, cat owners and veterinary health teams can unite for the greater good of the felines in our care.

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The Ins and Outs of Feline Nutrition and Gastroenterology

7th WORLD FELINE VETERINARY CONFERENCE

October 12 – 15, 2023 Renasant Convention Center, Memphis, TN & Virtual

SATURDAY, OCTOBER 14, 2023

Schedule is in Central Daylight Time

TIME	SESSION TITLE		SPEAKER	ROOM	SPONSOR/ PARTNER
6:00 - 7:00 am	Early Riser Yoga Class*	IPO		Sheraton Hotel - Heritage Ballroom	
6:45 - 8:00 am	Breakfast			Ballroom Foyer	
7:00 - 7:50 am	*Breakfast Symposium*: Controlling OA Pain in Cats: Where Do I Start?	LS	Drs. Joyce Login & Michelle Meyer	Ballroom B	zoetis
8:00 - 8:50 am	Nutritional Management of Diabetes Mellitus	LS	Dr. Audrey Cook	Ballroom A	Boehringer Ingelheim
	The Feline Philosophy Behind Diagnosing GI Disease	LS	Dr. Craig Webb	Ballroom B	IDEXX
	Technician: Sippin' Through Straws: Taking the Stress Out of Feline Neonate Tube Feeding	LS	Ellen Carozza	Ballroom C	sleepypod
8:55 - 9:45 am	Nuanced Nutrition: Calcium Oxalate Urolithiasis	LS	Dr. Audrey Cook	Ballroom A	Dechra
	The Feline Pyramid of Poop	LS	Dr. Craig Webb	Ballroom B	endoscopy support services, inc.
	Technician: Chew With Your Mouth Closed! Preventing Food Phobias & Fighting at the Dinner Table in the Multi-cat Household	LS	Ellen Carozza	Ballroom C	sleepypod
9:45 - 11:00 am	Networking Refreshment Break			Exhibit Hall	Boehringer Ingelheim
9:50 - 10:15 am	AAFP Membership Meeting	LS		Ballroom C	
10:20 - 10:50 am	ABVP: Is it for Me?	LS		Ballroom C	ABVP
11:00 - 11:25 am	Cobalamin: Diagnostic & Therapeutic Implications	LS	Dr. Audrey Cook	Ballroom A	Dechra
11:00 - 12:15 pm	No Way Out! Constipation, Obstipation, Megacolon: Panel Discussion	LS	Drs. Adam Rudinsky, Betsy Swanson, & Craig Webb	Ballroom B	ROYAL CANIN
	Technician: RECOVER CPR Guideline Updates: Feline Focus	LS	Ken Yagi	Ballroom C	NAVTA
11:25 - 12:15 pm	Modifying the Microbiome: The Role of Probiotics in Feline Practice	LS	Dr. Audrey Cook	Ballroom A	visbiome vet.
12:15 - 1:40 pm	Lunch			Exhibit Hall	
12:30 - 1:30 pm	*Lunch & Learn #1:** Feline GI Immunity's Inextricable Links to Dietary & Microbiome Components	IPO	Dr. Alison Manchester	102 - 104	PRO PLAN VETERINARY DIETS
12:30 - 1:30 pm	*Lunch & Learn #2:** Why is This Kitty Skinny? What Should I Do About It?	IPO	Dr. Jessica Pritchard	105 - 107	Dechra
12:30 - 1:30 pm	*Lunch & Learn #3:** Let's Get Digital: How Smart Pet Tech Can Make a Big Impact on Cat Care	IPO	Dr. Sheryl Gamble	113 - 115	MERCK Animal Health
1:40 - 2:30 pm	Management of Liver Disease	LS	Dr. Adam Rudinsky	Ballroom A	wedgewood PHARMACY
	Diagnostic Testing in Feline Chronic Enteropathy Demonstrates Evolution from Inflammatory Bowel Disease to Intestinal Lymphoma	LS	Dr. Anne Avery	Ballroom B	PRO PLAN VETERINARY DIETS
	Technician: Nursing & Nutrition for the Critical Feline Patient Who Just Won't Eat!	LS	Dr. Ashlie Saffire	Ballroom C	ROYAL CANIN
2:30 - 3:15 pm	Networking Refreshment Break			Exhibit Hall	Boehringer Ingelheim
3:15 - 4:05 pm	Liver & Biliary System: Peri-Operative Care, Surgical Evaluation, & Diagnostic Sampling	LS	Dr. Betsy Swanson	Ballroom A	
	The Role of Microbiome: Supporting, Immune Modulating, & Stress Lessening Probiotics in GI Diseases	LS	Dr. Michael Lappin	Ballroom B	PRO PLAN VETERINARY DIETS
	Technician: Discussing Diabetes Mellitus: Empowering Technicians	LS	Ken Yagi	Ballroom C	Boehringer Ingelheim
4:10 - 5:00 pm	Interpreting Liver Biopsies	LS	Dr. Adam Rudinsky	Ballroom A	IDEXX
	Update on the Diagnosis & Management of Infectious GI Diseases	LS	Dr. Michael Lappin	Ballroom B	PRO PLAN VETERINARY DIETS
	Technician: Practical Application of Feline Emergency Transfusions	LS	Ken Yagi	Ballroom C	NAVTA
5:00 - 5:30 pm	Cat Friendly Practice®: Because You're Worth It	LS	Dr. Kelly St. Denis	Ballroom C	Cat Friendly Practice

LS Live Streamed

IPO In-person Only

*Separate registration required. No fees associated.

Controlling OA Pain in Cats: Where Do I Start?

Joyce Login, DVM, CPH & Michelle Meyer, DVM

Feline OA is an underdiagnosed non-curable condition that, left untreated, can negatively affect a cat's quality of life.[1] Nearly 40% of cats with OA demonstrate pain-related signs,[2] with radiographic changes reported in 60% of cats older than 6 years of age,[3] and 90% in cats older than 12 years of age.[4] Despite the alarming prevalence of arthritis in cats, the disease continues to elude diagnosis and treatment for several reasons, including:

- Lack of awareness of prevalence of cats with OA pain
- Lack of awareness on how to identify feline pain
- Feline-specific barriers to veterinary care (e.g., transportation, veterinary stress and anxiety, at-home medication administration[1])
- Lack of safe, effective long-term feline pain medications

Sadly, when left untreated, pain becomes its own disease, progressing to maladaptive pain and central sensitization. In osteoarthritis, maladaptive pain refers to the body's response to chronic joint degeneration, where pain signals persist long after the initial injury has healed. This pain response becomes disproportionate and no longer serves as a protective mechanism. Central sensitization, on the other hand, is a neuroplasticity phenomenon where the central nervous system becomes hyperexcitable, amplifying pain signals from the affected joint. This heightened sensitivity can lead to the perception of pain even in response to non-painful stimuli. Together, maladaptive pain and central sensitization significantly contribute to the persistent and often debilitating nature of osteoarthritis pain, highlighting the importance of targeting both peripheral and central pain processing mechanisms for effective pain management.

Diagnosis, or even identification of osteoarthritis is particularly hard in cats because the changes are often subtle and are primarily related to behavior changes vs. limping or crying. They are commonly dismissed as "just getting old" and often associated with the cats' decreased agility and reluctance to move around.[5,6] There are 6 behavior changes that have been proven to screen for the presence of OA pain[7]:

1. Going up steps
2. Going down steps
3. Jumping up onto higher surfaces like beds or chairs
4. Jumping down from a higher surface,
5. Chasing toys
6. Running. An interactive checklist with these 6 behaviors can be found at www.CatOAChecklist.com

An interactive checklist with these 6 behaviors can be found at www.CatOAChecklist.com

In addition, the cat is far more difficult to evaluate for chronic pain because of their evolution as solitary hunters. They need a smaller repertoire of inter- and intra-species social communication compared with the dog. Cats are often described as "aloof" and "independent" which could stem from the lack of obvious facial expressions and visually expressive characteristics of the dog.

Cats in the wild live alone and must compete with each other for food and other resources. Letting on that a good meal is nearby or that a safe resting place has been discovered will not result in a good outcome for that cat. Conversely, letting on that one is injured, sick or exhausted may lead to becoming another's prey. *The subtlety of signaling has led to a misunderstanding of the health care and quality of life care cats require*.

As if that's not enough, we must layer in the experience of the cat in the veterinary setting. Separation anxiety is recognized in dogs when their owners are away. For the territorial cat, separation anxiety occurs when they are taken from their place of safety. The sensations of pain induce behavioral change that may look like the experience of a cat experiencing stress. Defensive aggression, withdrawing or inhibiting behavior, changes in maintenance behaviors such as grooming or eliminating can be indicative of either. The cat is usually not willing to walk for a gait evaluation in the exam room and may avoid contact with a stranger that could indicate either fear or pain. The place for evaluation of OA pain then becomes the home. Validated pain assessment tools give the caregiver the ability to assess change in behavior and daily routine.

Educating caregivers require easy, short video experiences and clear educational materials. By teaching them the difference in common behaviors between OA pain and normal behavior we can then ask them to submit video of their cat in a normal home circumstance for assessment. The distance from the cat should be 3 – 4 feet to give the cat room to move and to capture the motion of the whole body and try to get one or two actions in 2 minutes or less. The first few attempts can be quite discouraging. A staff member can help by viewing a submission and coaching the caregiver to create a more useful segment.

Once an understanding of the signs of pain in cats has been conveyed and the importance of its control understood by caregivers. A plan for treatment of OA pain that balances the goals of the caregiver can be created. These goals go beyond the successful management of pain and include the preservation of the loving relationship between cat and caregiver. Thus, the plan must be one that considers the ability and commitment of the caregiver, cost of care, the availability of resources. The owner will be more likely to embrace the suggestions in a multimodal pain management plan if they feel really involved in its formulation, if the goals and objectives are important to them, and if they don't feel pressured, tested or judged. How the owner approaches the task will differ from one individual to another. Nurturing the trusting relationship between caregiver and veterinarian will simplify planning.

Feline OA is very common and there is opportunity to diagnose this painful condition in more cats. Early screening can establish a cat's baseline. Checklists can help owners to identify signs of osteoarthritis in cats. There are many opportunities for intervention, including analgesics, environmental adjustments, activity, and surgery as needed. The newest approved product to control OA pain in cats is an injectable monoclonal antibody. With prolonged duration of activity (1 month) and easy administration to cats with a subcutaneous injection, this new therapeutic antibody approach may be the solution for which veterinarians, cat owners, and cats suffering from OA have been waiting.

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NOTES:

Nutritional Management of Diabetes Mellitus

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Introduction

Over the last couple of decades, there has been a profound shift in our approach to feeding all cats, with an increased recognition of their status as an obligate carnivore and an increased appreciation of what it takes for a cat to thrive, rather than merely survive. Much of this new understanding is reflected in current 'best practices' regarding the nutritional needs of diabetic cats, but there is still much to be learned about how to optimize dietary plans for these patients.[1]

Feeding the diabetic cat – current paradigms

Most cats with diabetes mellitus (DM) fit the criteria for human type 2 DM, in which the primary driver behind inadequate insulin secretion is chronic insulin resistance. However, it is important to bear in mind that other factors may be at play, including heritable tendencies, and/or chronic pancreatitis. Although most experts endorse the routine use of a low carbohydrate, high protein diet for diabetic or prediabetic cats, there is a dearth of hard evidence to support a particular stance regarding dietary management. In addition, other factors such as feeding strategies (i.e., meal v ad libitum), formulation (i.e., wet v dry v home cooked), energy density, fiber content, antioxidant levels and the presence of co-morbid conditions must also be considered.

Carbohydrates

Cats are simply not designed to eat substantial amounts of CHO. This is evidenced by their inability to taste sugars, their incretin responses, and their default to hepatic gluconeogenesis, in which amino acids are used to produce glucose. Several studies have demonstrated that both diabetic and non-diabetic cats have improved glycemic control on low CHO diets. This may impact the likelihood of diabetic remission in insulin-dependent cats. In one study, 63 cats with DM were fed either a 12% CHO diet (based on metabolizable energy, ME) or a 26% CHO diet. The low CHO diet was also substantially lower in fiber (0.1 v 3.1 g/100kcal ME). The remission rate for cats on the low CHO diet was significantly higher, at 68% v 41% (P=0.03).[2] Although an in-depth review of the factors influencing diabetic remission in cats concluded that the evidence to support the use of low CHO diet was sparse[3], this is the current recommendation by both the International Society of Feline Medicine and the American Animal Health Association.[4,5]

Protein

Many commercial diets are now regarded as borderline adequate with respect to their protein content. Current AAFCO guidelines for an adult maintenance diet require >6.5 gm of protein / 100kcal.[6] If we assume that a 5 kg cat needs 300 calories, this cat will take in less than 20 gm protein a day if the diet contains the bare minimum. This is less than 4 gm/kg. However, work done looking at nitrogen balance and lean body weight demonstrated that cats need at least 5.2 gm/kg.[7] High protein diets support muscle mass and likely mitigate the age-related muscle loss (i.e., sarcopenia). It is particularly important to ensure adequate protein intake when a cat is on a weight loss program. Maintaining a robust muscle score is particularly important in cats with DM, as muscle is a great 'sink' for glucose. The protein should be of high biological value.

Fat

The impact of dietary fat in the feline diabetic is unclear. It is likely that many cats with DM have chronic pancreatitis, in which case dietary fat content may be a consideration. However, unlike their canine counterparts, most cats with pancreatitis have a more insidious, chronic form, characterized by a lymphoplasmacytic infiltrate[8]; cats rarely manifest acute neutrophilic or necrotizing pancreatitis. Although some experts recommend fat restriction in cats with clinical evidence of pancreatitis, the consensus does not support fat restriction in this subpopulation of cats.

Fat restriction is indicated in cats with severe hyperlipidemia (i.e., serum triglycerides > 1000 mg/dL). These levels are often seen in poorly controlled diabetics, and it can be difficult to determine if the lipid disorder is a consequence or cause of DM.[9] However, these levels warrant dietary modification, with or without drug therapy, as they are associated with various complications including ocular disease and peripheral neuropathy.

Fiber

In the 1990s, there was a strong push towards the use of high (primarily insoluble) fiber diets in cats with DM. This was driven by a small number of studies that showed modest improvements in some glycemic parameters in cats on high fiber diets.[10]

Arguments to support the inclusion of fiber include increased satiety and delayed release of nutrients due to changes in gastrointestinal (GI) transit. In people, high (primarily soluble) fiber diets have been shown to improve peripheral insulin sensitivity and overall glycemic control; the mechanism for this is unclear but may reflect changes in the GI microbiome and altered secretin of key GI hormones such as peptide YY and some of the incretins.[11]

Chromium and vanadium
Chromium plays a key role in the function of insulin by increasing its binding to receptors and the number of receptors expressed. Chromium deficiency has been associated with decrease tissue responsiveness to insulin. In one study of healthy non-obese cats, supplementation was associated with lower blood glucose concentrations, but other studies have been less encouraging.[12] Vanadium has a similar effect on insulin function. However, supplementation of either element is unlikely to provide a significant benefit and is therefore not indicated unless the cat is deficient.

Antioxidants
There are clear associations between obesity and increased oxidative stress. Similarly, oxidative stress is higher in diabetic individuals in many of the species studied; it is unclear however if this is a cause or consequence of DM. Super oxide dismutase (SOD) was reported to be lower in cats with DM when compared to controls[13]; this enzyme plays a key role in the development and progression of oxidative damage. Although there is scant information about the impact of antioxidants in our feline diabetics, there is an argument to support judicious supplementation.

The Incretins
Many of the advantages provided by high protein, low CHO diets likely reflect the impact of diet on the secretion of these key hormones by the GI tract. The incretins are relative newcomers to the world of endocrinology, but it is clear that they have substantial and wide-reaching effects on energy metabolism, GI function, endocrine pancreatic function and health, and satiety. The incretins are secreted by specialized enterocytes, that essentially 'taste' the ingesta and pre-emptively adjust numerous metabolic processes so that absorbed nutrients are handled efficiently and appropriately.[14] Several incretins have now been identified, but the most important to date (with respect to DM) is glucagon-like peptide 1 (GLP-1). This triggers the release of insulin before sugars are absorbed and is simultaneously trophic to the pancreatic β-cells. This hormone also suppresses gluconeogenesis by the liver and triggers feelings of satiety within the brain. It is telling that CHOs have very little impact on GLP-1 secretion, and do not trigger the release of another key incretin (glucose-dependent insulinotrophic peptide: GIP) at all. This is in stark contrast to dogs and people, in which CHO is the primary incretin trigger.

Making a nutritional plan
A logical approach is needed to make an effective nutritional plan for any patient. As a general rule, most cats with DM will benefit from a 'diabetic' diet, but this transition should be made gradually. Assuming that the cat will be started on a sodium-glucose linked transporter subtype 2 (SGLT-2) inhibitor or insulin, it is often prudent to wait a couple of weeks before introducing a new food.

Establish caloric needs
Caloric needs are determined by body and muscle condition score; these are used to estimate a desired body weight. I routinely use an online calculator (https://petnutritionalliance.com) for this process, assuming that the cat is overweight. Calorie needs can be calculated using several different formulas, which often provide a daunting range of estimates:

40-66 kcal/day
$(Kg^{0.75} \times 70) \times 1.3$
$(Kg \times 30) + 70$

It can be helpful to calculate current caloric intake, as this can help to contextualize the numbers derived from these various formulas.

If the cat is overweight, a weekly loss of 1.5-2% is ideal. This should be monitored closely, as rapid weight loss suggests insulin insufficiency or inadequate intake and may predispose the cat to developing hepatic lipidosis. It can be helpful to consider the energy density of the food provided, as this will impact feelings of satiety. It can be difficult for an owner to stick to the diet if the cat is manifesting hunger on a regular basis. Of the three main diabetic diets, RC Glycobalance has the lowest energy density at 320 kcal/cup; Purina DM is 605 kcal/cup.

Establish protein needs
Using 5.2 gm/kg lean body weight as a guide, calculate the protein intake. This can be calculated from the protein % on an as fed basis, or on a gm/100 kcal basis. Consider also the biological value and digestibility of the protein provided.

Consider caloric distribution
The caloric distribution can be determined from the food label or feeding guide. The guaranteed analysis (GA) on the food bag or can is regarded as the minimum; it is often more useful to find the typical nutrient analysis (TNA) provided by the manufacturer.[1]

Foods are broken down into protein, fat, and the nitrogen-free extract (NFE). This is the digestible / metabolizable CHO component plus the dietary fiber. It is very important to realize that the % CHO / NFE on a dry matter basis is not the same as the % of ME from CHO.

Wet v Dry
From a nutritional perspective, wet foods are often superior as they are usually lower in CHO and the increased bulk may improve feelings of satiety. The moisture content may also be beneficial, as hyperglycemia will trigger polyuria and makes patients more vulnerable to dehydration. Unfortunately, cats create strong food preferences at an early age, and it can be very difficult to get a cat that has eaten dry kibble for years to accept a wet food. He or she may nibble at the new food but is unlikely to consume enough calories. Some cats even become fixated on the shape of their dry food and are very reluctant to eat one that appears different.

Consider co-morbidities
Many diabetic cats have other concurrent conditions which may be mitigated or stabilized with specific dietary manipulations. A s a general rule, it is most appropriate to create a nutritional plan with the other condition in mind, rather than prioritizing the DM.

Create a feeding schedule
Cats are adapted to very frequent small meals and have a long and modest post-prandial change in blood glucose. Consequently, there is really no need to switch the average diabetic cat to meal feedings, unless it is on lente insulin (Vetsulin®). This is often a poor choice for cats, as it tends to cause marked glycemic variation over the course of the day, and the fast-acting component can cause rapid declines in blood glucose in a fasted cat.

Future considerations
SLGT-2 inhibitors and diet
As the therapeutic effect of the SGLT-2 inhibitors is dependent upon some endogenous insulin secretion, it makes sense to provide as much support as possible for the pancreatic β-cells. Based on current understanding, that would include the provision of a high protein, low CHO diet, fed in amounts appropriate to achieve a normal body condition score.

Advanced glycation end products (AGEs)
AGEs are proteins or lipids that have been permanently modified by exposure to glucose or another reducing sugar.[15] This is a non-enzymatic glycation and is familiar to any keen home cook as the "Maillard reaction", by which meats and other protein-rich foods become browned and more flavorful when exposed to high temperatures.

These chemicals are derived from both foods and endogenous sources and are associated with numerous chronic disorders such as diabetes and its complications, atherosclerosis, hypertension, and neoplasia.[16,17] Two mechanisms behind the toxicity of the AGEs have been proposed, namely the trapping and cross-linking of proteins, and the synthesis of cytokines and chemokines as the result of the activation of AGE receptors on various cells. This process has also been associated with oxidative stress, cell proliferation and apoptosis.

The interplay between DM and AGEs is complex, as hyperglycemia drives the production of AGEs. We all routinely measure serum fructosamine concentrations in our diabetic cats: the fructosamines are a group of glycated proteins, primarily albumin, and are in fact AGEs.

The contribution of dietary AGEs (dAGEs) versus endogenous is unclear, but in most people, it is estimated that dietary sources account for 30-60%. dAGEs are present in most foods, but the amount is markedly influence by the degree and nature of the processing of that particular raw ingredient. Exposure to high temperatures (e.g., grilling or broiling) generates large amounts of AGEs, whereas lightly poaching has much less effect.

Rodent studies have shown that restriction of dAGEs prevents various conditions, including both type 1 and 2 DM. This is telling, as it suggests that food processing (not just macronutrient profile) may impact pancreatic health. Most cats live on highly processed foods; canned foods, for example, are subjected to 250°F for 80 minutes, and dry foods are extruded at very

high temperatures. Could food processing be contributing to the increase in feline DM? We have been focusing on weight and exercise, but maybe we also need to consider dAGEs as part of this kaleidoscope of predisposing factors. There is still much to be learned about dAGEs and feline health, but this new information certainly gives us food for thought.

Summary

Every diabetic cat deserves a personalized nutritional assessment and plan. As a general approach, there is good evidence that low CHO diets convey significant advantages, and most experts would support their routine use. However, calorie and protein needs should be determined carefully, and co-morbid conditions considered when making a nutritional plan.

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NOTES:

Nuanced Nutrition: Calcium Oxalate Urolithiasis

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Introduction

Calcium oxalate (CaOx) urolithiasis is a cause of significant morbidity and mortality in cats. The incidence of CaOx stones appears to be on the rise in this species, which interestingly mimics recent patterns in human medicine.[1,2] Although we tend to consider CaOx urolithiasis to be one disorder, it is likely that various factors, including genetic predispositions, diet, water intake, urinary proteins, the gastrointestinal (GI) microbiome, and numerous hormonal influences determine an individual's risk for stone formation. Current estimates suggest that 40-50% of feline uroliths are CaOx monohydrate; however, this stone type compromises the bulk of those found in the upper urinary tract.[1,2] Clinical signs directly attributable to CaOx urolithiasis include dysuria, urethral obstruction, ureteral obstruction and chronic kidney disease (CKD).[3] It is noteworthy that CKD is associated with urolithiasis even in the absence of ureteral obstruction or nephrolithiasis; this finding emphasizes the need to effectively mitigate stone formation in every patient.

Risk factors

Signalment

Most cats with CaOx stones are middle aged (7-10 years), and neutered males appear to be over-represented. Burmese, Himalyan and Persian cats also appear to be predisposed, and specific genotypes with an increased risk of stone formation have been idenfified.[4]

Inherent / metabolic influences

The number one determinant of 24-hr calciuria is serum ionized calcium (iCa) concentrations; over one third of cats with CaOx stones are found to be hypercalcemic.[5] For this reason, an iCa should be measured in every cat with urolithiasis, and hypercalcemia addressed immediately. Cats with idiopathic hypercalcemia are particularly vulnerable to CaOx stone formation, as iCa levels are often mildly increased for prolonged periods of time.[6] Measurements of total serum calcium are now known to be a very poor indicator of iCa, and normal concentrations should not be relied upon to rule out hypercalcemia.[7]

Specific molecules present in urine are thought to reduce crystal formation, and subnormal concentrations of these may increase the likelihood of CaOx precipitation. Tamm-Horsfall glycoprotein, nephrocalcin, and glycosaminoglycans have all been shown to reduce stone formation in other species; we have limited information about these endogenous stone inhibitors in cats, but it seems likely they play a similar role.[8]

The amount of oxalate present in urine reflects both dietary intake and the action of specific species of bacteria within the GI tract. In people, urinary oxalate excretion is a major determinant of stone risk; this may not be the case in cats, but oxalate intake and metabolism do still play a contributory role. *Oxalobacter formigenes,* a gram-negative rod and an obligate anaerobe, is a normal component of the colonic microbiome; this species digests oxalate and thereby reduces GI uptake and subsequent renal excretion.[9] Decreased abundance of *O. formigenes* is strongly associated with an increased CaOx stone risk in people, and lower levels of O. *formigenes* have been reported in dogs with CaOx urolithiasis.[10] I am not aware of similar work in cats, but again, it seems likely that this may play a role. *O formigenes* is rapidly depleted by many routine antibiotics.

The recent increase in CaOx nephrolithiasis in people has been linked with an increase in obesity, metabolic syndrome, and diabetes mellitus.[11] This is an interesting association, although this may simply reflect shared risk factors rather than a causal relationship.

The major players

Calcium - the exact role of dietary calcium in stone formation is unclear, and it is apparent that renal handling of calcium will impact the effect of oral intake. Although it would seem appropriate to strictly limit calcium intake in stone formers, low calcium diets are associated with increased GI uptake of oxalate in people and increase stone formation.[12,13] In addition, substantial calcium restriction impacts bone strength and contributes to age-related osteoporosis in humans.

Oxalate – This is the end-product of metabolism of vitamin C, glycine, and serine. It makes soluble salts with sodium and potassium but is very poorly soluble when complexed to calcium.[5] Deficiency in B6 increases urinary oxalate. Interestingly, 24-hr oxalate excretion has more impact than calcium on stone formation in people, and considerable effort is directed towards

reducing oxalate ingestion and subsequent uptake in human CaOx stone formers. There has been much less focus on oxalate in feline stone formers, but this may be an area that merits more consideration.[14]

Acid-base status – Metabolic acidosis will increase calciuria as calcium is released from bone to provide buffer. In addition, acidic urine limits the impact of the inhibitory molecules mentioned earlier, and decreases CaOx solubility.[2,5] However, as we all know, it is not sufficient to simply adjust urine pH if our goal is to prevent stone formation in cats.

Magnesium –As magnesium is a component of struvite stones, this micronutrient was restricted in the early iterations of "stone prevention" diets; this may have played a role in the gradual uptick in CaOx stone formation, as magnesium forms soluble salts with oxalate and robust intake is therefore protective against CaOx urolithiasis. However, the formulation of the magnesium must be taken into consideration; magnesium chloride is not protective, but magnesium oxide is.[15]

Phosphate – Calcium and phosphate have a complex relationship, so it is not surprising that dietary phosphate levels impact stone formation. Phosphorus restriction, such as in standard "kidney" diets, has been shown to increase the risk of stone formation.[16] This may be multifactorial, but is likely due to increases in vitamin D, and subsequent increases in GI uptake of calcium. In addition, less dietary phosphorus increases the bioavailability of calcium. Some cats will actually become hypercalcemic within just a few weeks of a transition to a low phosphorus diet.

Sodium – This electrolyte has a complex relationship with calcium within the renal tubules. Under normal circumstances, almost all (>99%) of filtered calcium is absorbed automatically in the proximal convoluted tubules, along with large amounts of sodium. If the filtrate is sodium rich, this tends to decrease calcium reclamation. We use this therapeutically to mitigate hypercalcemia in emergent patients.

Dietary considerations

Without a doubt, dietary modifications are the cornerstone of stone prevention.[2,5] However, it is important to bear in mind that simply switching to a "stone prevention" diet may not be adequate to prevent CaOx urolithiasis, and that not all diets are created equal. I recognize that there are several dietary options for CaOx stone-forming cats, and hope to provide some additional insight to better inform decision making.

Moisture content

This has a major impact on the risk of on-going stone formation, and cats maintained on a wet diet have a markedly reduced risk of stone formation than those maintained on an exclusively dry diet. Urine output in cats on wet food is >50% more than those on dry diets; this is due in part to the moisture content of the food but also reflects increased water intake due to the higher ash and protein contents normally found in wet foods.[2,5]

There are various strategies to increase water intake, such as providing water fountains, and offering hydration solutions such as Purina Hydra Care.[17] It can be helpful to add highly palatable liquids to water, such as very low sodium chicken broth or a dash of whipping cream. Due to the sodium content, tuna water or standard chicken broth are not advisable.

Calcium content

The current consensus is that dietary calcium intake does not appear to play a major role in CaOx stone risk, and the calcium content of widely used "stone prevention" diets ranges from 140 to 420 mg/ 100 Kcal. However, dietary calcium content may well play a role in the development of idiopathic hypercalcemia, and there is evidence than calcium intake should be < 200 mg/ 100 Kcal in affected cats (Valerie Parker, personal communication). In addition, calcium / phosphorus should be < 1.4 in these patients. I personally recommend following these guidelines in all cats with calcium oxalate urolithiasis, even if I am not concerned about idiopathic hypercalcemia.

Sodium content

Many "stone prevention" diets contain robust amounts of sodium in order to promote water intake and lower urine specific gravity. In normal (non-stone forming cats), this mild sodium loading does not seem to have a significant impact on renal calcium handling, but recent evidence suggests this may not be the case in cats with a vulnerability to CaOx urolithiasis.[17] It is noteworthy that sodium restriction is advised for people with CaOx stones. The sodium content of feline anti-stone diets is highly variable, even within a specific manufacturer's product line. I think that sodium content should be considered carefully, and diets with high sodium content should be avoided.

The following table provides some comparison of the calcium and sodium contents of some of the anti-oxalate prescription diets available for cats. Readers should always verify dietary information with current resources as formulations may change.

Diet	*Formulation*	*Calcium (mg/100 kcal)*	*Sodium (mg/100 kcal)*
Hills c/d Multicare	Dry	192	80
Hills c/d Multicare	Canned	195	85
RC Urinary SO	Dry	230	330
RC Urinary SO	Morsels	250	340
Purina UR	Dry	300	330
Purina UR	Wet	180	130

Protein content
Dietary protein intake influences systemic acid-base status, and high protein diets promote metabolic acidosis. They also increase calciuria and decrease urinary citrate (which forms soluble complexes with calcium and thereby decreases stone risk).[18] Every diet fed to a cat should meet its daily protein needs (est at >5.2 gm/kg).

Pyridoxine (vitamin B6)
The impact of vitamin B6 on oxalate stone formation is somewhat controversial, although one large study in women showed that a robust B6 intake lowered the risk of CaOx urolithiasis.[19] This vitamin metabolizes oxalates to glycine, and deficiency has been shown to increase urinary oxalate concentrations.

Probiotics
As was discussed earlier, *Oxalobacter formigenes* is a normal part of the colonic microbiome, and digests oxalates. Lower colonization rates have been reported in people with CaOx stones, along with higher plasma oxalate concentrations. Specific probiotics containing this species have been investigated in human medicine, but this is a challenging species to culture and maintain *ex vivo*.[9] However, it appears that there are global differences in the microbiota of stone-forming people, with less *Prevotella* and *Lactobacillus* spp.; this suggests that other bacterial species that improve diversity may confer benefit.[20]

Zucchini
A recent paper reported that adding cubed zucchini to a regular feline dry diet reduced the CaOx relative supersaturation (RSS) of the urine.[21] This was fed at 10 gm/kg/day and mixed in with the kibble. It was interesting to note that the RSS was markedly lower in cats fed zucchini and a regular diet, despite a USG > 1.060, suggesting a substantial decrease in either calciuria or oxaluria.

Essential fatty acids
Urolithiasis is uncommon in populations eating cold water fish and fish oils; these diets are robust in omega-3 fatty acids, such as eicosapentanoic acid (EPA) and docoahexanoic acid (DHA). It has been shown that arachidonic acid promotes calciuresis, so downregulating the arachidonic acid pathway with EPA and DHA may reduce the amount of calcium available for stone formation.[22] Some anti-stone diets are supplemented with essential fatty acids, but it is also easy to add this to the dietary plan for our feline patients.

Betaine
Betaine anhydrous is found in beets, spinach, and seafood. It converts homocysteine to methionine and may have an impact on CaOx stone formation in some individuals. In a recent study, cats with a specific genotype had a lower risk of stone formation when fed a diet containing betaine, green tea, tulsi and funigreek.[4] However, the effect was limited to individuals with key genetic markers.

Calcium oxalate urolithiasis and chronic kidney disease (CKD)
There is a clear link between urolithiasis and CKD in cats. It is interesting that CKD is associated with stones in any part of the urinary tract, so this connection is not simply a reflection of the physical damage done by a stone in the renal pelvis or ureter.[3] Instead, it has been hypothesized that tiny crystals forming within the renal tubules themselves cause injury, loss of tubular cell integrity, generation of radical oxygen species, chronic inflammation, and subsequent nephron loss.[23] We also know that idiopathic hypercalcemia is associated with both CKD and urolithiasis; this connection may be due to a direct effect of excessive calciuria or damage from microscopic crystals within the kidney. Bear in mind too that the absence of visible stones does not mean that a cat is not making damaging CaOx crystals.

Recent studies indicate that angiontensin-2 receptor blockers, such as telmisartan, mitigate tubular injury caused by crystal formation.[23] This drug is well tolerated when used for proteinuria or hypertension in cats, although we do need to check creatinine after 10 days of starting therapy to look for a decrease in glomerular filtration rate. I am now adding this drug to my standard management plan for every cat with CaOx urolithiasis, in the hope of mitigating on-going tubular injury.

Standard 'renal' diets are often an appropriate choice for cats with CKD and CaOx, as they have moderate protein and sodium concentrations, are alkalinizing, and contain supplementary essential fatty acids. I usually consider a renal diet in a cat with serum creatinine ≥2.2 mg/dL. However, the lower phosphorus content can be problematic as it may increase calcium uptake and calciuresis.[16] It is important to always check iCa after introducing a phosphate restricted diet, as overt hypercalcemia may be noted. We cannot rely on total calcium levels in cats with CKD are they are particularly discordant in this patient population. Zucchini may be a useful dietary addition in these cats, although it will decrease the energy density of the diet.

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Cobalamin: Diagnostic & Therapeutic Implications

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Background and biology

Cobalamin is a water-soluble vitamin and was first identified in 1948. However, over a decade earlier, physicians had recognized that a chemical found in hepatic tissue was able to reverse pernicious anemia, an insidious and progressive condition characterized by red cell macrocytosis. A team of doctors was awarded the Nobel Prize for Medicine in 1934 based on their discovery that a diet rich in bovine liver was curative. Unbeknownst to them, the most common cause of pernicious anemia is atrophic gastritis; this results in compromised cobalamin uptake and eventual deficiency. Liver is an excellent source of cobalamin, and ingestion of large quantities is enough to overcome the limitations imposed by underlying gastric atrophy.

Cobalamin is often referred to as vitamin B12, but this term is somewhat inappropriate as it refers to a collection of compounds, not all of which are needed by eukaryotic organisms. Cobalamin, which is only synthesized by bacterial species, is essential for eukaryotic health, and mammals are therefore totally dependent on exogenous sources.[1] Rumen bacteria produce copious amounts of cobalamin, and this vitamin is therefore abundant in red meat (beef, lamb, venison), the liver and kidneys of ruminants, and dairy products. Dietary deficiency is therefore very unlikely in companion animals eating traditional diets but is commonly reported in people consuming vegan diets.

The absorption of cobalamin is a complex process.[2] After release within the stomach from dietary sources, it is bound to gastric R-protein (sometimes also referred to as gastric haptocorrin). Compromised R-protein secretion occurs in people with atrophic gastritis, and a significant cause of non-dietary related hypocobalaminemia in this species. R-protein deficiency does not seem to be an issue in companion animals. Upon entry into the duodenum, cobalamin is cleaved from R-protein by pancreatic proteases and handed off to intrinsic factor; this is made by both the stomach and exocrine pancreas in dogs but is only made by the pancreas in cats. After transiting the length of the small intestine, the cobalamin-intrinsic factor complex attaches to specific receptors in the pits of the microvilli within the ileum. After absorption and entry into the vascular space, the cobalamin is bound to transcobalamin. This protein delivers cobalamin to all tissues, via receptor-mediated endocytosis. In people, about 20% of serum cobalamin is bound to transcobalamin. This has a short half-life of just a couple of hours. Most of the absorbed cobalamin is transported bound to haptocorrin; this only delivers cobalamin to the liver and has a half-life of 10 days. Studies using cobalamin supplementation in cats indicate that the overall half-life of cobalamin in this species is about 13 days; this however is significantly shorter (5 days) in cats with chronic enteropathy; this change reflect cobalamin loss due to compromised enterohepatic recirculation.[3]

Cobalamin is s co-factor for two key mammalian mitochondrial enzymes: Methionine synthase, which produces methionine; and methylmalonyl-CoA mutase, which produces succinyl-CoA. The consequences of cobalamin deficiency are therefore complex and wide-ranging. In people, this is associated with pernicious (megaloblastic) anemia, atherosclerosis, peripheral neuropathies, and dementia. Congenital deficiency in cats is rare but is associated with lethargy and failure to thrive.[4] Acquired cobalamin deficiency in cats has been associated with myelopathy and encephalopathy, but hyporexia appears to be the most common consequence.[5-7] It is noteworthy that cobalamin deficiency can cause hyperammonemia; patients may consequently be misdiagnosed with hepatic insufficiency.

It is important to recognize that hypocobalaminemia (i.e., a total serum cobalamin below the reference range) does not establish a diagnosis of cobalamin deficiency. This is because intracellular levels are not reliably predicted by serum concentrations. Instead, we need to measure methylmalonic acid levels in urine; this increases due to the build-up of methylmalonyl-coA. As a general rule, a cat with a serum cobalamin <200 ng/L is probably truly deficient, but bear in mind that some cats with serum cobalamin of 300 ng/L may also be deficient.[8]

Testing considerations

I measure serum cobalamin concentrations in every cat with a history of hyporexia or unexplained weight loss, or any clinical sign (diarrhea, vomiting) or imaging findings (abnormal intestinal wall thickness, mass effect, mucosal stippling) suggesting inflammatory or infiltrated gastrointestinal (GI) disease. It is important however to consider this result in conjunction with other markers of GI and pancreatic function, namely serum folate, trypsin-like immunoreactivity, and pancreas-specific lipase concentrations.

Folate (B9)
This is another water-soluble vitamin and is absorbed in the proximal small intestine. Serum levels reflect dietary intake, duodenal brush border enzyme activity, mucosal absorptive area, and the status of the microbiome. Hemolysis markedly impacts measured folate, so do not submit a sample if there is any evidence of hemolysis. Subnormal concentrations suggest intestinal dysbiosis or substantial duodenal disease. I think this test is relatively insensitive, and do not discount the possibility of significant GI disease just because serum folate is within the reference range.

Trypsin-like immunoreactivity (TLI)
This test is a highly reliable marker for exocrine pancreatic function. A subnormal level indicates exocrine pancreatic insufficiency (EPI); a value within the reference range rules this out, as long as the cat was fasted for at least 12 hours.[9] A high value has essentially no clinical relevance, although we do sometimes see this in cachectic cats. Most cats with EPI have very low cobalamin levels at the time of diagnosis due to lack of intrinsic factor secretion and require life-long supplementation. I do not routinely run a TLI unless I have a strong clinical suspicion of EPI, namely a patient with a voracious appetite and voluminous stools. Serum cholesterol may also be subnormal or borderline.

Pancreas-specific lipase (fPL)
This is a highly sensitive biomarker for pancreatic inflammation. I do routinely measure this in conjunction with folate and cobalamin, as many cats have concurrent pancreatic and GI disease, +/- cholangitis (so called 'feline triaditis').[10] Biochemical evidence of chronic pancreatitis may impact my decisions regarding medical and dietary therapy for cats with chronic enteropathy.

Clinical implications
There are several differentials for hypocobalaminemia:
- Dietary inadequacy (e.g., vegetarian homemade)
- Exocrine pancreatic insufficiency
- Ileal disease
- Intestinal dysbiosis
- Hyperthyroidism – this may self-resolve, but should be investigated if it persists[11,12]

In my practice, I tend to think that any patient with a serum cobalamin <400 ng/L merits attention, although the bottom end of the Texas GI Lab reference range is 290 ng/L. Assuming I have ruled out other causes of low cobalamin, I rely on this finding to indicate ileal disease. My routine endoscopy process does include retrograde biopsy of the ileum, but this becomes even more important in the cat with a borderline or low cobalamin status.

Several studies have tried to correlate cobalamin concentrations with severity of disease, and the results are somewhat mixed.[3,13,14] In a 2001 paper, 49/80 cats seen at a tertiary referral center for GI disease had subnormal cobalamin concentrations. These were particularly low in cats with a final diagnosis of GI lymphoma, and 50% of these cats had hypofolatemia too.[3] In a 2012 report, more than 40% of 261 cats seen at a university for GI disorders were hypocobalaminemic; over a quarter had markedly low values (<150 ng/L). These cats tended to have lower hematocrits, higher mean corpuscular volumes, higher neutrophil counts and lower serum albumin concentrations. The latter two findings likely indicate disease severity.[14]

Feline intestinal dysbiosis is still a poorly understood condition, and it is unclear if changes in the microbiome are the cause or consequence of chronic enteropathy in this species. However, shifts in bacterial populations are associated with increased use of cobalamin by bacteria, and a recent report looking at the dysbiosis index (DI) found negative correlation between the DI and serum cobalamin concentrations.[15]

Treatment of hypocobalaminemia
Although we have traditionally used parenteral cobalamin in cats with GI disease or EPI, recent studies have shown that oral supplementation is also effective.[16] If cobalamin is provided in large amounts, it can be taken up across the GI-tract by mechanisms independent of intrinsic factor. The parenteral dose is 0.25 mg/cat SQ every week; the oral dose is 0.25 mg/cat PO daily. Serum concentrations should be checked after 6 w4eeks and doses adjusted accordingly.

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Modifying the Microbiome: The Role of Probiotics in Feline Practice

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Introduction

Probiotics are defined as live microorganisms that, when ingested, convey a health benefit upon the recipient.[1] Various mechanisms of action have been proposed, including:

1. Prevention of pathogen adhesion
2. Release of compounds that inhibit the growth of pathogenic species
3. Alteration of the intestinal environment in such a way that pathogens are inhibited
4. Stimulation of immune function and immunomodulatory cells
5. Competition with pathogens for growth factors and nutrients

However, this is likely a substantial oversimplification of what probiotics may do and is predicated on the idea that particular species of bacteria are "good" or "bad". We probably need to move away from this viewpoint and focus instead on the overall status of the gastrointestinal (GI) microbiota (i.e., the complete collection of bacteria, yeasts, viruses colonizing the bowel). This is best thought of as an adaptive, complex, integrated ecosystem, much like a tropical rain forest or the ocean. Individual species should not be labeled as good or bad; it is the relationships between species and their interactions with the environment and each other that determine overall GI tract health and function.

Until recently, there was limited understanding of the GI microbiome, as only culturable species could be identified. With the advent of PCR techniques, the full extent of the microbiome is now evident. Less than 10% of the species that routinely live in the GI tract are culturable bacteria; the microbiome includes huge numbers of other bacterial species, along with numerous yeasts and viruses. The average cat likely has more individual organisms within its GI tract than there are people of the face of the earth. These organisms affect dozens of digestive and metabolic processes within the host, and changes from the normal population ("dysbiosis") can substantially impact GI tract function, including motility, permeability, nutrient absorption. There is also evidence to support a wider impact, with effects on psychology, energy metabolism and global immune responses.

Decreased diversity of the GI microbiome has been associated with numerous disorders in human medicine, such as inflammatory bowel disease (IBD), obesity, and type 2 diabetes mellitus. Changes in specific populations have also been implicated in changes in GI hormone secretion and various neurological conditions. It is unclear for some of these disorders if these population shifts are causative or consequential, but there is tremendous interest in manipulation of the GI microbiome.

There is clear evidence – based on high quality studies – that probiotics have a positive effect with certain specific disorders in people, including the management of lactose intolerance, prevention of antibiotic-associated diarrhea, recovery from acute diarrhea in children, and the maintenance of remission with inflammatory bowel disease. One consistent finding is that only specific products (strains, or combinations of species) are associated with a response. It is misleading to say 'probiotics help with diarrhea'; instead, we need to recognize that *Lactobacillus paracasei* strain ST11 ameliorates non-rotaviral diarrhea in children, and that VSL#3 has been shown to support remission in adults with mild to moderate ulcerative colitis.[2,3]

The ideal probiotic

A probiotic is defined as a food supplement containing specific strains of live microorganisms, usually bacteria. An ideal probiotic needs to fit the following criteria:

1. Survive gastric acid and duodenal bile
2. Adhere to the GI tract mucosa
3. Colonize the target host species; persist and flourish when the product is discontinued
4. Limit pathogen growth
5. Grow readily during commercial production; survive processing, shipping, and storage
6. Have a proven positive effect on the host
7. Be entirely safe, with no risk to the consumer

Prebiotics and symbiotics
Prebiotics are compounds that support a probiotic species and include fructooligosaccharides and soluble fibers. Products containing prebiotics and probiotics are called synbiotics. The idea behind combining the two is enhanced survival/persistence/effect for the probiotic species, but prebiotics may also support members of the native microbiome.

The feline perspective
There is relatively little peer-reviewed literature regarding probiotics in cats with spontaneous disease, and most studies have reported on their effects in healthy individuals.[4-6] Although these studies can demonstrate survival +/- persistence, it is hard to extrapolate their findings to cats with spontaneous disease. It is reassuring however when these products are shown to be safe and well tolerated.

In a placebo-controlled study, administration of *Enterococcus faecium* SF68 (FortiFlora®) to cats in a shelter setting reduced the incidence of persistent (>2 day) diarrhea.[7] A substantial number of these cats had concurrent parasitism, which may have confounded the results. The same product was given to kittens in another study; there was no measurable effect on weight gain, fecal quality or Clostridial enterotoxin when compared to the control group. Kittens in the treated group had a significantly higher percentage of CD4+ lymphocytes, but other immune parameters were similar.[8] In contrast, a study following over one thousand orphaned kittens, of which over 10% developed diarrhea, failed to demonstrate a positive effect from the administration of *E. faecium* SF68.[9]

In an open-label trial, a multi-strain synbiotic (Proviable-DC®) seemed to improve stool consistency in cats with undefined chronic enteropathy.[10] However, this was determined by the owner and the cats concurrently received other treatments, including dietary changes, although nothing new was introduced in the 3 weeks prior to synbiotic administration. It is unfortunate that this was not a blinded, placebo-controlled study, as the results would have been more meaningful.

One probiotic has been evaluated in cats with constipation +/- megacolon. After three months of administration of a high-dose probiotic, affected cats passed softer stools with less apparent discomfort.[11] There was a concurrent improvement in the number of interstitial cells of Cajal within the colonic walls; these cells play a key role in colonic neuronal activity.

In addition to GI based studies, probiotics have been looked at for other purposes. One is currently marketed for use in cats with chronic kidney disease. Despite encouraging data from the manufacturers, this product had no discernable effect on azotemia when tested independently in a double-blinded, controlled study, there was no discernable effect on azotemia.

Cats experimentally infected with FHV-1 had less episodes of conjunctivitis when receiving *E. faecium* SF68 in comparison to cats receiving a placebo. There was no effect on viral DNA expression or shedding. Unfortunately, administration of topical antiviral agents was a confounding factor in this study.[12]

A recent study looked at the effect of *E. faecium* SF68 on food intake, weight, and metabolic profile in overweight and obese cats. Eight cats received the probiotic for 2 months, and their status was compared to a placebo group. There were no significant differences between the two groups.[13]

Although a probiotic (*Bifidobacterium longum* BF999) is currently marketed for its 'calming' effects, the author is not aware of any peer-reviewed publications describing its positive effects.

Indications for use in cats
Based on the published literature, I feel comfortable using a probiotic (+/- other appropriate treatments, dietary changes etc.) in cats with both acute and chronic diarrhea. Having said that, I regard the probiotic as a low-level adjunctive therapy, and make it clear to the owner that this may be helpful but should not be regarded as a top priority; if adding a probiotic to a food appears to decrease intake, it should be immediately discontinued.

We do not have much information about what happens when we combine a probiotic with an antibiotic. It is likely that most routine antibiotics will inhibit or kill probiotic species, so it may be redundant to administer both together. In one feline study, SF68 (which has been shown to be susceptible to amoxicillin / clavulanate) was given 2hr before the antibiotic to healthy cats in an effort to prevent Ab-associated diarrhea.[14] Although the total fecal score for the cats getting the probiotic was lower, it did not protect against diarrhea or a decrease in diversity of the GI microbiome. However, meta-analyses of probiotics for the prevention of antibiotic associated diarrhea in people do suggest positive effects from certain species of probiotic. *Saccharomyces boulardii* (a yeast) appears to particularly useful for the prevention of *Clostridium difficile*. However, interpretation of the human data is confused by various doses and duration of therapy.

Picking a product

Probiotics are not drugs and are therefore not subjected to close scrutiny. In one study of 19 veterinary "probiotic" products, 5 had no live organisms at all, and the contents of the others all failed to match what was listed on the label.[15] It is therefore very important to use a product from a reputable manufacturer, and one which clearly lists species and strains, along with bacterial numbers (expressed as CFU/dose) and an expiration or best before date. Probiotics incorporated into foods are particularly problematic, as ensuring bacterial survival during routine processing is challenging.[16,17]

Common bacterial species used in probiotics include *Enterococcus faecium*, *Lactobacillus spp* and *Bifidobacterium*. Is one better than another? We simply do not know. In human studies, positive effects have been reported for very specific disorders using named strains or well-defined combinations of organisms. We should not regard these products as interchangeable, and failure to document a positive response with one does not mean that another product will have a similar lack of effect.

I personally have had the best results with products containing *Bifidobacterium*; however, this is hard to grow, due to its strict anaerobic requirements, and it not included in many veterinary probiotic products. There may also be some advantages to products that contain several different species of bacteria, as this may broaden their impact. Products containing prebiotics (i.e., synbiotics) may have some additional benefits, as these ingredients may support the indigenous microbiome even if the probiotic species have little positive effect.

The other issue to consider is dose; in the human field, there is considerable interest in the so-called 'high-dose' products, which provide many more organisms (e.g., 10^{12} v 10^{8}). One such product (VSL#3) is FDA approved for ulcerative colitis and pouchitis. The team at TAMU evaluated at this product in healthy cats and found an expected shift in fecal microbial populations during the administration period.[18] However, this was short lived, and the populations returned to baseline relatively quickly. The product was well tolerated however, and palatability was not an issue.

Summary

It seems likely that manipulations of the GI microbiome and therefore the microbiota impact health and metabolism in numerous ways. However, we are still at the dawn of our understanding of this complex system and have a long way to go before we can reach for probiotic products with confidence. In the interim, they should be regarded as possibly helpful adjunctive therapies for some GI disorders, but their use should not delay the establishment of a definitive diagnosis or replace traditional options for defined disorders.

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Management of Liver Disease

Adam Rudinsky, DVM, MS, DACVIM

General Treatments of Liver Disease1-3

There are a few fundamental roles of therapy for liver disease. First, you must eliminate the inciting or predisposing cause of disease. Second, attempt to provide individualized supportive care to allow time and optimal conditions for hepatic regeneration. And finally, prevent and/or manage hepatic complications if they occur. This approach will allow even the new graduate practitioner to construct a comprehensive plan for their patients.

Hepatoprotectant Medications

Signalment and History

The liver is at the epicenter of the body and as one of the three most important organs in the body (including the pancreas and gut) it is exposed to numerous insults. As a result, the liver has developed both antioxidant mechanisms (enzymatic and nonenzymatic) as well as prosurvival biochemical pathways to help support the liver during periods of oxidative stress. From the clinical standpoint, we are best able to manipulate the enzymatic (catalase, superoxide dismutase, glutathione peroxidase, glutathione transferase) and nonenzymatic (glutathione, vitamin E, beta---carotene, bilirubin) mechanisms of defense. Therefore, you will see the majority of the following drugs used to treat liver disease in some manner affect this area.
You must also remember that the following list of hepatoprotectants are all supportive medications rather than specific cures. The BEST treatment of any liver disease is aimed at the underlying disorder specifically (e.g. PSS shunt correction, antibiotics for bacterial cholangiohepatitis, etc…). These medications are instead use adjunctively with disease specific therapies as well as when there is no specific cure and we as clinicians are limited to supportive care and tincture of time.

S---Adenosylmethionine (SAMe)

SAMe is primarily produced in the liver and is known to be decreased in the majority of experimental models of liver disease. In the liver, SAMe is metabolized in three ways (transmethylation, transsulfuration, and aminopropylation) all of which have hepatoprotective effects. Therefore, we often add this medication to many hepatoprotective therapeutic regimens. It is most commonly available as Denosyl (Nutramax Laboratories) and is dosed at 20 mg/kg/day PO. The medication should be given on an empty stomach and all tablets should be enterically coated. The drug is poorly bioavailable and these are important to maximize absorption. [Side note – there are studies that have examined the relative SAMe amounts in various formulations which showed wide variety and many not meeting label claims! For this reason, remember to always give the formulations that have undergone more testing if at all possible]. When used clinically, this drug has few associated side effects and when they do occur, they most often are gastrointestinal in nature. Overall, current evidence indicates that this is a very safe supplement. Unfortunately, in veterinary medicine we are still lacking high quality studies clearly demonstrating the benefit to this medication and it is often empirical justification.

Silymarin

The mild thistle plant contain an active ingredient called Silymarin. This is a group of flavonoid compounds with antioxidant properties among other hepatoprotective properties. Specifically it is known to inhibit uptake of Amanita mushrooms in the liver and therefore is indicated as an antidote for toxic hepatopathies secondary to Amanita mushroom ingestion. In clinical use this is a safe and well---tolerated supplement. However, it does affect P450 drug metabolism and therefore, other drugs in your patients that typically undergo that type of metabolism should be monitored closely for changes. As you will see is a common theme, there is very limited data in veterinary medicine to support the use of this supplement. Its clinical recommendation comes from empirical evidence, high safety profile, as well as theoretical benefit based on drug mechanism. It is typically dosed at 10---15 mg/kg/day divided into either BID or TID dosing. The most commonly used formulation of silymarin include a combination product with SAMe (Denamarin) or combination product with vitamin E and zinc (Marin). Both of these are produced by Nutramax Laboratories. Additionally, due to the poor bioavailability of this supplement, there is a less commonly used but higher bioavailable complexed form called Siliphos.

Vitamin E

Vitamin E is a variety of antioxidant compounds occasionally used in a hepatoprotectant manner, with alpha---tocopherol being the most active of the family of compounds. Murine and human studies of hepatic diseases have shown a significant benefit with administration. However, direct evidence in our companion animals is still lacking. When used, the alpha---tocopherol

acetate form is dosed at 10---15 IU/kg PO SID. Emulsified formulations also exist for chronic cholestatic patients (vitamin E is a fat soluble vitamin).

N---acetylcysteine
This medication is used as an intravenous supplement of cysteine, which serves as a precursor to increase glutathione levels. It is used in two different clinical situations. It has proven to be very effective in acetaminophen hepatotoxicity specifically. However, the more common use is with hospitalized patients where oral antioxidants listed above are difficult to administer. It is dosed at 140 mg/kg IV initially, then 70 mg/kg QID for a total of seven treatments. This medication is not given orally due to the high incidence of gastrointestinal side effects.

Zinc
Zinc is an important co---factor in many important anti---inflammatory, antiapoptotic and antifibrotic processes in the liver. Zinc is used because it inhibits the uptake of hepatic copper and also as it is known to be low in some inflammatory hepatopathies.

Carnitine
This is an important factor in lipid metabolism in the body. It also plays a vital role in the maintenance of antioxidant systems. The most common use is in cats with hepatic lipidosis. It has been shown to increase lipid mobilization in fat cats. As a result supplementation at 250 mg/cat/day PO has been recommended in hepatic lipidosis cats.
Ursodeoxycholate (Ursodiol)

Ursodeoxycholate is the major bile acid in the bile of the chinese black bear and is known for its minimal hepatotoxicity. All bile acids have some hepatotoxic nature and it has to do with their hydrophobicity. Toxic bile acids disrupt cell membranes and stimulate apoptosis.

Ursodiol, when supplemented, augments the bile acid pool to a friendly gang. This has several cytoprotective effects include less hepatotoxicity, apoptosis inhibition and induction of choleresis. The choloretic properties of ursodiol are from direct stimulation of a bicarbonate rich bile flow in the ducts and also membrane transport mechanisms are upregulated which promote flow.

When used clinically, absorption is enhanced when this medication is given with food. Little information is available on the effectiveness of this medication but we commonly use it for its potential benefits and high safety profile. It is dosed at 10--- 15 mg/kg/day PO.

Immunomodulatory Medications
There is a wide variety of drugs that can be used WHEN INDICATED for immunomodulatory properties in hepatic disease. These should NOT be used empirically under most circumstances. Many veterinarians rely on them as 'go to' drugs but in reality they should only be used when there is a diagnosis or sound justification for their empiric use. The most commonly used immunomodulatory medications in hepatic disease are steroids and chlorambucil. Although others, including cyclosporine, mycophenalate and leflunimide have potential roles. Drug selection should be chosen based on side effects, onset of action and owner acceptance (cost and tolerance of side effects). The first line treatment in the vast majority of cases is prednisone.

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Liver & Biliary System: Peri-Operative Care, Surgical Evaluation, & Diagnostic Sampling

Betsy Swanson, DVM, MS, DACVS - Small Animal

Introduction

Many veterinarians shy away from surgery of the liver and biliary system because of its complexity and risk of significant complications. With some preparation, obtaining diagnostic samples of liver tissue and bile can be safely performed in general practice and can be an invaluable aid in diagnosing liver and biliary diseases in cats. This presentation will discuss presurgical workup, perioperative considerations, common surgical liver diseases, and indications and techniques for obtaining liver biopsies in cats. We will also review normal feline biliary tract anatomy and biliary diseases, how to evaluate the biliary system during surgery, how to collect a bile sample, and when to refer for surgery.

Indications for Hepatobiliary Surgery in Cats

The most common reason to obtain liver or bile samples is to diagnose a medical condition affecting the liver or the biliary system. Information from cytologic, histological, or microbiological testing is then used to guide treatment decisions. The most common hepatic diseases encountered in cats are hepatic lipidosis and inflammatory hepatic diseases, including cholangitis, cholangiohepatitis, and in older cats, lymphocytic portal hepatitis and chronic nonsuppurative cholangiohepatitis. Additionally, a high percentage of cats with cholangitis/cholangiohepatitis are diagnosed with concurrent pancreatitis and/or inflammatory bowel disease (IBD), a condition referred to as triaditis. Necropsy-based studies reported pancreatitis in 50-58% and IBD in 44-83% of cats with cholangitis or cholangiohepatitis, with one study reporting both in 39% of cats examined. A recent study by Center et al. identified pancreatitis in 93% and IBD in 88% of cats with cholangitis/cholangiohepatitis. Illness associated with these conditions may present with vague signs or with signs that overlap with other organ systems. While a complete history, physical examination, bloodwork, and diagnostic imaging lead to suspicion of disease, tissue sampling and examination is necessary for definitive diagnosis.

When less invasive techniques such as fine needle aspirates are non-diagnostic, biopsy can also be used to diagnose hepatobiliary neoplasia as part of oncologic staging and to aid surgical planning. For small or peripheral masses, biopsy can both treat and diagnose the lesion. Metastatic neoplasia, including lymphoma, mastocytosis, hemangiosarcoma, and carcinoma, is more likely to affect feline livers. Diseases where cells easily exfoliate, such as lymphoma and mast cell disease, are amenable to diagnosis via fine needle aspirates and cytology but may be identified through liver biopsies taken during an abdominal exploratory for other reasons. In all cases, liver biopsy is an important tool in staging the extent of disease.

Primary liver tumors are infrequent in cats and can be of biliary, hepatocellular, mesenchymal, or neuroendocrine origin. Tumors of the bile ducts are the most common primary hepatobiliary tumor encountered in cats. Biliary cystadenomas are benign and have a good prognosis with complete excision, while biliary carcinomas are associated with a high rate of metastasis and 100% perioperative mortality. Hepatocellular tumors account for 9%-24% of feline primary hepatobiliary neoplasms. The majority of these are benign hepatocellular adenomas, and excision is typically curative. Feline hepatocellular carcinomas are uncommon but are reported to have a 25% metastasis rate. Mesenchymal and neuroendocrine tumors are less commonly encountered (occurring 9%-14% and 4%, respectively) and carry a poor prognosis. Of the primary tumors of mesenchymal origin, hemangiosarcomas are the most common and are associated with high perioperative mortality (71%) and a short median survival time (77 days). Rare primary leiomyosarcomas, rabdomyosarcomas, osteosarcomas, and fibrosarcomas have also been reported. Neuroendocrine carcinoma is mostly found disseminated along the bile ducts and occasionally on the gall bladder. It has often metastasized at the time of diagnosis. However, one report found a longer median survival time following complete excision via cholecystectomy for masses isolated to the gall bladder.

Fine needle aspiration of bile from the gallbladder is indicated in cases of suspected inflammatory hepatic disease and cholelithiasis. For cats with cholangitis or cholangiohepatitis, culture of the bile is significantly more likely to result in positive culture than culture of the liver. [Wagner 2007] Cholelithiasis has been associated with infection in cats; thus, bile culture is warranted when noted. Very small choleliths measuring 3 mm or less that obstruct the major duodenal papilla have been reported to cause signs similar to pancreatitis and may be associated with triaditis. (Center)

Other surgical hepatobiliary diseases reported in cats include hepatic abscess and gallbladder mucocele. Referral for surgical treatment is recommended.

Perioperative Care

General Considerations

Cats with liver disease are often critically ill at the time of presentation. Perioperative care includes patient stabilization, identification of comorbidities, addressing the effects of liver dysfunction, and postoperative pain management. Patients with severe hepatobiliary disease may show signs of hepatic dysfunction including an increased risk of hemorrhage due to decreased production of clotting factors, hypoproteinemia (particularly albumin) from impaired protein synthesis, and impaired drug metabolism especially of opioids. Patients are often unstable under anesthesia and in critical condition postoperatively, requiring constant monitoring and advanced care. Surgeons and anesthetists should be prepared to administer blood products in response to hemorrhage, manage hypotension, and be able to recognize the signs of opioid overdose.

Pre-Operative Workup

Laboratory:

Preoperative work up should include a CBC, serum chemistry, PT/PTT, and urinalysis. While it is rare to encounter life-threatening hemorrhage from a biopsy or fine needle aspirate of the liver, it is prudent to type +/- cross-match the patient's blood prior to surgery in case transfusion is needed.

Imaging:

Imaging of the hepatobiliary system may include radiographs, ultrasound, CT, or MRI. Radiographs are useful for determining liver size and for identifying large masses and cholelithiasis. Ultrasound of the liver allows for evaluation of the liver parenchyma and visualization of the biliary tree. It is excellent for identification of discrete masses, but less so for diffuse disease. Color flow Doppler is used to evaluate hepatic vasculature and blood flow through the liver. Ultrasound alone cannot reliably diagnose the type of disease present. New technologies, such as contrast enhanced harmonic ultrasonography, are emerging that are able to differentiate benign and malignant neoplastic lesions. When evaluating the biliary system with ultrasound, it is important to follow the common bile duct to the level of the major duodenal papilla to evaluate for biliary obstruction from choleliths, tumor, or pancreatitis as part of a complete evaluation. The normal width of the common bile duct in cats is 3-4 mm. To differentiate between ductal dilation from an active obstruction and chronic dilatation after an obstruction has cleared, the biliary tree should be evaluated over several days. Increasing dilatation indicates a current obstruction. In general, the common bile duct will distend within the first 48 hours of obstruction and the intrahepatic ducts will start to distend by one week after obstruction. Most choleliths are echogenic with acoustic shadowing. Ultrasound alone is unable to determine if the duct is patent at the site of a stricture. Advanced imaging, particularly computed tomography, may be used to determine the size and location of a mass for surgical planning. Studies to date show no difference in the ability of CT and ultrasound to differentiate between benign and malignant tumors. Magnetic resonance imaging has been tested in dogs for this purpose with promising results.

Non-surgical tissue sampling:

Ultrasound-guided fine needle aspiration and cytology of the liver is indicated for diagnosis of discrete solid or cystic hepatic lesions, diffuse hepatic disease, and bile abnormalities. It is simple to perform and has a low risk of complications. Accuracy of diagnosis is poor, however, and is reported to be around 50%, except in cases of visceral mast cell disease and lymphoma. Ultrasound-guided needle core biopsy obtains a larger sample for histopathological evaluation and provides an accurate diagnosis in 48%-83% of cases. There is a greater risk of complications including hemorrhage that may require treatment or death. The greatest risk of bleeding is associated with thrombocytopenia and an increased APTT. Care must be taken to avoid major blood vessels and bile ducts. Vagotonic shock and death has been reported after the use of a rapid fire automatic biopsy needle in cats, especially those with extrahepatic biliary obstruction. Because of this, biopsy needles with an automatic or mechanical firing mechanism should not be used. FNA and needle core biopsies should not be used on cavitated lesions because of the increased risk of rupture and life-threatening hemorrhage.

Sedation and Anesthesia

Patients with severe liver or biliary disease will have difficulty processing many drugs that are metabolized in the liver. This can easily lead to an overdose of these drugs, even at appropriate doses. Therefore, drugs commonly used for sedation and anesthesia such as benzodiazepines and opioids should be used cautiously or avoided altogether. Dosages may be modified by decreasing the dose or increasing the intervals between doses. Propofol, although metabolized in the liver, is considered safe for induction in for patients with liver disease. Isoflurane or sevoflurane are the preferred inhalant anesthetics.

While under anesthesia, anesthetists should be prepared to provide manual or mechanical ventilatory support in patients with large masses that impede movement of the diaphragm. Likewise, cardiac arrhythmias, particularly ventricular premature

contractions, accelerated idioventricular rhythm, and ventricular tachycardia may develop after removal of a large abdominal mass. Clinicians should be able to recognize these arrhythmias and understand when and how to treat them.

Perioperative Antibiosis
Broad-spectrum antibiotics that cover enteric bacteria as well as anaerobes, such as cefoxitin or ampicillin/sulbactam, are appropriate for perioperative antibiotic administration. Aerobic, strict anaerobic, and facultative anaerobic bacteria have been cultured from healthy livers. The most common bacteria isolated from the livers of patients with suppurative hepatobiliary disease include *E. coli*, *Enterococcus* spp, *Bacteroides* spp, and *Clostridium* spp. If cholangitis, cholangiohepatitis, or other infection is suspected, broad-spectrum antibiotic coverage should be continued postoperatively pending culture and susceptibility results.

Surgical Approach
General Considerations
For the most accurate diagnosis, hepatic biopsy samples must include at least 3-12 complete portal triads. Samples for histopathological evaluation should be obtained from two different lobes, even in cases of apparent diffuse disease. An open surgical approach via a midline celiotomy is readily available to all clinicians and provides the largest tissue specimens. Biopsies can be easily obtained concurrently with other abdominal procedures. Liver biopsies are most often obtained using guillotine, wedge, or punch biopsy techniques. With the development of smaller laparoscopic instrumentation, laparoscopic liver biopsy can be safely and effectively performed in cats. Generally, 5 mm instruments and scopes can be used for larger cats, and the newer 3 mm instrumentation for smaller cats. It is necessary to collect multiple samples from at least two different liver lobes to obtain an adequate amount of tissue for diagnosis. There is good correlation in diagnosis between laparoscopic and open liver biopsy samples.

Anatomy of the Feline Liver
The feline liver has six lobes that are grouped into three divisions. The left division consists of the left lateral and left medial lobes, the central division consists of the quadrate lobe and the right medial lobe, and the right division consists of the right lateral and caudate lobes. The clefts between the left lateral and medial lobes and the left medial and quadrate lobes are complete, providing easier access to the hilus of each lobe. The lobes on the right side have partial clefts, and the lobes are fused proximally. Additionally, the caudal vena cava runs through the parenchyma of the right medial and caudate lobes before passing through the caval foramen into the thoracic cavity. The liver is attached to the diaphragm by the left and right triangular ligaments. Caudally, it is held in place by the hepatorenal ligament, the hepatoduodenal ligament, and the hepatogastric ligament. The hepatorenal ligament connects the caudate lobe to the right kidney. The hepatoduodenal ligament and hepatogastric ligament are formed from the lesser omentum and connect the porta hepatis to the duodenum and lesser curvature of the stomach, respectively. The majority of the liver lies to the right of midline. The cranial pole of the right kidney nests into the renal fossa of the right lateral lobe. The stomach abuts the left lateral and medial lobes.

Vasculature of the liver may vary between individuals, but generally consists of afferent flow from the portal vein and hepatic artery and efferent flow from the lobar veins into the caudal vena cava. The portal vein provides 80% of the blood flow to the liver, and the hepatic artery provides 20%. Each carries about 50% of the oxygen supply for the liver. The portal vein in cats divides into three branches that supply each respective division of the liver. The hepatic artery forms branches that supply each liver lobe and the cystic artery of the gall bladder. A lobar vein drains each liver lobe and may join with adjacent lobar veins before emptying into the caudal vena cava in a spiral, with the right divisional branches entering most caudal, and the left divisional branches entering cranially near the diaphragm.

Anatomy of the Feline Biliary System
Bile flows from canaliculi into the interlobar ducts and then the lobar ducts. These become the hepatic ducts once they exit each lobe. The hepatic ducts empty into the common bile duct, which runs caudally through the hepaticoduodenal ligament to the duodenum. Once entering the wall of the duodenum, the common bile duct runs obliquely aborad before joining with the pancreatic duct. The common bile duct and pancreatic duct empty together at the greater duodenal papilla. Current thinking holds that this is a likely reason for the high frequency of triaditis in cats. The gallbladder sits at the opposite end of the common bile duct and is connected via the cystic duct. The location where the first hepatic duct enters the common bile duct is the delineation between the cystic and common bile ducts. The gallbladder stores bile between meals. Eating stimulates the gallbladder to contract, which then excretes the bile through the cystic duct and the common bile duct into the duodenum. The hepatic ducts, common bile duct, cystic duct, and gallbladder form the extrahepatic biliary tract.

Surgical Evaluation of the Hepatobiliary System

The liver is approached through a midline abdominal incision from the xyphoid to the pubis via the linea alba. A balfour retractor is placed to hold the abdominal incision open. Either the spoon from the Balfour retractor or the blade of an Army-Navy retractor or Senn retractor, depending on the size of the cat, can be used to elevate the xyphoid process. This allows easier visualization of the entire liver. A hand can be placed between the liver and diaphragm to retract the liver caudally, allowing for evaluation of the cranial surfaces of each lobe. Then the caudal (visceral) surface of each lobe is evaluated while pushing the liver cranially to reveal the porta hepatis. The appearance, thickness, and texture of each lobe should be noted. The lobes should be palpated to note any masses or soft areas within the parenchyma.

The normal liver has a uniform, deep red color. The lobar surfaces are smooth and the edges are sharp with variable notches. The texture of the parenchyma should be firm. The appearance of a diseased liver will depend on the disease process. Lesions may affect the liver diffusely or affect only some lobes and not others. Inflammatory hepatic disease causes the affected liver lobe(s) to become plump with rounded edges. The notches at the edges of the lobes are usually no longer evident. The color of the parenchyma can be red, but often is paler than a healthy lobe. Significant cholestasis can give the lobe a tan or yellow tinge. The texture of the lobe is still firm, but the capsule or parenchyma may be more friable and bleed easily. Hepatic lipidosis gives the liver a distinctive appearance. The lobes are plump with a characteristic tan or yellow reticulated pattern. Liver masses are typically distinct and easy to identify. The specific appearance varies based on size and type of tumor. It is important to note that physical characteristics may overlap and it is not generally possible to identify benign versus malignant pathology based on appearance alone. An end-stage, cirrhotic liver, appears diffusely nodular from attempts at regeneration and feels tough and rubbery. Because of the nodular appearance, a cirrhotic liver can be confused with hepatic neoplasia.

The gallbladder is located in a fossa formed between the quadrate and right medial liver lobes. To visualize the entire extrahepatic biliary tract, the gallbladder is displaced cranially. This exposes the porta hepatis and straightens the common bile duct. The hepatic, cystic, and common bile ducts should be identified and any changes noted. The normal gallbladder wall is thin and pale to green in color. It is not uncommon to find bilobed gallbladders in cats. This and the rare trilobed gallbladders are considered normal variations. The gallbladder is typically full in surgery in fasted patients but it should not feel turgid when palpated. A gentle squeeze should easily express bile from the gallbladder. No distension of the bile ducts will be observed if bile is able to flow freely into the duodenum. Distension of the extrahepatic bile ducts indicates obstruction. Damage or stricture of the duct may be noted. The presence of bile indicates rupture of the biliary tree. Gall stones appear as dark objects visible through the thin walls of the bile ducts. The gallbladder wall may be thickened in cases of cholangitis.

Surgical Techniques for Diagnostic Sampling of the Hepatobiliary System

After completing a thorough abdominal exploratory, the liver can be displaced caudally by either having an assistant place a hand between the diaphragm and liver and gently push the liver caudally or placing one or two moistened laparotomy pads between the diaphragm and liver.

Guillotine Technique

Identify the desired biopsy site. The natural notches at the edge of a lobe are excellent points to catch the suture as it is tied around the tip of the lobe. If the lobe edge is rounded and no notches are present, Mosquito hemostatic forceps can be used to crush the tissue at the desired location. A loop of 3-0 PDS or Vicryl is formed, and then is placed over the tip of the lobe to the level of the notches. The suture is then pulled tight, catching at the notches so that it doesn't slip off. The suture should cut through the liver parenchyma to tighten around the vessels and bile ducts deep in the tissues. Then the remainder of the knot is tied. The biopsy is transected using either a scalpel or Metzenbaum scissors, leaving a stump distal to the ligature so that it doesn't slip. An empty suture packet can be placed under the sample during transection to act as a cutting board. A piece of Gelfoam can be placed on the cut edge to control oozing. Any significant bleeding should be addressed by placing a new ligature or placing hemoclips on visible bleeding vessels.

Wedge Technique

The wedge technique is essentially a partial liver lobectomy technique that can be used both to remove peripherally located tumors and obtain biopsy samples of the liver. Full thickness interrupted mattress sutures are placed through the liver parenchyma starting at the lobe's edge and continuing in an overlapping pattern (like a chain) across the lobe. The sutures are tightened so that they cut through the parenchyma and tighten around the deep vessels and ducts. The tissue is then transected using Metzenbaum scissors. Minor veinous oozing can be controlled by placing a piece of Gelfoam at the excision site.

Punch Biopsy Technique
The punch biopsy technique is useful to biopsy superficial lesions in the body of the liver lobe. A 4 or 6 mm Baker Skin Biopsy Punch is used to obtain samples. The depth of the punch should not exceed 50% of the lobe thickness to avoid lacerating the deep blood vessels. Hemostasis is obtained by placing a piece of gelfoam into the biopsy site and applying manual pressure with a sterile 4x4 gauze.

Laparoscopic Liver Biopsy
Either a multiple-port or single-port technique can be used to enter the abdomen. After placing ports and examining the abdominal cavity, 5 mm biopsy forceps are used to obtain samples from the periphery of two different liver lobes. At least two samples should be obtained for histopathology. The biopsy forceps are closed over the parenchyma, held tight for about 5-10 seconds, and then twisted to separate from adjacent tissue. This method has been demonstrated to provide good samples with minimal bleeding. Gelfoam can be placed over the biopsy sites. The area should be monitored to ensure that bleeding has stopped before exiting the abdomen and closing.

Bile Aspiration from the Gallbladder
A 3 cc sterile syringe with a 25 or 23 gauge hyperdermic needle is used to puncture the gallbladder at it's apex. Bile is carefully extracted. A sterile gauze or cotton tipped applicator is placed over the needle at the puncture site while the needle is removed to prevent leakage of bile. A piece of gelfoam can be moistened and placed over the puncture site to help seal over the puncture. Care must be taken to avoid laceration of the gallbladder wall.

Postoperative Care
Veterinary teams should be prepared to manage a critical patient postoperatively. Generally the patient should be on IV fluids, blood pressure, heart rate, pulse quality, should be monitored at regular intervals along with vitals. Pain management should be monitored closely to avoid opioid overdose if liver function is compromised. A PCV should be checked after surgery and at least 12 hours later to monitor for postop hemorrhage. The author prefers to position the patient in sternal recumbency during the recovery period. The body weight helps to tamponade any minor bleeding from the biopsy site.

Recommended Reading

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Interpreting Liver Biopsies

Adam Rudinsky, DVM, MS, DACVIM

Do you need a liver biopsy?

Liver biopsy can be a daunting diagnostic in the eyes of cat owners. Regardless of the merit of liver biopsy, it is still a difficult step for many clinicians to recommend and even more so for owners to consent to for their pet. Liver biopsy is also not a one size fits all diagnostic. It has definitive value in establishing definitive diagnoses (e.g. neoplasia, inflammatory liver disease) and treating conditions (e.g. vascular shunts, EHBDO, masses). In addition to these perceptions of liver biopsy, it is also typically a higher cost diagnostic. However, regardless of these reasons for hesitation, liver biopsy and associated surgery presents an opportunity to obtain samples for mineral quantification, culture samples, and lesion removal. Furthermore, once the diagnosis is achieved, the liver biopsy (or repeat biopsy) may help guide treatment decisions and provide prognostic information which can be relayed to the owner. This is, on the condition, that the biopsy is interpreted correctly and maximally including an assessment of the structural integrity of the liver tissue, the type and degree of injury, and the patient's response to that injury.[1, 2]

Contraindications to a liver biopsy?

The primary contraindications for liver biopsy are routine risks for clinical patients. Most notably, if a cat has a high risk of bleeding during the procedure, is not a good anesthetic candidate, or has acute hepatobiliary disease (most of the time) liver biopsy is not advisable. Lidbury JA. VCNA 2017 provides more specific criteria for liver biopsy contraindications:

- Platelet count less than 80,000/mL
- Buccal mucosal bleeding time greater than 150 seconds for cats
- Prothrombin or activated partial thromboplastin times greater than twice the upper limit of the reference interval
- Plasma fibrinogen concentration less than 50% of the lower limit of the reference interval
- Infectious disease that could be disseminated by biopsy
- Presumed hemangiosarcoma (excisional biopsy may be possible)
- Ascites (relative contraindication; try to treat first)

Despite the potential complications, when appropriate patient selection is implemented, the risk associated with liver biopsy is minimal. The main safety data available for cats is from a retrospective study including 124 cats undergoing ultrasonography-guided percutaneous hepatic and renal biopsies.[3] In this study, minor bleeding occurred in 22% (all animals) and major bleeding occurred in 6% of all animals. Complications were less common with liver biopsy compared to renal biopsy. Bleeding was less likely in patients undergoing hepatic biopsy than renal biopsy. Bleeding was more likely when cats had prolonged coagulation times.

Understanding sample handling, biopsy quality, additional testing, and technique

The first step in maximizing the utility of your liver biopsy starts with strategic sampling, appropriate sample handling, and diagnostic selection. As a rule of thumb, it is best to get three liver biopsies from three separate areas within the liver. Sampling error (missing lesions) is common in liver biopsy interpretation if multiple varied biopsies are not submitted. This is because many diseases are heterogeneously distributed in the liver with variation between liver lobes. The clinician can minimize this impact and maximize identification of histologic lesions by submitting multiple samples.

Size also matters when biopsying the liver. Studies in dogs have shown at minimum 3 to 12 portal triads are necessary for accurate histopathologic interpretation by the pathologist.[4] The standard recommendation is to have at minimum the high end of this range (12 portal triads). Unfortunately, similar data is not published in cats and therefore is currently extrapolated from data in dogs. Regardless, a good liver pathologist will provide a number of triads evaluated and an adequacy of biopsy statement in the report. This provides an indicate to the clinician on the reliability of the diagnostic results.

Clinicians should also strategically biopsy gross lesions to maximize results. For example, a solid, parenchymal liver mass in a cat should ideally be completely excised. Once excised (or if complete excision is not possible) peripheral lesions should be submitted to avoid potential necrotic tissue at the center of the lesion. Another example is how biopsy of different tissues can affect mineral analysis.

The last consideration is ensuring that the samples are submitted promptly, appropriately submitted in formalin or other fixatives depending on testing, and with all ancillary diagnostics requested. In feline hepatology, this usually consists of special panel of stains (copper with rhodanine or rubeanic acid, staining for iron (hemosiderin) with Prussian blue, staining for lipofuscin with Schmorl stain, and staining for collagen/connective tissue with Masson trichrome or Sirius red), culture of bile +/- liver tissue, as well as tissue for mineral analysis. Additional testing like IHC can be submitted after preliminary results are reported from the pathologist.

Finally, the person that is reading the biopsy also impacts the repeatability of the results. Since the lvier is a complicated organ, it is advisable to submit to a specialty liver histopathology service. This is a well-recognized concern in human medicine and a major reason for specialty hepatopathologists. Multiple veterinary histopathology services offer specialty assessment of liver tissue. This will also enhance the relationship with the pathologist and the integration of the clinical history for the interpretation. Communication between the clinician and the pathologist is vital for a successful outcome, particularly in challenging cases.

Clinical Correlation

As the clinician ordering the biopsy, it is important to integrate the complete clinical picture with the histopathologic diagnosis and ancillary testing results. The lecture will discuss case example and features of biopsies that clinicians can use to maximize the diagnostic results. However, to do this it is helpful to understand basic hepatic anatomy and histopathology. Particularly, the language used by histopathologists (per WASVA recommendations) are sometimes at odds with colloquial language regarding primary disease processes. For example, cholangitis is defined as inflammation of the large bile ducts and is the preferred term by the WSAVA in cats. This disease can have different recognized subtypes (e.g. neutrophilic cholangitis). Alternatively, cholangiohepatitis is defined as extension of cholangitis into the adjacent hepatic parenchyma and beyond the hepatic limiting plate. However, this term is not recommended by the WSAVA as a name for a specific disease . It is advised to be used specifically to describe histopathologic findings.

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The Feline Philosophy Behind Diagnosing GI Disease

Craig Webb, PhD, DVM, DACVIM

Introduction

If our patients read textbooks our job would be much easier. If our patients came to us with Presenting Complaints such as "GI eosinophilic sclerosing fibroplasia", or "low-grade alimentary lymphoma" our job would be much easier. If our patients restricted themselves to one disease at a time, our job would be much easier. If our patients segregated themselves such that the positive predictive value of our diagnostic tests were through the roof, our job would be much easier. And if our prescribed therapy never failed, our job would be much easier. Our job is not very easy. But there are some fundamental philosophical principles that can serve as a foundation for us; a number of them will be discussed, others are highlighted in these proceedings.

Specific Philosophical Principles that will be discussed using clinical case examples include:

1) By failing to prepare, you are preparing to fail
2) Doubt the conventional wisdom; verify with reason and experiment
3) We are not makers of history. We are made by history
4) Don't jump to conclusions; there maybe a perfectly good explanation for what you just saw
5) Elementary, my dear Watson
6) One finger in the throat and one in the rectum makes a good diagnostician
7) Do you believe in magic?

The Appointment

When a client pays for an appointment they are paying for the clinical expertise of the veterinarian (well, that and the electricity, the receptionist's salary, the mortgage on the building, etc.). The clinical expertise of the veterinarian has a profound impact on how much more the client will pay on diagnostic testing, how effectively and efficiently a diagnosis is identified, and the likelihood the patient leaves the appointment with the correct diagnosis and the appropriate treatment. But even the best clinicians encounter diagnostic dilemmas where the presenting complaint or the clinical signs scream for one diagnosis while much softer signs suggest an alternative interpretation. The gastrointestinal tract offers a number of interesting examples to consider. The gastrointestinal tract also highlights the concept that failed therapy does not mean failure. Instead, failed therapy often represents an important diagnostic clue and if considered thoughtfully, will likely have a significant and beneficial impact on case management.

Additional Basic Principles in Practice

- Verify the Problem: Define the Problem
- Signalment, Presenting Complaint, History, Physical Examination
- Diagnostic tests are only as good as you are
- Treatment: Know your drugs before you use them
- Cats are not Small Dogs
- Cats and Concurrent Diseases go together

Understanding Cognitive Medical Errors in an effort to understand yourself.

A cognitive error is defined as an error in clinical reasoning due to lack of or erroneous knowledge, data gathering, or synthesis (Canfield et al. JFMS, 18:240-247, 2016).

Bias, in its many forms, is the factor that most often contributes to cognitive errors. The following table of common biases and their relationship to cognitive error is adapted from Canfield et al. JFMS, 2016, Table 1 (with permission).

> Confirmation bias: tendency to search for, interpret, focus on and remember information in a way that confirms one's preconceptions about a case
>
> Anchoring bias: tendency to rely too heavily on one trait or piece of information

Gambler's fallacy: tendency to think that the probability of a cat having a particular diagnosis or prognosis is influenced by preceding but independent cases.

Availability bias: tendency to overestimate the likelihood of events that have a greater 'availability' in memory.

Feedback bias: tendency to interpret any feedback in the context of personal attitudes instead objective and measurable facts.

Overconfidence bias: Confident diagnosis based on a belief of infallibility.

Omission bias: tendency towards diagnostic "inaction" because of lack of confidence or fear for owner consequences if diagnosis is serious or terminal illness.

Hindsight bias: false confidence in future diagnostic ability based on retrospective confirmation of correct diagnosis, i.e. ignoring the previous diagnostic challenges faced in "real time"

Visceral bias: tendency to harbor negative (or positive) feelings towards owner (or breed), which may result in a diagnosis being missed or ignored

Shared information bias: tendency for group members to spend more time discussing familiar or shared information than is spent working through information that is not shared by all group members.

It is important to take time for "metacognition": to think about how you think (Canfield & Malik, JFMS 18: 2016). This will help you to avoid, or at least better understand those times when you make cognitive errors. Canfield et al. offer the following metacognitive strategies for managing cognitive errors.

Develop an understanding of common cognitive errors (above).

Reflection, review problematic cases, personal bias, and decision-making process

Assess the Big Picture and accept uncertainty

Take time or make time for review, and objectively review results that agree, and disagree, with a presumed diagnosis.

Consider alternative diagnoses.

Acknowledge the emotional component to clinical performance.

Be openly accountable and seek constructive feedback as well as advice

Develop checklists based on difficult cases for future direction.

Suggested Reading

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The Feline Pyramid of Poop

Craig Webb, PhD, DVM, DACVIM

Introduction

Clinical signs associated with the gastrointestinal tract - diarrhea and vomiting being the most outwardly obvious, with weight-loss and a change in appetite frequently present - are one of the most common reasons a feline is brought to the veterinary clinic. Cats are complex creatures and there are a myriad of reasons why a cat might present to you with diarrhea, but Albert Einstein encourages us to attempt to fashion our approach to these patients by making them as "simple as possible, but no simpler." The approach to feline diarrhea can at least start with some relatively simple assumptions, and by following a few horizontal (i.e. age) and vertical (i.e. clinical severity) trends, create a "pyramid" approach to the diagnosis of diarrhea in cats.

Rule #1

Rule #1: the clinical signs consistent with primary gastrointestinal disease also happen to be the same clinical signs that are consistent with secondary, non-gastrointestinal disease.

Starting at the Base

The most prevalent causes of diarrhea in kittens are parasitic and infectious. Fortunately, the vast majority of these causative agents can be found within the diarrhea. Unfortunately, many of these agents can be found in formed stool as well, not causing much of anything. Regardless, after obtaining a complete and compelling history, and after performing a razor-sharp physical examination (both are of critical importance in these cases), a very logical next-diagnostic-step is to pick apart the poop.

Fecal Examination

Direct Fecal Smear: Feces: the fresher the better, "match head" amount, a drop of 0.9% saline, warm the slide, apply cover slip, examine under 100X & 400X [consider second slide with dilute iodine added to cover slip edge]. Although this is easily performed and very rewarding if a tritrichomonas darts by or a Giardia trophozoite falls leaflike to the bottom of the slide, in the vast majority of cases fecal examination should involve centrifugation. There are any number of great resources for fecal flotation procedures (Todays Veterinary Practice; https://todaysveterinarypractice.com/todays-technician-diagnosis-of-internal-parasites). A particularly useful resource for those of us who did not pass this portion of the NAVLE exam is the Companion Animal Parasite Council (capcvet.org). CAPC is a free, user friendly, and very useful website than includes, for example, an article on "Avoiding common pitfalls in fecal examinations," and a diagram of the *Isospora felis* life cycle!

It is beyond the scope of this presentation to adequately review the numerous diagnostic tests used to further delineate who is or is not present in the poop (e.g. Zn-sulfate centrifugation for Giardia; culture techniques for Tritrichomonas (In-Pouch), or Salmonella & Campylobacter; fluorescent antibodies for Giardia; acid-fast for Cryptosporidium; ELISAs for enterotoxins and viruses; PCR for Tritrichomonas & Giardia; serology, immunohistochemistry, fluid analysis, and PCR for FIP, etc.), the most effective deworming strategies, or the optimal treatments…or non-treatments for those differentials that form the very broad base of our poop pyramid. This base is dominated by younger, otherwise healthy patients, a number of whom may have a self-limiting problem (when's the last time set up a Drs. appt for a day or two of diarrhea?). With the advent and popularity of diagnostic panels utilizing the most advanced technology available (e.g. "Diarrhea PCR Panels") the clinician is likely able to find most any organism they might want to find in the poop of most any patient. Warning: Presence does not equal Responsibility. This highlights an important statistical concept for the clinic floor. Positive Predictive Value (the probability that a cat with a positive test result truly has the disease) is dependent on the prevalence of the disease in the population that's being tested. The presence of the disease in the population you decide to test depends on…YOU! Have you done your due diligence as a clinician, whether by script recognition or clinical reasoning, to arrive at a clinical diagnosis before ordering the diagnostic test?

What are we most often looking for within the foundation of our poop pyramid?

Parasites: *Tritrichomonas, Giardia, Cryptosporidium, Coccidia*, Roundworms, Hookworms

Bacteria: *Clostridium, Campylobacter, Salmonella*

Viral: Panleukopenia, Enteric coronavirus, FIP, FeLV

Moving Up the Pyramid

As we move up the pyramid our patient population starts to age, and their diarrhea starts to present as a more chronic problem, in general. This next level is dominated by diet. Starting with the vocabulary:

Chronic enteropathy: GI signs present for > 2 weeks

Food-responsive diarrhea, Diet-sensitive enteropathy, Adverse food reaction

Food allergy or Dietary hypersensitivity: Immunologic response to an antigen

Food intolerance: Nonimmunologic reaction, enzymatic, idiosyncratic, pharmacologic

Dietary indiscretion or Intoxication: Garbage gut, fungal toxins, etc.

The dietary intervention that may be useful in these patients includes a wide variety of choices and geared towards the most likely diagnosis. An "upset tummy" or "sensitive stomach" might respond to an 'easily digestible' diet; large bowel diarrhea (colitis) might warrant a high fiber diet; a food allergy requires a hypoallergenic or hydrolyzed diet; a specific-ingredient food intolerance may explain the response to a "boutique" diet that happens to be devoid of the offending ingredient.

For young adult, otherwise healthy cats presenting for chronic enteropathy, diet actually becomes a critical diagnostic test. If a cat has GI signs are due to a food allergy the diagnostic test of choice is a 2-week diet trial using a true hypoallergenic or hydrolyzed diet – there is no other diagnostic test that will reliably identify this etiology (dermatologic signs, if present, may take months to respond to a diet trial).

Approaching the Peak of the Pyramid

As we climb to the top of our poop pyramid we most often encounter the question, does this cat have inflammatory bowel disease (IBD) or GI lymphoma? At this level the cats are often a bit older, the problem more chronic and often impacting the cat systemically (e.g. weight-loss, decreased appetite, lethargy, etc.). As we move up the poop pyramid non-GI or secondary causes of the same clinical signs become more relevant; hyperthyroidism, diabetes, cholangitis, pancreatitis, etc., and a thorough extra-GI work-up is recommended.

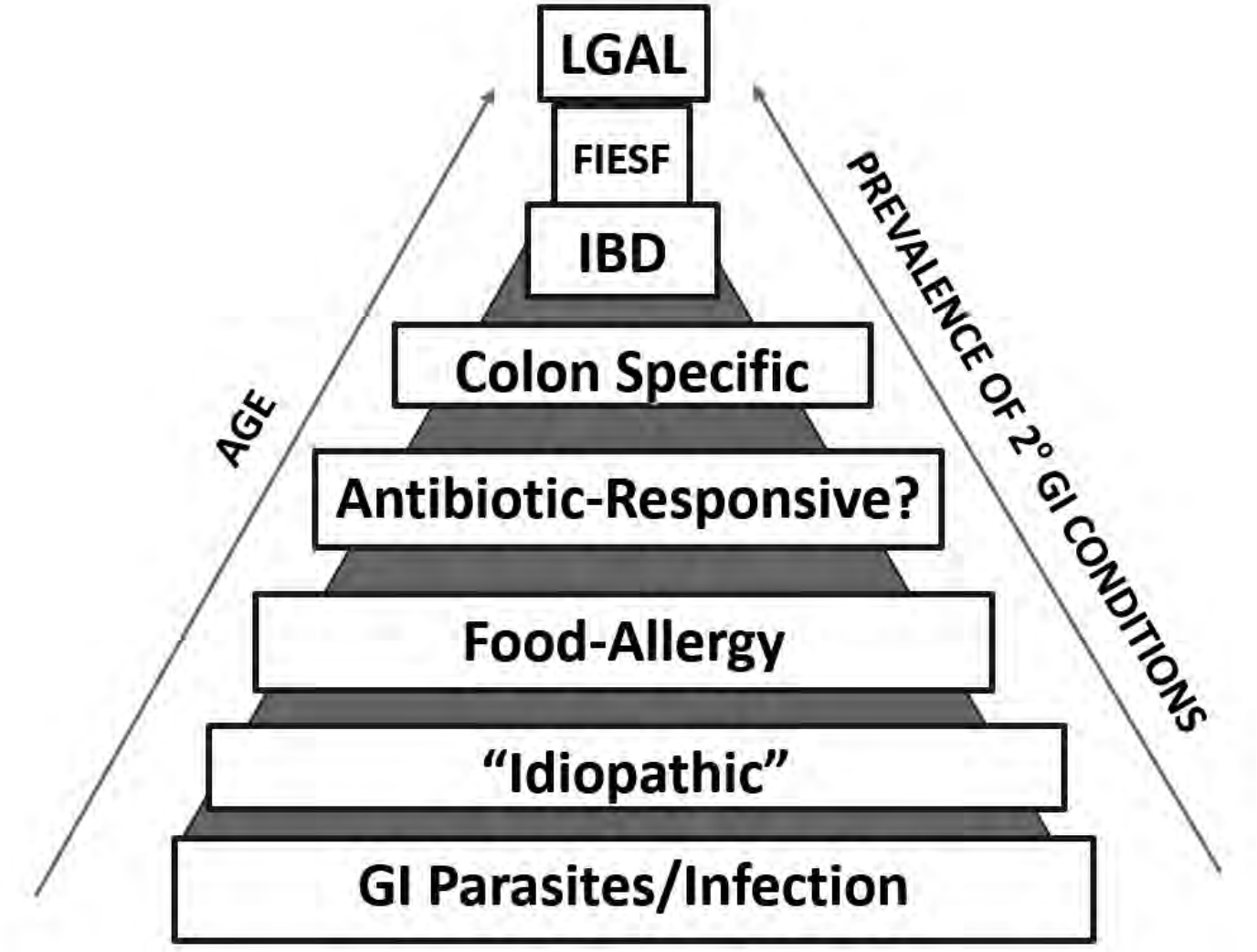
By definition, IBD is a histopathologic diagnosis, meaning the clinician would need tissue from the patient. The definition of GI lymphoma is seemingly obvious, but diagnostic challenging, even with histopathology. An important distinction is between B-cell and T-cell lymphoma, with B-cell having a very poor prognosis. Fortunately the majority of cats with GI lymphoma are T-cell, or small cell, or low-grade, GI lymphoma. If the clinician is able to obtain biopsy samples, we can now go beyond histopathology and utilize molecular testing, including PARR (PCR for antigen receptor rearrangement), immunohistochemistry (IHC), and flow cytometry. All three are efforts to identify clonality, and at CSU we often find it helpful to incorporate this technology for further clarification. (Available from Dr. Anne Avery, CSU Clinical Immunology Laboratory, http://csu-cvmbs.colostate.edu/academics/mip/ci-lab).

The treatment of these cases includes dietary intervention (hypoallergenic/hydrolyzed for IBD, probably the case for GI lymphoma but not well established), prednisolone or budesonide, and then, for GI lymphoma (T-cell), chlorambucil appears to be key (2 dosing regimens that show similar outcome: 2 mg every other day, or 20 mg/m2 once every two weeks). Chlorambucil can be expensive, less so if using a compounding pharmacy, but with the uncertainty inherent in any compounded medication.

Welcome to the top of the poop pyramid.

Rule #2

Rule #2: Sometimes the pyramid is upside down!



[FIESF: Feline Intestinal Eosinophilic Sclerosing Fibroplasia]

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No Way Out! Constipation, Obstipation, Megacolon: Panel Discussion
Adam Rudinsky, DVM, MS, DACVIM, Betsy Swanson, DVM, MS, DACVS (Small Animal) & Craig Webb, PhD, DVM, DACVIM

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Diagnostic Testing in Feline Chronic Enteropathy Demonstrates Evolution from Inflammatory Bowel Disease to Intestinal Lymphoma

Anne Avery, VMD, PhD

Introduction

Diagnosing a cat showing signs of chronic enteropathy poses a challenge for practitioners. After ruling out infectious and parasitic causes, food-responsive enteritis and systemic diseases causing gastrointestinal signs, intestinal biopsies are obtained by endoscopy or exploratory laparotomy, and this is where the challenge begins. The three most common histologic diagnoses are:

1. Lymphocytic plasmacytic enteritis (LPE) - a specific subtype of inflammatory bowel disease,
2. Suspicion of intestinal lymphoma due to an increase in intra-epithelial or lamina propria lymphocytes,
3. Definitive small cell intestinal T-cell lymphoma, also known as SCL or low-grade alimentary lymphoma (LGAL) in the literature. (Stein et al., 2010) (Moore et al., 2012) Pathologist confidence in a definitive diagnosis of lymphoma varies, and multiple pathologists can interpret the same biopsy differently. (Briscoe et al., 2011) Additional objective information about the disease process would be useful for determining prognosis and treatment.

Cats develop other forms of intestinal lymphoma, including B-cell and large-cell granular lymphocytic lymphoma. However, these two forms typically present with more dramatic clinical signs, are more straightforward to diagnose by histology, and have poorer outcomes. Therefore, this talk will focus on the complexities of diagnosing small cell intestinal T cell lymphoma once a biopsy has been obtained. Diagnostic and outcome data from an ongoing study of cats with clinical signs of chronic enteropathy will be discussed.

Clinical presentation and diagnostics

Signalment and clinical signs

Both LPE and SCL are commonly observed in older cats. Most studies report a median age of 9-10 years for these diseases, with a notable predominance in male cats (Burke et al., 2013; Janeczko et al., 2008). The most common clinical signs of both diseases are weight loss, vomiting, anorexia and diarrhea (extensively reviewed in (Marsilio, 2021)), but beyond these clinical observations, there are no consistent, imaging, biochemical or hematologic abnormalities that identify a cat with SCL, nor that would distinguish a cat with LPE from one with SCL. While hypocobalaminemia points to an intestinal (rather than extra-intestinal) cause of clinical signs, it is not specific for a particular disease.

Histology: Small intestinal biopsies of cats with signs of chronic enteropathy will show varying degrees of inflammation characterized by increased proportions of lymphocytes and plasma cells in the lamina propria, and variable numbers of other inflammatory cells (neutrophils and eosinophils). When there is a mixture of inflammatory cells, usually dominated by lymphocytes and plasma cells, the diagnosis is LPE. Histologic suspicion for SCL increases as the proportion of lymphocytes increases compared to the other cell types, and importantly, as increased number of lymphocytes between the epithelial cells lining the intestine (intra-epithelial lymphocytes or IELs) are detected (Briscoe et al., 2011; Moore et al., 2012). A definitive diagnosis of SCL is made when there is significant infiltration of a monomorphic lymphocyte population in the lamina propria and/or the mucosal epithelium. When immunohistochemistry is used to identify B and T cells, a higher proportion of T cells in the epithelium or expanding the mucosa will heighten suspicion for SCL. It is important to note, however, that IELs are invariably T cells, both in inflammation and neoplasia. The most common sites of involvement are reported to be the ileum and jejunum, although endoscopic biopsy most commonly samples the duodenum.

In an ongoing study of feline chronic enteropathy that will be presented at this talk, 3 pathologists were given 158 duodenal and ileal endoscopic biopsy samples from 85 cats with clinical signs of chronic enteropathy. The pathologists were blinded to each other's diagnosis and to any other testing. They were asked to provide one of three bottom-line diagnoses: enteritis, possible lymphoma, definitive lymphoma. All three pathologists agreed on the diagnosis in only 37% of samples, but at least two pathologists agreed on the diagnosis in 96% of samples. The two pathologists were not always the same pair. This finding highlights the variability in histologic interpretation of intestinal biopsies in this disease, and the need for additional, objective diagnostics.

Clonality testing/PARR: Clonality testing determines if a tissue or blood sample contains a population of cells that is dominated by a single clone. Clonal expansion of cells is a hallmark of neoplasia, and the finding of a clonal population of T cells favors a

diagnosis of lymphoma over enteritis. If approximately 5 – 10% of the T cells in a sample are derived from the same clone, then the PARR assay will indicate clonality, although this proportion will vary depending on a variety of factors.

Clonality testing is a PCR based assay performed on DNA (reviewed in (Keller et al., 2016)). The PCR reaction amplifies a portion of the T cell receptor. T cell receptors differ in length between T cells, but when a T cell divides, the daughter cells have the same sized receptor. If a sample has PCR products of multiple different sizes, then the result is called "polyclonal" and indicates there are many different T cells in the sample – more consistent with a reactive process. However, if a single sized PCR product is seen in a sample, then the result is considered "clonal" and supports a diagnosis of T cell lymphoma. The PARR assay is performed by several laboratories in the U.S., but all labs perform the assay differently. Therefore, the sensitivity and specificity of the assay for lymphoma is specific for the laboratory performing the test – sensitivity and specificity for lymphoma provided by one lab cannot be applied to results from a different lab.

97% of samples that were called lymphoma by all three pathologists in the study described above were clonal, indicating a high level of sensitivity for T cell lymphoma. 30% of samples with no histologic suspicion for lymphoma were also clonal. This observation raises the question of the status of these cats – do they have early lymphoma, not detected by histopathology, or is this a non-neoplastic clonal expansion of T cells? It is difficult to answer this question without a gold standard diagnostic for lymphoma. One explanation for the findings is that lymphocytic plasmacytic enteritis and lymphoma are a continuum of a single disease process, and the point at which T cells become neoplastic is earlier than can be detected by histopathology. The discovery of lymphoma-associated mutations, and testing cats at various stages of disease for these mutations, may help to clarify this hypothesis. STAT5B is the first of such mutations that has been described.

STAT5B mutation testing: T cells are activated to proliferate and produce cytokines when they receive an external signal. This signal can be through the T cell receptor after the T cell recognizes antigen, or it can be when growth factors such as cytokines bind to their receptors on the cell surface. One important pathway that transmits signals from the cell surface to the nucleus is the JAK-STAT signaling pathway. When cytokines or growth factors bind to their surface receptors, JAK proteins are activated, and in turn they phosphorylate STAT proteins. STATs are transcription factors, which enter the nucleus and initiate transcription of a variety of genes (Hu et al., 2021).

In 2021, a group of investigators identified a STAT5B mutation in a subset of feline intestinal lymphoma (Kieslinger et al., 2021). This mutation is seen in many human T cell lymphomas and is considered an important cancer driver. The effect of this mutation is to cause STAT5B to be constitutively phosphorylated, and therefore activated, without any external signals. This in turn leads to unrestricted T cell activation and proliferation. Indeed, a second group (Freiche et al., 2021) found that STAT5B was commonly phosphorylated in feline SCL, further corroborating the role of this signaling pathway. This discovery provides important insight into the possible pathogenesis of this disease. It also provides an additional objective diagnostic tool.

The STAT5B mutation is present in 64% of samples that were unequivocally diagnosed by 3 pathologists as lymphoma. The samples without the mutation will likely have other mutations affecting the JAK-STAT or other signaling pathways, and it will be important to continue to search for mutations that will expand the repertoire of testing that can be applied to these cases.

The STAT5B mutation is also present in samples that had suspicion for lymphoma butwere not definitively diagnosed with lymphoma by any pathologist. 78% of these samples STAT5B mutant samples also demonstrated clonality with the PARR assay. This observation again raises the question of whether neoplastic transformation precedes detection by histology. Although these cases do not meet criteria for a histologic diagnosis of lymphoma, they exhibit other important features of cancer; namely, clonal expansion and the presence of cancer driver mutations.

Outcome

A retrospective analysis of the survival data from this cat cohort showed that clonality testing and histology have similar correlations with overall survival. Cats that had clonally rearranged T cell receptor genes in their intestine had a shorter survival than cats without, regardless of histology, and cats with a definitive histologic diagnosis of lymphoma had a shorter survival, regardless of clonality. Survival associated with STAT5B was not analyzed because 36% of samples with true lymphoma will not carry the mutation. Ultimately, multivariable analysis of many clinical features, including signalment, clinical signs, and diagnostic testing, will be needed to determine which set of parameters are the best predictors of outcome.

When to treat?

In this study, most cats with a clear histologic diagnosis of lymphoma had supporting findings of either clonality, STAT5B mutation, or both. Therefore, a histologic diagnosis of SCL most likely has good specificity for this disease and could be treated accordingly. The more problematic situation for the clinician is a cat with equivocal or no histologic evidence of lymphoma, but

which exhibits clinical signs. If additional testing shows that this cat has a clonally expanded T cell population and/or a STAT5B mutation, how should that cat be treated? There is currently no objective data available to answer this question. Prospective clinical trials that stratify cats by different diagnostic criteria and by treatment would be ideal, and some of these trials are in the planning stages. While the challenges in diagnosing and treating cats with chronic enteropathy remain, advancements in understanding the disease and its markers, such as clonality and STAT5B mutation, are paving the way for more precise and effective treatments and outcome predictions. Importantly, a better understanding of the types of T cells that are involved in this disease may help us implement preventative strategies.

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The Role of Microbiome: Supporting, Immune Modulating, & Stress Lessening Probiotics in GI Diseases

Michael Lappin, DVM, PhD, DACVIM

Introduction

Stress associated illnesses in cats are common and include in part, diarrhea, recurrent respiratory tract disease signs, and chronic or recurrent signs of lower urinary tract disease that often relate to feline interstitial cystitis (FIC).[1-4] The proposed pathophysiological pathways resulting in the clinical manifestations of FIC were recently reviewed.[2] The reference also provides a great description of the use of multimodal environmental modification (MEMO) in the management of cats with chronic or recurrent lower urinary tract disease signs likely due to FIC.[2] In my experience, many of the components of MEMO can be beneficial in the management of some causes of diarrhea and some causes (particularly feline herpesvirus 1 [FHV-1} of the recurrent upper respiratory tract disease syndrome.

In the lecture associated with these proceedings, several research studies completed in the Center for Companion Animal Studies that evaluated the use of nutrition in the management of feline disease syndromes that likely are exacerbated by stress will be discussed.

Effect of a commercially available probiotic on the fecal microbiome of cats undergoing mild stress

The safety, immunomodulating properties, and clinical efficacy of the probiotic *Enterococcus faecium* SF68 have been described in a number of feline studies.[5-7] In one study, cats that were chronic carriers of FHV-1 had stress induced by moving from group housing to caged housing and back repeatedly.[6] The cats supplemented with a placebo were more likely to have increased activation of FHV-1 associated conjunctivitis compared to cats supplemented with probiotic.[6] At the time, these observations believed to exclusively relate to the immune stimulating effect of this probiotic.[5,8] However, it was also one of the first experiments to show that stress in cats leads to decreased fecal microbiota diversity and that supplementing with the probiotic led to a maintenance of microbiota diversity.[6] Thus, this probiotic appears to have both immune enhancing and stress modulating characteristics.

Effect of *Bifidobacterium longum* 999 supplementation on stress associated findings in cats with feline herpesvirus 1 infection

The following abstract was presented at the American College of Veterinary Internal Medicine (ACVIM) Annual Forum in 2021 and provides evidence that a different probiotic, *Bifodobacterium longum* strain 999 (BL999) can modulate stress by interacting with the fecal microbiome. For this proceedings and meeting, only the information presented previously at ACVIM will be discussed as the manuscript resulting from the work is in review.

> *Bifidobacterium longum* strain 999 (BL999) is a probiotic (Purina® Pro Plan® Veterinary Supplements; Calming Care) that has been shown to lessen anxiety in dogs and is known to be safe in cats. Feline herpesvirus 1 (FHV-1) is the most common infection of cats and clinical disease can be exacerbated by stress. The primary hypothesis was that cats supplemented with the BL999 containing product would have higher relaxation scores, lower stress markers, and lower FHV-1 clinical scores than cats supplemented with the same product, but without BL999 as a placebo when mild stress was induced by changing the type of housing.
>
> This 12-week study enrolled 24 cats with chronic subclinical FHV-1 infection that were randomly divided into two groups. The cats were supplemented with BL999 (group 1) or placebo (group 2) daily. After BL999 was supplemented for 42 days to achieve probable maximal effects, the cats were moved from the individual gang rooms into cages, back into gang rooms, and then back into cages to induce stress over the next 42 days while behavioral, clinical, and biochemical markers were measured.
>
> Both supplements were well tolerated and there was no obvious vomiting or diarrhea. During the stress periods, the cats supplemented with BL999 were significantly less likely to have abnormal serum cortisol concentrations ($P = 0.0059$) or sneezing ($P < 0.00001$). During the times cats were housed in cages, those supplemented with BL999 were significantly more likely ($P < 0.0001$) to reach out to the scorers through the cage bars and were significantly less likely ($P < 0.0003$) to pace in the cages.

The results of the study suggest that BL999 is well tolerated by cats, reduces stress, reduces stress associated problems like activated FHV-1, and increases social interactions between cats and people.

Additional field studies are ongoing to collect additional clinical information from client owned cats with anxiety or stress associated illnesses. Further information to explain the interactions between the gut and the brain of cats and other species is needed.

Effect of 2 urinary diets on hematuria in shelter cats with suspected interstitial cystitis

Recently, feline diets have been formulated that dissolve struvite cystoliths and prevent recurrent of both struvite and calcium oxalate cystoliths. An open trial with one of the diets (Purina Pro Plan Veterinary Diet UR Urinary St/Ox) was recently completed in cats with radiodense cystoliths that had been relinquished to animal shelters due to periuria and other signs of chronic or recurrent lower urinary tract diseases.[10] In that trial, 5 of 12 cats had the stones resolve within 2 weeks of starting the diet suggesting struvite cystoliths. The other 7 cats had stones that would not be expected to have been dissolved by the diet.[10]

When the open trial was completed, we continued accruing cases for either attempted dissolution of the cystoliths or to assess the effect of 2 diets on resolution of hematuria associated with presumed idiopathic FIC.[11] The following abstract was presented at the American College of Veterinary Internal Medicine (ACVIM) Annual Forum in 2020 and provides evidence that a veterinary diet could be of benefit managing cats with presumptive FIC. For this proceedings and meeting, only the information presented previously at ACVIM will be discussed as the manuscript resulting from the work is in review.

There are multiple different veterinary prescription diets that are purported to aid in the management of struvite and calcium oxalate crystalluria and to dissolve struvite cystoliths. Whether positive effects are induced by these diets in cats with suspected feline interstitial cystitis (FIC) that is possibly associated with stress is unknown. The purpose of this pilot study was to determine if there were differences in clinical outcomes in cats with suspected FIC that were fed one of two different veterinary prescription diets.

In this IACUC approved study, cats relinquished to animal shelters in North Central Colorado that were noted to have hematuria and clinical signs of lower urinary tract disease were transferred to the Veterinary Teaching Hospital. All cats had 2 view abdominal radiographs made, were assessed by abdominal ultrasound, and had urine collected by ultrasound guided cystocentesis for urinalysis and aerobic bacterial culture and sensitivity. Cats with hematuria but no other abnormalities (classified as FIC) and cats with radiodense cystoliths were gang housed in 2 different housing chambers and were randomized to be fed one of two veterinary prescription diets (Purina St/Ox or Hill's c/d Multicare). Cats in the FIC group were housed overnight individually in cages on Days 2, 6, 9, 13, 16, and 20 with Purina Tidy Cat® Litter System without absorbent pads to collect free catch urine for repeat urinalyses. Cats with radiodense calculi were radiographed weekly, with stone removal and analysis planned if the cystoliths did not dissolved after 28 days of dietary management.

At the time of abstract submission, 21 cats had been evaluated. A total of 4 cats either did not meet the entry criteria and were returned to the shelters (2 cats) or had concurrent underlying diseases (IRIS Stage II CKD or development of clinical FIP while on study) and so were excluded. All 4 cats with radiodense stones were fed St/Ox. The cystoliths dissolved in 2 cats and the 2 cats that required surgery had calcium oxalate cystoliths. Of the 13 cats with suspected FIC that completed the dietary trial, 6 were initially fed St/Ox and 7 were fed c/d. Five of 6 cats with suspected FIC fed St/Ox had hematuria resolve in the 28 day observation period. In contrast, 6 of 7 cats with suspected FIC fed c/d had persistent hematuria and were switched to St/Ox. This difference in response to the first diet was statistically significant ($p = 0.03$). Of the 6 cats with persistent hematuria on c/d, 3 resolved while fed St/Ox and 3 had persistent hematuria.

Significantly more cats with suspected FIC had apparent first-time responses to St/Ox than to c/d in this mild stress model. The cystoliths that dissolved on St/Ox were presumed struvite and the calcium oxalate stones are not expected to dissolve with dietary management. Continued data should be collected from additional cats to verify the results of this study.

It is proposed that cats are naturally chronically dehydrated, and so inducing increased water consumption may have the added benefit of lessening stress due to dehydration in cats (Dr. Deb Greco, personal communication). The Purina diet has a higher sodium concentration (1.2%) than the alternate diet (0.37%). Whether this characteristic explains the differences between groups in study described will be evaluated in future studies.

During the lecture, we will also discuss several other studies of diets or supplements that may play a role in the management of stress associated diseases in cats.[12-14] Data showing immune modulating properties of Enterococcus faecium strain SF68 will also be presented.

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Update on the Diagnosis & Management of Infectious GI Diseases

Michael Lappin, DVM, PhD, DACVIM

Clinical problem and differentials

Vomiting is the forceful ejection of stomach and proximal duodenal contents through the mouth. Vomiting can be induced by vestibular, vagal, chemoreceptor trigger zone, or direct input to the emetic center. Diarrhea is a characterized by increased frequency of defecation, increased fluid content of the stool, or increased volume of stool. Markedly increased frequency of defecation, small volume stools, tenesmus, urgency, hematochezia, and mucus are consistent with large bowel diarrhea. Slight increase in frequency of defecation, large volume, melena, steatorrhea, and polysystemic clinical signs are more consistent with small bowel diarrhea. Mixed bowel diarrhea is a combination of characteristics or clinical signs.

Gastrointestinal (GI) signs can be the result of primary diseases of the GI system or secondary GI diseases. The secondary GI diseases are generally those of the kidneys, liver, pancreas (pancreatitis or exocrine pancreatic insufficiency), endocrine system (hypoadrenocorticism; diabetic ketoacidosis; hyperthyroidism), or central nervous system. Differential diagnoses for primary GI diseases are often grouped into obstruction (masses, foreign body, and intussusception), dietary intolerance, drugs/toxins (garbage gut), inflammatory gastric and bowel diseases, neoplasia, infectious diseases, and parasites. The primary bacteria associated with gastrointestinal tract disease in cats include *Salmonella* spp., *Campylobacter jejuni*, *Clostridium perfringens*, *Helicobacter* spp., bacterial overgrowth syndrome, bacterial peritonitis, and bacterial cholangiohepatitis. The primary viral agents include feline coronaviruses, feline leukemia virus, feline immunodeficiency virus, and feline panleukopenia virus. The primary nematodes are *Ancylostoma*/*Uncinaria, Strongyloides cati*, *Dirofilaria immitis* (vomiting), *Toxocara cati*, *Toxascaris leonina*, *Ollulanus tricuspis*, and *Physaloptera* spp. Enteric protozoans include *Giardia* spp., *Cystoisospora* spp., *Cryptosporidium* spp., *Entamoeba histolytica*, and *Tritrichomonas foetus*. The cestodes *Taenia*, *Dipylidium*, and *Echinococcus* generally cause subclinical infection.

Diagnostic plan

Please also see the section in the procedures on feline diagnostic tests for additional information. Occasionally, otherwise healthy cats with acute vomiting and normal physical examination findings can be handled conservatively by withholding food for 24 hours followed by introduction of a bland food for several days. For all cats with diarrhea with no apparent cause on physical examination, I will perform a fecal flotation, fecal wet mount examination, complete blood cell count (CBC), and rectal cytology if diarrhea is present. While the CBC generally does not lead to a specific diagnosis, the presence of eosinophilia makes inflammatory bowel diseases and parasitism more likely.

I perform acid-fast staining of a fecal smear or immunofluorescence antibody staining (Merifluor *Giardia/Cryptosporidium*, Meridian Diagnostics) on all cats with diarrhea to assess for the presence of *Cryptosporidium felis* oocysts. A wet mount examination may aid in identifying trophozoites of *Tritrichomonas* and *Giardia*. If neutrophils or spirochetes are evident on rectal cytology I recommend fecal culture (or PCR) for *Salmonella* spp. and *Campylobacter* spp.. If spore-forming rods consistent with *Clostridium perfringens* are present in large numbers, fecal enterotoxin assays or PCR assays can be performed to help confirm the diagnosis. However, these assays can be positive in healthy cats as well and so have less than 100% predictive value.

A biochemical profile, urinalysis, FeLV antigen assay, and FIV antibody assay are indicated if secondary GI diseases are on the differential list or if dehydration is present. I generally perform a total T4 on all cats with vomiting or small bowel diarrhea that are greater than 5 years of age. While amylase and lipase are poor predictors of pancreatitis in cats, a pancreatic lipase immunoreactivity assay has now been validated. It can be used to diagnose pancreatitis (increased) in cats. The positive predictive value is better for acute pancreatitis than chronic pancreatitis. The negative predictive value (negative test correlates well with a lack of pancreatitis) appears to be high. If an cat with suspected pancreatitis has abdominal effusion, assay lipase concentrations in the serum and effusion; if pancreatitis is occurring the effusion lipase is usually greater than serum.

Fecal fat assessment with Sudan IV stain can help confirm malabsorption/maldigestion but is not specific for a single disease. If the MCV is low, chronic iron deficiency should be suspected; this occurs almost exclusively with gastrointestinal diseases. A serum iron panel can be used to confirm iron deficiency. Panhypoproteinemi is often associated with gastrointestinal tract

disease. Measurement of B12, folate, and trypsin like immunoreactivity (TLI) are also used to screen animals for small intestinal bacterial over growth syndrome, inflammatory bowel disease, and exocrine pancreatic insufficiency (TLI).

Most commonly used imaging techniques include radiographs, contrast radiographs, and ultrasound. I commonly perform abdominal radiographs in cats to support my palpation findings. I use contrast radiographs occasionally; often I perform endoscopy or exploratory laparotomy based on physical examination and abdominal radiographic findings. Ultrasound of the intestinal tract can be hard to interpret and is operator dependent. However, some findings can be used to support the decision to move forward with biopsies and direct the biopsy method, especially in cases with IBD or neoplasia.

Diagnosis of gastric foreign bodies and diffuse inflammatory diseases can be made by endoscopy. Endoscopically obtained biopsies are small; I generally take at least 8-10 biopsies from stomach, duodenum, colon, and ileum if possible. Even if a lesion is present, endoscopically obtained biopsies can be falsely negative requiring full thickness biopsies. Gastric biopsies should be placed on urea slants to assess for urease which is found in the cell wall of *Helicobacter* spp.. Full thickness biopsies can be made by using laparoscopy to pull appropriate loops of bowel to the abdominal wall and performing a key hole incision for biopsy procurement.

INFECTIOUS DISEASE TREATMENT OPTIONS

There are multiple drugs used in the treatment of gastrointestinal parasitic infections. For all kittens, the strategic deworming recommendations for the control of hookworm and roundworm infections from the Centers for Disease Control and the American Association of Veterinary Parasitologists should be followed by veterinary practitioners.

Kittens should be administered an anthelmintic at 3, 5, 7, and 9 weeks of age and then periodically monitored or treated. If the kitten is not presented to the clinic until 6-8 weeks of age, administer the anthelmintic at least 2-3 times, 2-3 weeks apart. Pyrantel pamoate and fenbendazole are usually effective drugs for use in strategic deworming programs and for the treatment of nematodes causing gastrointestinal tract disease. Albendazole is more likely to cause hematologic side-effects than fenbendazole and so should not be used in cats. Even if anthelmintics for hookworms and roundworms are administered, a fecal flotation should be performed to evaluate for other parasites.

Monthly *D. immitis* preventatives can help control or eliminate some nematode infections as well as prevent heartworm infection. Ivemectin at heartworm preventative doses is effective for control of hookworms but not roundworms. Thus, selamectin, milbemycin, or moxidectin should be used in regions where roundworm infections are common. Selamectin and imidocarb-moxidectin have the advantage of controlling fleas as well and so may lessen the potential for *Bartonella* spp., *Rickettsia felis*, and *Haemobartonella* (*Mycoplasma*) spp. infections. In a recent study in our laboratory, administration of imidacloprid-moxidectin monthly blocked flea transmission of *B. henselae* amongst cats. *Dipylidium* and *T. taeniaformis* infestations usually are eliminated by praziquantel or espiprantel; fenbendazole is effective for *Taenia taeniaformis*. Since *Echinococcus multilocularis* can be a significant zoonosis transmitted to cats by carnivorism, hunting cats in endemic areas should be treated up to monthly. Administration of a pyrantel/praziquantel combination may be effective in these cats since praziquantel is approved for the treatment of *Echinococcus* and roundworms are also transmitted by carnivorism.

Withholding food for 24 to 48 hours is indicated in cats with acute vomiting or diarrhea. Highly digestible, bland diets are used most frequently if vomiting and small bowel diarrhea are the primary manifestations of disease. High fiber diets are generally indicated if large bowel diarrhea is occurring. Diarrhea associated with *Giardia* spp. generally resolves during or after administration of fenbendazole or metronidazole. Metronidazole induces a GI dysbiosis whereas fenbendazole does not and so should be used first in the treatment of giardiasis. In one study, cyst shedding resolved in 26 cats after the administration of metronidazole benzoate at 25 mg/kg, PO, q12hr for 7 days. If inflammatory changes exist, metronidazole may also be beneficial due to inhibition of lymphocyte function. Central nervous system toxicity occasionally occurs with this drug; it is unlikely if no more than 50 mg/kg, PO, total daily dose is given. Fenbendazole has not been studied extensively for treatment of giardiasis in cats. In one experiment study of cats coinfected with *Giardia* spp. and *Cryptosporidium* spp., four of eight cats treated with fenbendazole at 50 mg/kg, PO, daily for 5 days stopped shedding *Giardia* cysts. The combination product of febantel, pyrantel, and praziquantel has been shown to have anti-*Giardia* activity in dogs. When given at the febantel dose of approximately 56 mg/kg, PO, daily for 5 days, *Giardia* cyst shedding was eliminated in some cats. Metronidazole and fenbendazole can be given concurrently in resistant cases. A single dose of secnidazole was evaluated in one trial and is being used with groups of cats need to be treated in the United States.

Albendazole has been evaluated for treatment of giardiasis in a limited number of dogs, but has been associated with neutropenia. Furazolidone (4 mg/kg, PO, q12hr, for 7 days) and paromomycin (appropriate dosing interval for cats is unknown) are other drugs with anti-*Giardia* effects but have not been evaluated extensively in cats. There are no known advantages of

using tinidazole or ronidazole compared to metronidazole in cats and ronidazole has a greater risk of CNS toxicity. Previously, the feline *Giardia* spp. vaccine could be attempted as an immunotherapy but the vaccine has been discontinued. In some cats with *Giardia* and diarrhea, administration of a probiotics or addition of fiber to the food and retreating can result in resolution of diarrhea. In one study in our laboratory, use of *Enterococcus faecium* SF68 with metronidazole was superior to metronidazole alone in a study of shelter dogs with diarrhea (Nestle Purina; FortiFlora). The primary goal of *Giardia* therapy is to resolve diarrhea. It is unlikely the infection can be eliminated in most cats and reinfection is common. If treatment is to be monitored, a fecal flotation (not antigen assay) could be performed within 14 days of ending therapy.

Multiple drugs have been evaluated for the treatment of cats with *T. foetus* infections; until recently no drug eliminated infection and diarrhea rarely resolves during the treatment period. Recently ronidazole at 30 mg/kg, PO, q24hr, for 14 days eliminated clinical signs of disease and trophozoites from cats infected with one strain of the organism. Ronidazole is more neurotoxic than metronidazole and so should be used carefully. In another one small study, administration of metronidazole and enrofloxacin lessened diarrhea in kittens but it is unknown if the organisms infecting those cats was *T. foetus*. It is possible that some cats with *T. foetus* have other enteric coinfections and so anthelmintics or drugs with activity against *Giardia* spp., *Cryptosporidium* spp., and enteric bacteria like *Campylobacter* spp. are often prescribed. Use of 2 different *Enterococcus faecium* probiotic strains (including strain SF68) showed a potential beneficial effect in a model. Paromomycin should be avoided cats with bloody stools because of the potential for being absorbed and inducing renal disease or deafness. In one study, 23 of 26 cats with diarrhea and *T. foetus* infection had complete resolution of diarrhea a median of 9 months after initial diagnosis. Quinolones, especially pradofloxacin, may be an alternate therapy for cases resistant to ronidazole.

Cryptosporidium spp. associated diarrhea sometimes resolves after administration of tylosin (10-15 mg/kg, PO, BID for at least 14 days) or azithromycin (10 mg/kg, PO, daily for at least 14 days). If the cat is responding to therapy, continue treatment for 1 week past clinical resolution. Some cats may require several weeks of treatment. Nitazoxanide at 10 mg/kg, PO, twice daily for at least 14 days has been effective for controlling *Cryptosporidium* spp. diarrhea, but is a gastric irritant that commonly induces vomiting.

The *Toxoplasma gondii* oocyst shedding period can be shortened by administration of clindamycin, sulfadimethoxine, or ponazuril. *Cystoisospora* spp. generally responds to the administration of sulfadimethoxine or other sulfa-containing drugs. Clindamycin, trimethoprim-sulfa, or ponazuril are also options. Ponazuril and toltrazuril are very safe for kittens. Use of ponazuril at 50 mg/kg, PO, daily for 3 days was superior to other protocols in one study.

Since many of the gastrointestinal parasites that infect cats are transmitted by carnivorism, cats should not be allowed to hunt or be fed raw meats. Additionally, infection of cats by many feline parasites results from ingestion of contaminated water. Clinical disease in some parasitized cats can be lessened by eliminating stress and providing a quality diet and clean environment.

Clostridium perfringens and bacterial overgrowth generally respond to use of probiotics. Enterococcus faecium SF68 was used to lessen non-specific diarrhea in cats in a shelter from over 20% to < 5%. We also used this probiotic to lessen diarrhea induced by amoxicillin-clavulanate. Some C. perfringens cases will also require an antibiotic; tylosin, metronidazole, ampicillin, amoxicillin, or tetracyclines. The drug of choice for campylobacteriosis is erythromycin; however, oral administration of quinolones is often less likely to potentiate vomiting. Salmonellosis should only be treated parenterally due to rapid resistance that occurs following oral administration of antibiotics. Appropriate antibiotics for the empirical treatment of salmonellosis while awaiting susceptibility testing results include chloramphenicol, trimethoprim-sulfa, amoxicillin; quinolones are also effective. *Helicobacter* spp. infections are usually treated with the combination of metronidazole and tetracycline or amoxicillin and metronidazole in dogs. Clarithromycin or azithromycin may be logical choices in cats since the species is often difficult to treat with multiple drugs. Whether to concurrently administer an antacid like famotidine is controversial but seems to lessen vomiting in some cats.

Cats with apparent bacteremia due to enteric bacteria should be treated with parenteral antibiotics with a spectrum against anaerobic and gram negative organisms. The combination of enrofloxacin with a penicillin or first generation cephalosporin is generally effective. Second generation cephalosporins or imipenem are also appropriate choices.

Cats that have hepatic infections and signs of bacteremia should be treated with antibiotics that kill gram positive, gram negative and anaerobic bacteria as discussed before. Non septic hepatic infections generally respond to amoxicillin, amoxicillin-clavulanate, first-generation cephalosporins, or chloramphenicol. Decreasing numbers of enteric flora by oral administration of penicillins, metronidazole, or neomycin can lessen the clinical signs of hepatic encephalopathy.

Panleukopenia virus, feline leukemia virus, feline immunodeficiency virus, and coronaviruses are the most common viral causes of gastrointestinal tract disease in cats. Viral diseases are managed by supportive treatment. Make sure to maintain hydration, correct hypoglycemia, and maintain normal potassium concentrations. Use of jugular catheters is superior to leg veins since blood samples can be drawn and CVP can be measured. Based on results in dogs with parvovirus infection, administration of plasma or serum (1 ml/kg) from your hyperimmune blood donor cat may lessen morbidity in cats with panleukopenia due to passive transfer of immunity. This is effective because parvoviruses induce a viremic state; virus particles are complexed by the antibodies transferred passively. Administration of interferon alpha at 10,000 U/kg, SQ, once daily may have anti-viral effects. Antibiotics effective against gram negative and anaerobic bacteria are commonly indicated. Vaccines are available for the prevention of parvovirus, coronaviruses, and feline leukemia virus infection.

Histoplasma capsulatum infection is the most common fungal infection of the gastrointestinal tract of cats in the United States. Treatment with itraconazole can be effective.

Zoonotic considerations

Infection of people by feline enteric agents is usually from contact with feces in the environment, by ingestion of contaminated food or water, or by ingestion of undercooked meat (*T. gondii*). Contact with infected cats is an unlikely way for humans to acquire infection. The following guidelines may lessen the risk of transfer of feline enteric zoonotic agents to people.

- Perform a thorough physical examination and zoonoses risk assessment on all new cats.
- Perform a physical examination and fecal examination at least once or twice yearly.
- Take all cats with vomiting or diarrhea to a veterinarian for evaluation.
- Fecal material produced in the home environment should be removed daily, preferably by someone other than an immunocompromised individual.
- Use litterbox liners and periodically clean the litterbox with scalding water and detergent.
- Do not allow cats to drink from the toilet.
- Follow the CDC strategic deworming guidelines.
- Wear gloves when gardening and wash hands thoroughly when finished.
- Filter or boil water from sources in the environment.
- Wash your hands after handling cats.
- Maintain cats within the home environment to lessen exposure to other animals and their feces.
- Feed cats only commercially processed food.
- Do not share food utensils with cats.
- Avoid being licked by cats.
- Control potential transport hosts like flies, rodents, and cockroaches.
- Cook meat for human consumption to 80 C for 15 minutes minimum (medium-well).
- Wear gloves when handling meat and wash hands thoroughly with soap and water when finished.

References available on request to mlappin@colostate.edu

NOTES:

Technician: Sippin' Through Straws: Taking the Stress Out of Feline Neonate Tube Feeding

Ellen Carozza, LVT, VTS (CP-Feline)

Tube Feeding Kittens

Tube feeding is a valuable skill set that anyone in veterinary medicine should know how to perform confidently, however, the smaller the patient, the more delicate the skill is. Knowing how to choose the right style tube for use, measuring and placement is all part of the process.

Tube Styles:

- **Red rubber** (various styles of soft/firm to very soft/floppy latex) catheters with 2 opposing eyes for fluid uptake or distribution
    - Dover Red Rubber Robinson Catheter
    - Covidien* Rob-Nel Catheter- latex free! - typically used in veterinary medicine, polyvinyl chloride tubing that becomes stiff when chilled.

Many brands available on the market will have a catheter funnel tip that can be trimmed to fit other sizes of catheter tips such as a luer lock.

- **Polyurethane PVC Feeding Tube**
    - Argyle
    - Kangaroo

Smaller catheter tip available, or use for luer lock syringes

Parts of the catheter:

- Tubing
- Cather funnel (attached to the syringe)
- Eyelets (single or double)

What you need for tube feeding: Each kitten gets their OWN tube- do not share tubes. This not only prevents cross contamination, but each kitten will have their own measurements

- Tube of choice
- Permanent Marker
- Bandage scissors to trim the funnel
- Syringe of appropriate size to fit the funnel

TIP: NEVER use >12ml syringe for tube feeding neonates/pediatrics as the pressure to eject the formula is too great and can cause significant issues such as aspiration pneumonia.

Measuring the kitten for tube length:

- **Pick the appropriate size of tubing for the kitten. Premature kittens and kittens <80g should be started with a 3.5-5F tube. (When in doubt start small to prevent esophageal rupture or overstretching- you will need to snip off the eyelets for ease of administering liquids)**
- **Kittens >80g can usually fit 5F with little to no resistance**
- Measure from the tip of the nose to the last rib. Mark the tube at the nose! Do not feed the catheter past that mark or you risk the tube curling up around inside the stomach causing either a knot or back wash
- You can snip the eyelets off POLYVINYL tubing with little to no risk of scratching the esophagus as the vinyl is very soft, however, the stiffer red rubber catheter can scratch the esophagus if not clipped straight across.

How to tube feed: Step by Step

(NEVER tube feed a non-responsive neonate food. Sugar support only on the mucous membranes)

1. Pick out the correct size (F) tube and syringe and cut to fit (this is also where you make the decision to snip off the eyelets)
2. Measure your kitten from the tip of the nose to the last rib- mark your tube.

3. Prepare your warmed formula and draw it up into the syringe needed
4. Ensure there are ZERO clumps in the formula or you risk the tube becoming clogged
5. Attach the syringe to the feeding tube and gently charge the tube with formula so there is no air in the tube. You can place a small amount of formula, water or even a bit of water based lubricant (very little) to help the tube glide down easier, but the kitten may be adverse to the taste of the lubricant. The author prefers either water or formula to moisten the tubing.
6. Gently restrain the head and body of the kitten in your non dominant hand and gently squeeze at the commissures of the mouth to get the kitten to open their mouth with your thumb and forefinger (many times you may not have to do this as once they taste the formula at the end of the tube and they will get excited for their meal and attempt to swallow the tubing.)
7. Feed the tube gently down the left side of the mouth and STOP if you feel any resistance or if the kitten begins to gag as you may be tapping the larynx. Gently pull back and readjust if needed. If your kitten is squawking past the tube, you are in the correct space. They cannot cry if you are in the larynx while they are coherent and will gag and attempt to spit out the tube.
8. Feed the tube up to the marked line
9. Slowly administer the food over 30 seconds to 1-2 minutes depending on the amount being fed. This helps prevent backwashing if feeding too quickly and allows them to adjust to the feeding.
10. Once the syringe is empty, bend and pinch off the tube and gently pull out of their mouth to ensure no fluid falls back into their esophagus when removing the tube.
11. Clean the tube with hot soapy water and hang to dry for use again

Notes:

- Yes, you 100% can train kittens with cleft palates to eat via tube feeding until they are able to have surgery. While a small mouth gag may be needed to prevent the kitten from chewing the tube, it is absolutely possible to perform this technique when they have teeth. You CAN create mouth gags with TB syringe barrels for older kittens that have tooth eruption and may attempt to chew on the tubing.
- Feeding too fast can cause the formula to backwash up into the esophagus with the potential to cause aspiration pneumonia.
- Feeding charts are only a guide, NOT exact amounts to feed as each kitten is different, particularly if they are ill.
- Only feed fresh, warmed formula that is clump free.
- If a kitten will not bottle feed (ie- recently taken from mom or ill, tube feeding is a viable option for nutrition until the kitten will nurse from a bottle)
- NEVER tube feed a kitten milk replacer to a hypothermic and/or hypoglycemic kitten. Always tube feed warmed (~95-100 degrees fahrenheit) CLEAR pedialyte or LRS with a bit of 50% dextrose added until the kitten is normothermic and normoglycemic.
- Monitor kittens for bloating as ileus can occur in kittens and overfeeding can cause neonatal GI distress or death.
- NEVER use a feeding tube that was placed in a cooler without warming it up to room temperature first.
- You CAN use Emeraid-HDN for your kittens if you do not have formula at the hospital: https://emeraid.com/vet/emeraid-cat-critical-care-hdn/

YOU GOT THIS! Tube feeding the smallest and most fragile patients in the hospital is incredibly rewarding when you see positive responses. Thank you for being the advocate in your hospital for the neonates and pediatrics in practice. They are your future patients and deserve the same opportunity at a successful life.

Painful oral inflammation provides difficult diagnostic and therapeutic challenges in cats, owing to our poor understanding of many causes of the problem and poor patient and owner compliance during treatment.[1] Clinical signs may vary from mild gingivitis to refractory gingivostomatitis (GS) affecting most of the soft tissues of the oral cavity. The prevalence of the problem in primary-care practice in the United Kingdom recently was reported as 0.7%.[2]

NOTES:

Technician: Chew With Your Mouth Closed! Preventing Food Phobias & Fighting at the Dinner Table in the Multi-cat Household

Ellen Carozza, LVT, VTS (CP-Feline)

Feeding Challenges in the Multi-cat Household

The multi-cat household poses many challenges to the pet owner when it comes to food. Not only does one have to take in account for overeating or cats on particular Rx diets but food resource guarding. In turn, cats become obese, can have diet related issues due to improper nutrition or have increased anxiety or malnutrition due to bullying at the bowl. Developing plans for clients that provide a variety of methods to help ease the stress at meal times can make a difference for the household. However, *it is ultimately up to the client to succeed.*

Recommended Reading:

1. Feline Feeding Programs: Addressing behavioral needs to improve feline health and wellbeing https://journals.sagepub.com/doi/10.1177/1098612X18791877
2. Common feline problem behaviors: Aggression in multi cat households. https://journals.sagepub.com/doi/10.1177/1098612X19831204

Food Puzzles:

Food puzzles are stimulating not only for the mind, but fills a niche for the need to hunt for prey. Puzzles come in all sorts of levels of mental stimulation and physical challenges. Whether they are purchased already assembled or DIY, it's important to rotate the toys to eliminate boredom. *Clients should consider rotating toys out once the cat grasps the concept and is successful with the puzzle*. Puzzles that are too challenging for the cat need to be modified for success OR removed and the cat given an easier toy until they build up to the more challenging ones as frustration can occur and create a negative side effect with not wanting to use puzzles in the future. Cats can and do become easily bored and will not entertain toys that do not have a positive side effect.

http://foodpuzzlesforcats.com/

https://www.purina.com/articles/cat/feeding/diy-cat-puzzle-feeder

https://petkeen.com/diy-cat-feeder-puzzles/ <- incredibly creative and fun ways using cardboard for low cost puzzle feeders! Check out the kitty vending machine!

Cat Food Stations:

Not all cats appreciate eating near each other. While kittens learn to eat by watching siblings and their mom, as they age, they prefer their own space. Some of the challenges are small living spaces that cannot accommodate separate rooms for feeding. Feeding cats at least 3 feet apart can alleviate some of the stress, however, eating in private can be better. While it is not the best situation to feed an additional cat in a bathroom near their litter pans, simply providing a barrier so the cats cannot see each other can make a difference in many situations.

Level feeding is also an option. Large cat trees that have shelves where cats can be trained to eat at their personal spot can also alleviate some of the stress when it comes to dining with each other. In many households, such as mine, I feed the cat who tends to be bullied on the counter away from the other cats where she can eat in peace. Each home is different and while some people may not appreciate their cats on the counter tops happily tippy tapping away with their toilet toes, they need to put in the effort to help the cat who is being pushed out of the way or bullied allow a safe place to eat.

Box feeding stations are also an option. These generally work very well for cats that are obese to prevent them from stealing more food, cats on a medical diet or have kittens on a higher caloric/protein diets and other cats need to stay out of their food bowls. Either pre-purchased or made with using a clear sterilite tub (with a cut out for the cat to eat and some small air exchange holes) the food is placed at the far end of the tub so the other cat cannot stick the head in or reach with their paws.

Microchip Feeders:
The latest technology for "feeding privacy." These work by locking out the cat that does not have the chip registered to the device. Yet, they can still be hacked by the cat who is not supposed to be eating out of them by hovering over the registered cat as they are eating and the thief putting their foot into the bowl to swipe out food as the trap door is open or pulling out the bowl entirely. These tend to be purchased first by clients as there is little effort other than making enrichment tools or feeding stations. While they work for some households, they do not work for all of them. These do not address boredom eating or replace food puzzles. They are simply used to lock out the cat the food is not intended for. Another downside to these is that the cat can still be bullied by resource guarding or pushing the cat out of the way and they cannot finish diets in time if they are wet, or raw fed when there is a limit to how long the food should be out before spoilage.

Feline Enrichment:
Cats, just like humans, will eat when bored as they have a dopamine and serotonin boost that makes you feel good and over time becomes a habit that can lead to obesity if you are not burning more calories that you intake. Providing the right amount of enrichment for the multi-cat household can help prevent food guarding and bullying. It is important to discuss and address the lack of environmental stimulation in the cat(s) home to prevent obesity and feline guarding behaviors.

https://catvets.com/education/conference/feline-enrichment-resources/
https://catfriendly.com/be-a-cat-friendly-caregiver/playing-with-your-cat/

NOTES:

RECOVER CPR Guideline Updates: Feline Focus

Kenichiro Yagi, MS, RVT, VTS (ECC) (SAIM)

Introduction

In June of 2012, the Reassessment Campaign on Veterinary Resuscitation (RECOVER) published the first evidence based guideline for veterinary cardiopulmonary resuscitation (CPR). The initiative was launched after considering the difference in success rates of CPR between human (20%) and veterinary (6-7%) settings, with the human counterpart having established evidence-based guidelines through the American Heart Association. There are physiologic and anatomic differences between human patients and veterinary patients, but one would expect a comprehensive, evidence-based treatment strategy on execution of CPR to improve the outcome through optimization of the CPR protocols. The RECOVER initiative was carried out through the involvement of over 100 experts from the American College of Veterinary Emergency and Critical Care (ACVECC) and American College of Veterinary Anesthesia (ACVA) of multi-national background evaluating published studies available to answer clinical questions organized into 5 different subtopics to arrive at a consensus guideline. This groundbreaking effort not only produced a guideline that is now utilized all over the world to refine CPR practices, but has also injected fuel into the drive towards evidence-based practices in veterinary medicine, and sparked many other movements in the process. Fast forward to 2023, the revision process of the RECOVER guidelines is about to be concluded and will contain updates through new evidence that has been published in the last decade.

Evidence in CPR

Many clinical questions asked in 5 different "domains" of (1) Preparedness & Prevention, (2) Basic Life Support, (3) Advanced Life Support, (4) Monitoring, and (5) Post-Cardiac Arrest Care were answered to confirm or disprove existing beliefs, provided new knowledge, and also allowed us to identify gaps in the knowledge available to come to definitive answers.

The guideline emphasizes importance in early initiation of CPR as a key factor in successful outcome. Preparation for swift intervention when a patient going into cardiac arrest can be accomplished through thorough training of the staff in both didactic (knowledge) and psychomotor (physical) aspects of CPR. CPR drills simulating the arrest and response allows staff members to better understand the sequence of events and potential turns the event may take. Periodic refresher training sessions at least every 6 months is recommended. Preparation of the facility through setup of a crash cart in a central location, which is regularly checked for stock with a detailed checklist will allow for easy access to supplies and equipment required for CPR. Cognitive aides consisting of the CPR algorithm, drug dosage charts, CPR priority checklist should be readily available in the emergency area, with the staff trained on their usage prior to the event, helping adherence to proper protocol.

Swift intervention is better made when cardiopulmonary arrest (CPA) is recognized quickly, and CPR initiated. Assessment of the patient for CPA should be performed in no more than 10-15 seconds through a standardized approach. If CPA is even suspected, chest compressions should be started right away since any delay can significantly reduce the chance of success, accurate assessment of a lack of a pulse is difficult without taking a long time, and performing compressions on a patient that is not in CPA brings very little harm. In an inpatient situation, clear identification of patients at risk of CPA to the staff should allow for earlier recognition.

Basic Life Support

CPR starts with provision of basic life support (BLS) as the priority, and most important aspect of CPR. The mnemonic CAB is now used to describe the priority order of circulation, airway, and breathing, because breathing is not helpful in oxygen delivery if circulation of blood has ceased. Evidence points towards delay in initiation of compressions leading to lower success rates in CPR. In regards to compressions, there were no evidence to show differences between right and left lateral recumbency. Chest compressions should be performed to 1/3 to 1/2 of chest width (which takes quite a bit of force for large animals, while moderation may be required for smaller patients like cats) at a rate of 100-120 compressions per minute while allowing full chest recoil in between. Cats should have compressions performed over the heart, and compressions may be performed with a one-handed, circumferential technique. A two handed, over the top technique is not recommended in cats because of the risk of performing compressions too forcefully. The use of a metronome, songs, or other methods of keeping the rate consistent to recommended rates is useful. Even when compressions are executed properly, it may only produce about 30% of normal cardiac output, which illustrates the need for swift and proper compressions during CPR. Interrupting of compressions significantly reduces the forward flow created through consistent application of compressions, and should be avoided unless absolutely necessary.

Compressions should not be stopped to auscultate the heart, check for pulses, assess the patient, or place an endotracheal tube for a full 2 minutes per cycle of compressions. 10-15 seconds in between 2-minute cycles should be used for assessment of the patient, and compressions resumed promptly if no change in CPA is seen. While it may be possible to perform one-handed circumferential compressions for repeated cycles, the compressor is recommended to be switched between cycles to prevent physical fatigue.

Endotracheal intubation should be performed without interruption of compressions, and ventilations performed approximately at 10mL/kg tidal volume (or 20cmH2O of pressure if no spirometer) at 10 breaths per minute with an inspiratory time of 1 second. Hyperventilation is best avoided to prevent vasoconstriction from low CO2 levels leading to poor cerebral perfusion. Mouth-to-snout ventilation may be used if supplies for endotracheal intubation are not available. In the case of single person CPR, 2 short breaths in between 30 chest compressions are recommended.

Advanced Life Support

With basic life support started, the attention of the CPR team should be directed to providing advanced life support, including monitoring, drug therapy, and electrical defibrillation. The two forms of monitoring that prove useful during CPR is the electrocardiogram (ECG) and end-tidal carbon dioxide (ETCO2) monitoring. Pulse oximeters and oscillometric or Doppler blood pressure monitoring is not effective in assessment during CPR due to movement and poor perfusion state. The electrocardiogram is also prone to motion artifacts during compressions, making interpretation difficult. Regardless, specific tracings may be seen during or in between compression cycles, guiding therapy. Asystole, pulseless electrical activity (PEA) and ventricular fibrillation (VF) are notable arrhythmias seen in CPR.

Capnography, or measurement of CO2 in the breaths coming out of the patient is monitored easily in a patient that is endotracheally intubated. ETCO2 measurement is the most reliable form of monitoring for effective compressions since the level of CO2 measured correlates to the level of perfusion the lungs are receiving, given there is no severe pulmonary pathology. ETCO2 levels higher than 10-15mmHg during CPR was observed to give a higher chance of return of spontaneous circulation (ROSC). Upon ROSC, ETCO2 increases significantly as perfusion to the lungs are re-established, and can be used as an indicator of ROSC.

Drugs can be administered intravenously (IV) or intraosseously (IO) during CPR, and access should be established without interruption of compressions. Vasopressors, parasympatholytics, anti-arrhythmics, reversal agents, IV fluids, and alkalinizing agents are used in specific situations during CPR. Vasopressors are indicated for use in CPR when non-shockable rhythms (asystole or pulseless electrical activity) are diagnosed in between compression cycles to increase systemic vascular resistance and optimizing perfusion through the reduced cardiac output. Epinephrine, an alpha-1, beta-1 and beta-2 adrenergic agonist causes vasoconstriction and is given at a low dose (0.01mg/kg) initially, and at a high dose (0.1mg/kg) with prolonged duration of CPR. Antiarrhythmics are considered with prolonged CPA with shockable rhythms. In cats, amiodarone is a better choice compared to lidocaine. Vasopressin is an alternative that may be used in place of epinephrine at 0.8U/kg. Both vasopressors are given every other cycle of compressions due to its half-life.

Atropine has traditionally been given as an anticholinergic and a sympatholytic drug. There is minimal evidence indicating benefits of atropine administration during CPR, though there is also no evidence of harm. Atropine is given at 0.04mg/kg IV or IO at the initiation of CPR or as soon as IV or IO access is established. Atropine may be warranted in patients suspected to be with high vagal tone. Anti-arrhythmics may be useful in ventricular fibrillation (VF) that does not respond to electrical defibrillation. Reversal of any anesthetic or analgesic drugs seems reasonable though no evidence is seen. Opioids can be reversed with naloxone (0.04mg/kg), benzodiazepines with flumazenil (0.01mg/kg), and alpha-2 agonists with atipamezole (0.1mg/kg) or yohimbine (0.1mg/kg), each IV or IO.

Intravenous fluids may be beneficial if the patient is known or is suspected of hypovolemia to help restore intravenous volume and perfusion, but is unlikely to be of any benefit (and may even be detrimental) to those that are euvolemic or hypervolemic. Corticosteroid administration may have been traditionally performed, though evidence suggests more potential harm than benefits, discouraging its use. Sodium bicarbonate administration is considered in patients with prolonged CPA (10-15 minutes) to counter effects of metabolic acidosis which is likely to be present.

Electrical defibrillation is useful in patients with shockable ECG rhythms (VF and pulseless ventricular tachycardia) and has been associated with a higher rate of ROSC. Electrical defibrillation delivers an electrical shock to the heart “resetting” the myocytes and allowing them to resume a more orderly conduction and contraction pattern. Monophasic and biphasic defibrillators are available on the market. Biphasic models are recommended over monophasic because of the higher success rate and less

damage caused by a lower current used. Defibrillation should be performed in between compression cycles to minimize interruptions and allow for recharging of the defibrillator should repeated discharges be necessary.

Post-Resuscitation Care
The survival to discharge rate of a patient that successfully achieves ROSC is quite low, reported to be 16% in one veterinary study. The final outcome has a multitude of factors including underlying disease, the cause of CPA, and damage to tissues sustained during and after CPR. Post-resuscitative care is directed towards respiratory optimization performed through monitoring and providing adequate ventilation and oxygenation, hemodynamic support with IV fluids, vasopressors, and inotropes as indicated, and neuroprotective therapy consisting of seizure control, permissive hypothermia, and intracranial pressure control. Optimization of the respiratory, cardiovascular, and nervous systems allows the best chance for patient life to continue while the underlying disease is treated.

Non-medical Aspects
Even when patients at risk of CPA are identified ahead of time and the team is prepared with the appropriate facilities to perform CPR, administration of CPR can be quite chaotic. The aim is to bring as much organization and order to the chaos as humanly possible. One of the biggest factors to keeping the order is the organization of a team. There are several roles to be established ahead of time in training for any one person to be comfortably able to fill all roles necessary. The roles needed are: CPR leader, compressor, ventilator, record keeper, drug handler, and the veterinarian. The CPR leader should be identified at the beginning of CPR, so assigning of subsequent tasks can begin immediately. Staffing permitting, the CPR lead should be freed from tasks aside from assigning and keeping the team organized. Compressor and ventilators provide the compression and ventilation, and may make sense to alternate with each other between compression cycles if staffing is limited. The record keeper should keep a detailed medical record during CPR, and this task is facilitated with a CPR record form. The drug handler will prepare and administer drugs in most cases. The veterinarian ideally is not fulfilling any of these roles, being able to focus on the patient and making judgments on whether CPR efforts should continue, decisions on drug administration, communication with the owners, and any medical interventions that are necessary for the patient.

Communication during CPR is also vital to inn organizing the effort and preventing mistakes. Closed-loop communication, performed through the person making a request addressing an individual clearly by name, the addressed individual repeating back their understanding of the request, the request being fulfilled being announced, and the requestor acknowledging the completion.

Keeping the communication loops closed each time may feel awkward if it is not used on a regular basis, but contributes to very organized communication allowing everyone on the scene to stay on the same page on the status of the CPR. Double checking each other on tasks being performed is also possible, preventing the preventable mistakes.
Debriefing is another form of communication that is hugely beneficial for the team, regardless of the outcome. After the conclusion of CPR, every member should participate in a 5-15 minute debriefing session discussing the CPR. The discussion will be lead by the CPR lead, discussing the following points:

1. What went well with this CPR session?
2. What could we have done differently?
3. Are there any goals we can set for ourselves for future CPR sessions?
4. Are there any serious concerns you would like to bring up?

Debriefing sessions will bring your team even closer together as a functional unit. This also provides opportunities for staff members to express any stress they may have faced in a productive and constructive manner, and a chance for better understanding of the event that passed. Debriefing is intended for us to be able to think towards bettering our effectiveness in CPR, providing each individual patient the best possible chance of recovery and positive outcome. Bring your open mind, active listening, and participation to each of these debriefings. Commend each other on what was done well, regardless of the outcome. Discuss what could be done differently to perform CPR better. Every opinion is important, and should be discussed in a professional manner. Being open in communication requires trust and willingness to give and take feedback without bias and being personally affected.

Potential Updates from the 2023 Revision
Updates from the 2023 revision of the guidelines are not finalized at the time of writing and will be shared during the presentation.

References

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4. Rozanski EA, Rush JE, Buckley GJ, et al: RECOVER evidence and knowledge gap analysis on veterinary CPR. Part 4: Advanced Life Support. *J Vet Emerg Crit Care* Suppl 1:S44-64. 2012.

NOTES:

Technician: Nursing & Nutrition for the Critical Feline Patient Who Just Won't Eat!

Ashlie Saffire, DVM, DABVP (Feline)

Inappetence in cats is a common complication of illness and hospitalization[1]. Hyporexia and anorexia in a species with high protein requirements can quickly result in many negative effects including loss of lean body mass, compromised wound healing, suppressed immune function, and reduced chance of survival[1-3]. Treating inappetence in the hospital setting is dependent on diagnosing and addressing the underlying cause in addition to creating a low stress/feline friendly environment.

Causes of inappetence are numerous. A cat may have a direct effect from an underlying illness, but may also experience non-specific indirect factors including pain, nausea, vomiting, gastrointestinal dysmotility (e.g. ileus or constipation), dehydration and electrolyte imbalances (e.g. CKD), inability to eat (e.g., neurologic disease, injury), adverse effects of medications, neoplasia, respiratory disease (e.g. URI), cardiac disease (e.g. CHF), pain, and stress[4]. Failure to address underlying causes of inappetence will result in ongoing food refusal.

All hospitalized patients should have a thorough nutritional assessment performed at intake. A cat's diet history including feeding preferences should be collected from the caregiver as offering food with unfamiliar taste and texture can result in inappetence and food aversion. Information collected from the cat's clinical history, physical exam findings and clinicopathological parameters should then be used to develop a feeding plan for the patient. As a rule, nutritional support should be instituted in any ill cat with inadequate food intake > 3 days, keeping in mind that most cats presenting with illness may have already been anorexic/hyporexic for more than 24 hours[1].

Once a patient is adequately resuscitated, increasing nutritional intake should be prioritized. Methods to achieve this include optimizing the clinic environment, increasing the palatability of food, initiating the use of medications such as antiemetics and appetite stimulants and if indicated, providing enteral nutrition via placement of feeding tubes[4].

Optimizing the Clinic Environment

Optimizing the clinic environment means understanding potential causes of distress to a hospitalized patient. Distress is defined as an unpleasant emotional experience that is harmful to one's mental wellbeing[4,5]. Distress, development of a negative emotional state and high emotional arousal consequently decrease food intake and recovery from illness[5,6]. Causes of distress in the hospital environment may include removal of the cat from their familiar territory, their inability to escape or hide, exposure to unfamiliar sounds/smells/sights, change in routine (altered feeding and sleeping times), restriction of movement (IV catheters, bandages, Elizabethan collars), unfamiliar food, lack of predatory and play behaviors, restraint for procedures and examination, and the sight and scent of other animals[4,5,7,8]. Cat friendly strategies have been developed for hospitalized patients to reduce as many causes of environmental distress as possible in addition to avoiding stressful human interactions while still meeting the cats' daily needs[5].

The hospitalization environment should be kept quiet. Calming synthetic pheromones near the hospitalization area should be used. Ideally hospitalized cats should be kept separate from other species, especially dogs. Familiar bedding and toys should be kept with the patient and only removed when soiled. Additional bedding provided should be soft and warm to help a cat stay comfortable and maintain body heat. Minimize cleaning of the kennels with harsh chemicals to prevent removal of familiar scents. When selecting a litter box, choose a size that fits with an individual's size and mobility. Hideaway spaces, such as a cardboard box, cat bed, carrier or litterbox lined with a soft blanket can provide a safe place for the cat to hide. Covering the cage with a blanket or dim lighting may also be beneficial for some patients[4,5,7].

Human interactions should be carefully implemented. The nurse should move quietly and slowly acting in a predictable manner. Direct eye contact should be avoided. Refrain from using strong perfumes and air fresheners. Pain and FAS scoring is recommended prior to any procedure to properly prepare for an individual cat's preference for handling and to administer analgesia if indicated. When restraint is required for a procedure or examination, it should be done so in a gentle way using continuous contact to avoid startling the cat. Prior to moving the patient from their cage, all required equipment should be collected preemptively and remain easily accessible to reduce traffic around the patient. If possible, allow the cat to remain hidden during procedures (e.g., under a towel). For receptive patients, offering positive, non-medical interactions such as grooming, playing, or petting and brief periods of exercise out of the kennel throughout their hospitalization can improve mental health and physical wellbeing, ultimately helping to speed recovery[4,5,7].

Increasing the Palatability of Food

As previously discussed, the nurse should get a thorough understanding of the cat's normal feeding routine and diet history from the caregiver. The cat should be fed its regular diet while hospitalized if possible. Transition to a therapeutic diet while in the hospital setting should be avoided and any diet change should only be made after the cat returns home and has

resumed a normal appetite. For those cats that are responsive to social interactions, offering treats or food items during a brief petting or grooming session may encourage food intake.

Food bowls should be placed in areas where the cat can easily move away if desired, and ideally not near a litter tray or bed. Offering small amounts of fresh food frequently is recommended, and any uneaten food (>30 min after offering) should be removed and not left with the cat for extended periods of time (exception to this would be at night if the cat is known to be an overnight eater). Offering too many options at one time can be very overwhelming and contribute to aversive behaviors. The food dish itself should be flat or wide-brimmed (such as a small paper plate) to prevent whiskers from contacting the sides and to make food more accessible[4]. In some cases, warming the food can be helpful to entice a cat to eat, however some nauseous cats may prefer reduced scent from unheated food. Syringe feeding, force feeding and wiping food on the cat's nose should not be performed as this will only contribute to food aversions and distress.

Initiating the use of Appetite Stimulants

The use of appetite stimulants can be considered to encourage voluntary food intake under certain conditions. They may be required for short term use during a diagnostic period or following surgery, long term for chronic disease such as CKD or pancreatitis, for behavioral or environmental causes while hospitalized, to help maintain caloric intake (if not consuming the full RER), or if placement of a feeding tube is not an option[4,9,10]. Appetite stimulants should be avoided in patients who have a physical condition that is causing decreased food intake (e.g. oral tumor, esophageal stricture, mass occupying lesion causing stomach compression), have uncontrolled pain, are considered critically ill, are actively vomiting or have uncontrolled nausea, or if there is evidence of ileus causing fluid and gas distension of the bowel. Common appetite stimulants used in the feline patient include mirtazapine, cyproheptadine, and capromorelin. Common anti-emetics and anti-nausea medications include mirtazapine, maropitant, ondansetron, and metoclopramide. Understanding the mechanism of actions, side effects and precautions is very important prior to administering.

Mirtazapine is a tetracyclic antidepressant with alpha-2-adrenergic receptor antagonism properties. It has appetite-stimulating effects in addition to anti-nausea and antiemetic properties. The dose of mirtazapine is 1.88-2 mg/cat PO or TD q 24 hrs[9,12]. The frequency of administration should be reduced to q 48 hrs in patients with renal or hepatic disease[10,11]. Side effects of mirtazapine include development of tremors, muscle twitching, hyperactivity, increased interaction and increased vocalization[10,12] which can improve following dose reduction.

Cyproheptadine is an antihistamine with anticholinergic and anti-serotonergic activity. The dose in cats is typically 1-4 mg/cat PO q 12-24 hrs[9,13]. The dose should be reduced in cats with kidney disease to 1 mg/kg q 12 hr. Cyproheptadine should not be used in patients with hepatic lipidosis, urinary or gastrointestinal obstructions or severe congestive heart failure[9,13]. Side effects can include sedation, agitation, and hemolysis. A unique feature of cyproheptadine is it can be used as an antidote for mirtazapine toxicity and reduce signs of serotonin syndrome[9].

Capromorelin is a selective ghrelin receptor agonist. It works by binding to receptors in the hypothalamus to stimulate appetite and in the pituitary to stimulate secretion of growth hormone (GH). Increased GH stimulates release of insulin like growth factor 1 (IGF-1) from the liver, which in turn stimulates weight gain. The dose in cats is 2 mg/kg PO q 24 hrs. Adverse effects include hyperglycemia, vomiting, hypersalivation, bradycardia, hypotension, behavior change and lethargy. It should be used with extreme caution in cats with cardiac disease, severe dehydration or hepatic dysfunction. It should be avoided in cats with acromegaly (and in the author's opinion diabetes) due to its effect on serum glucose.

Enteral Nutrition

Ultimately, the use of enteral nutrition via the placement of feeding tubes may be required. There are a variety of feeding tubes available for use in the feline patient including nasoesophageal/nasogastric tubes, esophagostomy tubes, gastrostomy tubes and jejunostomy tubes. A feeding tube should be considered in any patient who has been consuming < 80% RER for 3 or more days, is physically unable to eat, or is anticipated to not be able to consume adequate amounts of food[1,4]. Long-term feeding tubes can also facilitate medication administration at home by the caregiver.

Short-term versus long-term feeding requirements will determine the type of enteral feeding tube selected. Naso-esophageal (NE) and nasogastric (NG) tubes are commonly used as a short-term option in the hospital setting, especially for critically ill patients. They are easily placed, inexpensive, do not require anesthesia (although analgesia is recommended), and can be left in place for several days if needed. Due to the small-bore tube required for placement, only liquid diets can be administered as they are prone to obstruction. For safety reasons, these tubes should only be used in the hospital setting.

Common cases where placement of NE/NG tubes may be helpful include pancreatitis, ileus, acute renal crisis, pyelonephritis, hepatic lipidosis, post-surgery recovery, DKA, pyrexia, and for administering a PEG-3350 CRI for constipation[14,15]. NE/NG tubes can also be useful in cases of ileus for aspiration of residual gastric content. Placement of NE/NG tubes would be inappropriate for patients with evidence of nasal disease, facial trauma, uncontrolled vomiting, or coagulopathy. They should never be placed in a patient who is laterally recumbent, comatose, dyspneic, lacks a gag reflex or has evidence of esophageal dysfunction[4].

Placement of a NE/NG tube is rather straightforward and can easily be placed by a trained veterinary nurse. Sedation or general anesthesia may be required for some patients, but often good analgesia is sufficient. The author often uses a combination of gabapentin and/or butorphanol/buprenorphine to reduce stress and discomfort during placement. Application of 4-5 drops of a local anesthetic to the nostril should be performed first. (e.g., proparacaine). A 3F – 5F tube is tolerated in most feline patients and should be measured from the tip of the nose to the 7th-8th ICS (NE) or to the last rib (NG) while the cat is in sternal recumbency. For entry into the nasal cavity, the tube should be directed medial and caudoventrally. A dab of mineral oil can add lubrication and facilitate passage. The tube should pass easily without resistance and the patient should be monitored for swallowing as the tube passes the oropharynx. Once the tube is passed to the pre-measured length, correct placement should be confirmed and then the tube can be secured with sutures, staples, or tape/tissue glue.

Confirming placement of tube can be quickly performed using a variety of techniques. First, connect an empty syringe and draw back the plunger to confirm the presence of negative pressure (or gastric contents if an NG tube). Following this, approximately 5 ml of air can be administered into the tube and auscultation of the stomach should reveal borborygmi. The administration of 3-5 ml of sterile water through the tube can also be performed and the patient monitored for coughing which would indicate incorrect placement into the trachea. An end tidal CO2 monitor can also be attached to the tube to confirm correct placement into the esophagus as no CO2 should be detected. Lastly, thoracic radiographs should be taken to confirm correct placement to the desired length/location. In cases where a tube is not radio-opaque, 2-3 ml iohexol can be administered through the tube to aid in visualization.

Complications of NE/NG tubes are uncommon but can occur. Misplacement into the trachea can result in pneumonia. Due to the small-bore size, obstruction of the tube can occur if undissolved medications or thick food material is administered. Inadvertent dislodgment is common especially in uncontrolled vomiting cats or those with significant upper respiratory disease (eg. sneezing)[16]. Placement of the tube can sometimes cause epiphora in the ipsilateral eye, epistaxis, and sneezing/nasal irritation. Reduce complications by checking tube position at placement and before every use, administer antiemetics to control vomiting and secure an Elizabethan collar to prevent patient interference.

The patient's resting energy requirement (RER) should be calculated at **70 x (body weight in kg) $^{0.75}$** and used as an initial guideline for caloric intake. Tube feedings should be started at 25-50% of the RER over the first 24 hours depending on how long the patient had been anorexic to avoid refeeding syndrome[1]. The calculated total amount to be fed should be divided into bolus feedings of 5-10 ml/kg per feeding and given every 4-6 hours. Continuous rate infusions may also be performed. Bodyweight should be monitored daily and adjustments in volume fed should be made accordingly. Additionally, as enteral diets have a high water content, the amounts of intravenous fluids administered should be adjusted accordingly to avoid volume overload[1].

Tube feedings should ideally be performed in the patient's cage, however if needed the patient can be moved to a quiet area of the hospital[4]. The cat should be sternal but can remain hidden under blankets if preferred. Prior to feeding, the tube placement should be confirmed with one of the above methods. The tube should be flushed first with approximately 2-5 ml of water to confirm patency[4]. The diet should be warmed to room temperature and given slowly over 10-15 minutes to allow for gastric accommodation[1]. The patient should be monitored for any signs of discomfort both physically or emotionally (excessive lip licking or swallowing, backing away). Once the feeding is complete, the tube should be flushed again with 5-10 cc of water to ensure clearance of any debris and prevent obstruction[4].

Once the patient has been resuscitated, is deemed stable, and is voluntarily consuming food, the NE/NG tube can be removed (without sedation) and the patient discharged. Continued use of appetite stimulants may be required to maintain daily RER intake at home. If enteral feeding or long-term nutritional support is required to be continued following discharge, consideration for placement of an esophagostomy tube should be made. Examples of diseases requiring long-term nutritional support where an E-tube is indicated include hepatic lipidosis, facial surgery/jaw fractures, oral disease, severe periodontal disease or stomatitis, chronic debilitating diseases such as end stage chronic kidney disease or neoplasia, and pancreatitis. Advantages of an esophagostomy tube include a long term duration of use (tubes can remain in place for months at a time), they can be used by the caregiver at home, they are easy and inexpensive to place, canned/denser foods can be administered through the tube in addition to medications, they are generally well tolerated by the patient, although they require general anesthesia to place, they can be removed at any time without anesthesia[4,9].

In conclusion, the veterinary nurse plays an important role in caring for the critical feline patient. Recognizing patients in need of nutritional support and carefully planning and executing an individualized nutritional plan all while maintaining a cat-friendly hospitalization environment is essential for the successful recovery of these cats. The use of enteral feeding tubes can significantly improve outcomes and the veterinary nurse plays a vital role in helping to develop and execute a feeding plan for a critical patient. For more recommendations, the following guidelines are excellent resources and should be carefully reviewed: The 2022 ISFM guidelines on the Inappetent Hospitalized Cat[4], the 2022 AAFP/ISFM Cat Friendly Veterinary Interaction Guidelines: Approach and Handling Techniques[5], and The 2012 AAFP/ISFM guidelines on feline-friendly nursing care[7] (see references).

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Discussing Diabetes Mellitus: Empowering Technicians
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Technician: Practical Application of Feline Emergency Transfusions

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Introduction

The ability for a practice to perform emergency transfusions is crucial to have better chances in treating patients like the one described. While the patient was unable to be saved, time for diagnosis and the owner's decision making process was gained. In many less extreme cases of hemorrhaging and anemia, red blood cell (RBC) transfusion is a life-saving therapy. Present day, transfusions are not uncommon. Many practices bank blood products in-house with most relying on commercial banks for supply, while some develop their own donor program and even process blood components in-house.

Step 1: Know when a transfusion is required

When an animal loses a significant amount of blood, replacing the blood may seem like common sense. In actuality, not all patients who have lost blood require blood to be transfused in order to prevent shock.

Blood circulating within the vasculature serves to deliver oxygen to various tissues. Oxygen is required for efficient production of cellular energy in the form of adenosine triphosphate (ATP), utilized for maintenance of life at molecular levels. Cell signaling, DNA and RNA synthesis, cytoskeletal maintenance, active transport, and muscle contraction are just some of the critical processes utilizing ATP. Oxygen delivery is determined by arterial oxygen content and cardiac output (how fast the blood can be pushed around the body).

As long as there is adequate blood volume, even an anemic patient can deliver sufficient oxygen to meet metabolic oxygen demands. This required blood volume can be provided for the short term with crystalloid infusion. There is a point, however, where the anemia is severe enough that restoring blood volume is not sufficient to provide adequate oxygen delivery. As hemorrhaging progresses, blood volume replacement with crystalloids will continue to dilute the blood, decreasing the packed cell volume (PCV) to the point that the compensatory increase in cardiac output (through increasing heart rate and stroke volume) is insufficient to keep up with oxygen demand. When the patient reaches, or is expected to imminently reach this critical oxygen extraction level, a transfusion of RBCs is required.

Determining when a patient has reached this "critical oxygen extraction" level is important because transfusions are not benign; they may cause immunosuppression, immunologic reactions, or inflammatory consequences. If a transfusion is not truly necessary, these effects are only harmful to the patient.

Clinical signs of anemia will be seen in patients reaching critical oxygen extraction levels, such as weakness and impaired mentation even though they may be considered to be at a good fluid balance. Patients would also exhibit compensatory signs of shock including tachycardia, increased respiratory effort, pale mucous membranes and prolonged capillary refill time.

Laboratory values evaluating acid-base status would point towards metabolic acidosis with an increased plasma lactate level if the anemia is significant and prolonged. The decision to perform a RBC transfusion cannot be based on any laboratory value such as PCV or hematocrit alone, but on the presence of these signs of hypoxia in the patient.

Step 2: Use the proper type of blood product

With severe hemorrhaging, whole blood is lost, i.e. RBCs, platelets, leukocytes, and plasma. Replacing this loss with a whole blood transfusion is reasonable, and sometimes even beneficial, preventing dilutional coagulopathy. However, each of these components possesses the potential to cause negative effects when transfused. Each component has antigenic elements which stimulate the immune system to react. Because of this, component therapy, or the act of replacing only the components required by the patient in a purposeful manner, is advocated. Whole blood is separated into components and stored separately to be used at a later time.

In the case of reduced oxygen carrying capacity due to anemia (low RBC level in blood), only red blood cells (RBCs) are required. Whole blood is centrifuged and the plasma removed. The remaining RBCs, packed RBCs (PRBC), are a concentrated solution that can be used for RBC transfusions. Leukocytes can also be removed through a process called leukoreduction, further reducing the immunologic potential. The cost of filters required for the process makes regular application of leukoreduction difficult in veterinary settings, though many blood banks will provide leukoreduced PRBC on request.

Plasma contains hemostatic proteins, albumin, and other plasma proteins. Due to the concentration levels of each of these plasma components, therapeutic use of plasma transfusions are appropriate only to replace hemostatic proteins for coagulation factor deficiencies and the resultant hemorrhaging. Plasma is no longer preferred in hypoalbuminemic patients because in order to increase serum albumin by 1 g/dL, a dosage of 40-50 mL/kg is required. The risks of immunologic complication and fluid volume overload, as well as the drain on both financial and biological resources, would be reasons against using plasma for albumin supplementation.

In a similar manner, platelet supplementation may be desired in cases of thrombocytopenia or thrombopathia. It is difficult to maintain a healthy stock of platelet products as its shelf-life at room temperature is short (approximately 5 days). The viability of frozen platelets are significantly reduced using the current methods of cryopreservation. In most practices, platelets are provided in the form of whole blood, where the quantity available to the patient will be limited by a typical concentration of platelets in whole blood. Repeated whole blood transfusions for the sake of replacing platelets is not a good option due to the potentially unnecessary components and volume of RBCs and plasma.

The majority of emergency transfusions will be performed to supplement oxygen carrying capacity for anemic patients via PRBC. Transfusion of cellular components, such as RBCs, are accompanied by a strong antigenic (foreign substance triggering the immune system) load. RBCs are accompanied by a set of erythrocyte antigens which are used to characterize the blood type of an individual and affect the compatibility of RBC transfusions from a donor to a recipient.

In felines, the AB system and the *Mik* antigen have been identified as existing blood types. A cat can express either A, B, or AB as their phenotype. Type A blood will be most compatible with type A cats, and type B blood will be most compatible with type B cats. Type A cats have a mild level of anti-B antibodies circulating in the plasma, causing significant, but often non-life threatening transfusion reactions when transfused with type B blood. Type B cats have a high titer level of anti-A antibodies, causing severe, acute hemolytic transfusion reaction and anaphylaxis when transfused type A blood. Cats with blood type AB have both A and B antigens on their red blood cells.

In addition to the AB system, cats have also been identified with other blood group antigens, including the Mik antigen. The Mik antigen is found on the red blood cells of about 10% of cats. Cats with the Mik antigen can develop antibodies to the Mik antigen, which can lead to a hemolytic reaction if they receive a blood transfusion from a cat that does not have the Mik antigen.

There have been other non-AB antigens described in cats. These antigens include FEA 1-5. The prevalence of these antigens in cats is not well-known, but they have been associated with hemolytic reactions in cats that received blood transfusions from cats that did not have the same antigens.

Because of the lack of commercial kits for many RBC antigens, crossmatching is an important form of compatibility testing, especially if the patient has been exposed to previous transfusions (and potentially sensitized). Crossmatching tests for the potential for immunologic complications by mixing recipient and donor plasma and observing for agglutination or hemolysis. A positive result in agglutination or hemolysis indicates the likelihood of immunologic complications occurring if the transfusion goes forward. The major cross-match tests for the likelihood of donor RBCs being hemolyzed by the recipient, and is performed by mixing donor RBCs with recipient plasma. The minor cross-match tests for the likelihood of donor plasma proteins affecting the recipient RBCs, performed by mixing recipient RBCs with donor plasma. Any positive result makes the match non-ideal for transfusion. Blood type matching and cross-matching is recommended for cat transfusions. If the patient cannot afford the time to crossmatch, blood type matching is recommended at a minimum.

Keeping both type A and type B blood on hand is the most ideal scenario in the case of emergency need for transfusions because there is no universal blood type with cats. Storing of type B PRBC is both a financial and biological resource commitment, however, since the majority of the population is type A. However, without stored type B RBCs available, your type B patients will be left to wait for donors to come in and have whole blood collected, or in worse cases be left without the option of RBC transfusions. Especially for type B blood products, though not exclusive, creating a regional network with neighboring veterinary practices to help each other in the case of dire need is beneficial.

Step 3: Keep other sources of blood in mind

Traditionally, blood transfusions are performed in an allogenic manner, or performed between one member to another within the same species. There are, however, some other forms of transfusions that can be used in specific situations which reduce the demand for blood products from donors and may prove its usefulness in emergency situations; autotransfusion and xenotransfusion.

Autotransfusion

The first of which is autotransfusion, or the act of salvaging blood lost by the patient and reinfusing the blood into the same patient. In veterinary medicine, autotransfusion is most commonly performed as unwashed red cells transfused through a filter. This is accomplished through transfer of suctioned blood into an intravenous fluid bag and administered with a blood administration set. An alternative method involves the use of a 3-way stopcock attached to a syringe and extension sets. The stopcock is first opened to the extension leading to a blood-filled cavity (e.g. abdomen) and the syringe, and blood pulled into the syringe. The stopcock is then turned to be open to the syringe and another extension leading to an intravenous catheter, and the blood pushed through an in-line blood filter into the patient. The syringe method can also be employed prior to surgical intervention, through percutaneous insertion of a catheter into a body cavity the hemorrhaging is occurring in. Autotransfusion is observed to be effective in alleviating compensatory signs from anemia and improvement in consciousness in a study involving severely anemic subjects, whereas replacement of the volume with lactated ringers did not result in the same effect.

Autotransfusion has advantages in addition to alleviating RBC product demand. By administering autologous blood, the concerns of immunologic complications are eliminated. Blood typing and cross-matching can also be omitted, since there should be no better match to a recipient than their own blood. The effects of storage lesions can be avoided through autotransfusion, since storage time is not involved. Storage lesions, which include accumulation of hazardous levels of electrolytes, metabolites, and inflammatory mediators, as well as RBC changes (which reduces their efficacy as oxygen carriers), occur in blood stored longer than 14 days causing it to be less effective in the treatment of anemia, have shorter cell survival time, and incite negative effects in the recipient.

Xenotransfusion

A news report of a feline patient who was determined to require a RBC transfusion with the alternative being death reminds us of the challenges of obtaining feline blood matching our patient can be. A practice, for example, with an in-house bank has two units of type B blood banked regularly, with a type B donor in the donor program ready to donate at beck-and-call would be considered very well prepared for a type B patient requiring transfusions. Such a situation is rare, however. Even then, the practice still would be out of options for RBCs of this rare feline blood type if a patient requires multiple transfusions, or multiple patients come in and happen to be of the same type. Many practices face shortage of RBC products in general, regardless of the type. In this particular news report, the feline patient received canine blood as a part of his treatment and survived; an example of xenotransfusion in practice.

Xenotransfusions, or transfusion of blood products between individuals from different species, has been recorded in literature dating back to 1667 involving transfusion of blood from lambs, calves, and dogs to human for various reasons. Xenotransfusion has been employed in the 1800's with a good degree of success, though the discovery of blood types and improved knowledge on blood compatibility from the 1900's encouraged the practice of intraspecies, or homologous, transfusions. The practice of intraspecies transfusions has significantly improved the safety and effectiveness of RBC transfusions. While veterinary transfusion medicine is largely practiced in this manner, maintaining adequate feline blood supply is challenging with the small donor pool and more complicated collection process. Being able to use, for example, canine donors of a typical donation volume of 450mL to supply our feline patients with a typical whole blood unit volume of 50mL would allow a single donation to give us enough blood for nine transfusions. This seems like a great opportunity for a solution to the blood shortage. Let's discuss this further.

In order to implement xenotransfusion into our practices, we would first need to ensure the effectiveness and safety of xenotransfusions. There are several published studies specifically evaluating the effects of canine to feline transfusions, evaluating pre-transfusion predictors of immunologic complications, immunologic complication signs seen during and after transfusions, and the same on repeat xenotransfusions at varying timings.

Efficacy: The studies that have been conducted heavily focused on compatibility testing and immunologic complications, and less information on efficacy of the transfusion is available. Literature giving insight to the efficacy of canine to feline transfusion indicates a rapid improvement of clinical symptoms, leading to the conclusion that a positive effect of the transfusion is expected. In a case report involving a type B cat receiving blood from a Labrador Retriever resulted in an increase in PCV taken after the transfusion performed over 48 hours. The effect is relatively short lived, however, since the transfused RBCs seem to have an average lifespan of 4 days. In comparison, a typical life span of RBCs of homologous feline transfusion is 30 days. The loss of transfused RBC is attributed to delayed hemolytic transfusion reaction resulting from antibody production against RBC antigens introduced. The production of antibodies by the immune system when exposed to foreign antigens (sensitization) occurs in a delayed manner reaching significant titer levels 4-7 days post transfusion, allowing the transfused RBC to persist for

4 days on average. The recipients have been observed to develop icterus from increased intravascular hemolysis and bilirubin load.

Safety: Statements regarding safety of canine to feline transfusions can be separated into three specific situations. In almost all transfusions performed in these studies, there were no acute clinical consequences to performing canine to feline transfusions as long as there was no history of previous canine blood transfusions. Subsequent transfusions performed within 4 days of the initial exposure also were performed without acute symptoms of immunologic complications. Subsequent transfusions performed more than 4-6 days past initial exposure resulted in anaphylaxis, which was often fatal.

Cats seem to be tolerant of the first canine blood transfusion they receive without signs of acute hemolytic or allergic reactions, indicating a lack of naturally occurring antibodies against canine RBC antigens. These observations correlate with the majority of compatibility testing methods (slide agglutination and cross match hemolysis testing) showing no signs of incompatibility. Occasional positive reactions were seen on the minor (recipient RBC mixed with donor plasma) cross match, which upon transfusion would cause some hemolysis of recipient RBC. This effect is minimized from the use of PRBC, containing little plasma, and dilution by recipient blood volume upon transfusion. Cats in the studies rarely exhibited signs of complications, and when they did, they were mild, involving tachypnea and pyrexia during or within 24 hours of the transfusion. Delayed hemolysis occurring after 4-7 days of transfusion seems inevitable, with presence of anti-canine RBC antibodies made evident through positive slide-agglutination and cross match results when performed after this timing. Subsequent transfusions after the initial exposure but within the 4-7 day period did not result in clinical signs. Slide agglutination and cross match tests performed during this time period did not result in a positive reaction as well. This indicates a "grace period" in which antibodies are being produced to incite an anamnestic response when the next exposure occurs. Felines in the study that were given doses of canine RBC 1 and 2 days after initial exposure did not exhibit signs of immunologic complications. Test subjects having subsequent transfusions performed later than 6 days after the initial exposure showed signs of anaphylaxis with more than 66% resulting in death. Some of these cats were treated with cyclophosphamide as an immune suppressant prior to second exposure with the hypothesis of immune suppression reducing chances or severity of immunologic complications, with no positive effect seen. This serves as further evidence of the ineffectiveness of immune suppressive agents as premedication for transfusion (Human studies show premedication to be ineffective).

Example Uses: Several articles relating to dog to cat transfusions have been published since. One involved a 0.5 kg kitten presenting anemic from a flea infestation and possible *Mycoplasma hemofelis* infection. The kitten received 5 mL of canine PRBC after a lack of response to antibiotic and supportive care and being unable to receive feline blood due to financial constraints. There were no signs of acute or delayed transfusion reactions and the kitten made a full recovery.
Another case report described two cats presenting with hypovolemic shock (one with a penetrating abdominal trauma and another with flea infestation) and blood loss being given 20 mL/kg of canine blood. There were no signs of complication during the transfusions and the transfusions were effective in raising the PCV and hemoglobin levels. CBC, total protein, albumin, electrolytes, urea, creatinine, and bilirubin levels were measured at two days, one week, and one month post transfusion. The bloodwork at two days showed no abnormalities, while the blood smears showed anosocytosis which was attributed to the difference in diameter of canine and feline RBCs. At seven days, an elevation in the bilirubin level and spherocytosis was seem, indicating the presence of extravascular hemolysis from a delayed hemolytic reaction. The article did not indicate the results obtained one-month post-transfusion.

A third case report described two cats receiving canine blood. The first cat was suffering from acute blood loss related to a coagulopathy during a surgical procedure. The blood typing was inconclusive in whether the patient was type B or type AB which led to the necessity to use canine blood on an emergency basis. The cat was behaving normally (eating and grooming) one hour after transfusion with bleeding stopped by 4 hours after transfusion. There were signs of hemolysis 24 hours by 1 day post-transfusion and further PCV decline by day 4. The patient recovered fully over the next 3 weeks with normal PCV and coagulation test results. The second cat was determined to be type A through in-house testing but had severe acute reaction when infusion of type A blood was started. Given that the cat showed major crossmatch incompatibilities with all available type A blood, dog blood was opted to be given which resulted in a successful transfusion with no adverse reactions with an increase of PCV from 6% to 22%. Signs of hemolysis were seen in the subsequent days, and the PCV fell to 7% four days post-transfusion. Both of these cases illustrate the usefulness of dog blood in patients with uncertain blood types or unpredictable response to type-matched blood, though the benefits are short-lived.

A fourth case report published described dog blood being injected into the left ventricular chamber of a cat in cardiopulmonary arrest. Blood was opted to be injected into the ventricular chamber guided by ultrasound because IV access was unable to be established. The patient achieved return of spontaneous circulation, and was given additional dog blood through a jugular catheter. The patient recovered fully with signs of regeneration with minimal changes to bloodwork (some bilirubin seen 2 days

post-transfusion), and later determined to be type B. This case described a situation where dog to cat transfusions may be useful on an extreme emergency basis.

Summary: Transfusion of canine blood, whether whole blood or packed RBC, can be performed without immediate consequences if it is the first transfusion of this kind. However, the benefit is short lasting, and should be reserved for patients are in dire need of blood. The basic considerations in employing this therapeutic option should include situations where all of the following are conditions are met. (1) The patient has no source of RBCs with compatible blood type (type B cat with no stocked blood, donor, or nearby hospital with stock, for example) or hemoglobin-based oxygen carrier solution. (2) The patient is imminently going to pass away or is thought to be in danger of sustaining irreversible hypoxic damage (certainly up to clinical judgment) without the ability to obtain compatible blood in a timely manner. (3) The patient is expected to benefit from a short-term oxygen carrying capacity gain. In this case, the patient may have a condition where the cause of anemia can be controlled swiftly enough to allow regenerative response to take over, or allow for time to obtain sources of compatible RBCs in the meantime. (4) The patient has never received canine blood products. (5) The owner understands the risks and consequences of performing a canine to feline transfusion. As the method is non-traditional, the owner should know our exact state of knowledge and potential consequences to give fully informed consent to the procedure.

If these conditions are met, use of transfusions of canine RBC to feline patients can be a life-saving therapeutic option in true emergency situations. If a xenotransfusion is decided on, a major and minor cross match should be performed to screen donor-recipient matches resulting in any signs of immunologic complications, and a therapeutic plan formulated with the benefit lasting 4-7 days in mind. Clear understanding of outcomes of future canine to feline xenotransfusion by the owners is important in preventing a second exposure beyond the 4-7 day mark. As responsible veterinary professionals, xenotransfusion should not become common practice in its current state. Effort invested in maintaining a good source and stock of feline RBC products should not decrease simply because “we can always turn to dog blood if we really need to”.

Other uses of xenotransfusions: There are several other articles of interest related to xenotransfusions. These are related to bovine blood being used for transfusions in wildebeest calf and goats, and dog blood being transfused to an island fox. Each of these reports describe the xenotransfusions being viable for a short-term duration.

A pilot study evaluating *in vitro* compatibility of canine and human blood saw that crossmatches shows strong reactivity with significant hemolysis or agglutination on all samples, indicating that human blood being given to dogs will not result in favorable outcomes.

Conclusion

Preparing ourselves to be equipped for emergency transfusions requires a working knowledge in the assessment of an anemic patient, when a patient truly needs transfusions, blood types, preparation in creating multiple sources of blood products and components, and utilize some situation specific options that will further expand the ability to provide transfusions. Is your practice prepared for emergency transfusions?

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Feline GI Immunity's Inextricable Links to Dietary & Microbiome Components

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Introduction

Chronic intestinal issues are a common reason for cats to be presented to their veterinarian. Clinical signs can range from obvious issues like recurrent vomiting, or be more insidious, such as progressive weight loss. Optimal management of these conditions requires an understanding of the particularities of the feline gastrointestinal tract. Much remains to be investigated in this species; here, we will review current understanding of feline gastrointestinal (GI) physiology. Gut luminal contents, namely, dietary components and microbes, play a pivotal role in the development, functionality, and disease progression of the entire GI system. Recent publications probing the connections between diet, microbiome, and feline enteropathy will be visited with the aim of providing information that will optimize management of clinical patients today.

Function of the healthy feline gastrointestinal tract

Knowledge from studies of other species (e.g., humans and mice) are frequently extrapolated to domesticated small animals; this may be acceptable for some topics and problematic for others. Gastrointestinal and nutritional aspects of the domestic cat (*Felis catus*) have been studied more far the most extensively compared to other members of the order *Felidae*, still, there remains a great deal of lumping together of canine and feline intestinal health. Here, we'll focus on a few highlights of feline gastroenterology.

Anatomically, the cat GI tract is unique in its shorter length compared to that of the dog, with an average length (esophagus to anus) of approximately 200 cm[1]; for context, average human intestinal tract is about 4.6 m long. Cats are monograstric, lack a functional cecum, and have the three characteristic segments of the small intestine as seen in other species. Biliary communication with the small intestine most typically involves fusion of the common bile duct and major pancreatic duct prior to arrival at the major duodenal papilla[2]. This difference from other species has been postulated as a cause for concurrent pancreatic and biliary disease.

Gastrointestinal transit times in fed and fasted states been recently evaluated in research colony cats (Telles JFMS 2022). Anatomic location was inferred based on local pH. Cats showed marked intra-individual variation despite a homogenous population in terms of age, genetic background, and current diet. Median overall GI transit time (GTT) was 28.9 and 46.5 hours in the fasted and fed state, respectively. This difference was not statistically significant; total GTT were comparable to similar investigations in dogs[3]. Somewhat shockingly, 5/6 cats had esophageal retention of capsules for > 15 minutes, including multiple instances where the capsule remained in the esophagus for 5 hours[4]. Clearly, pilling a cat with a 6 mm × 5 mm × 25 mm capsule does not replicate normal food consumption, but this study nonetheless provides important insight into possible outcomes of orally medicating a cat, and some insight into expected feline GTT.

Cats are obligate carnivores. Essential nutrients for cats are therefore derived from animal tissues, including but not limited to arginine, taurine, niacin, and vitamins A and D[5]. Cats have lower intestinal mucosal carbohydrate digestive enzyme activities (e.g., maltase, sucrase, isomaltase) compared to dogs and pigs[6]. Feeding of starches has *not* been found to have an inductive effect on these enzymes[7]. The high protein requirement of cats may be related to their limited ability to control activities of aminotransferases[8]. The upshot of this is that cats are very efficient mobilizers of protein building blocks for gluconeogenesis. This enables cats to do well despite prolonged periods of fasting. Normal cat feeding behavior involves grazing and foraging; left to their own devices, cats may eat up to 20 times per day. Ad libitum feeding may therefore better replicate natural feline feeding behavior[9] with the potential increased risk for development of obesity.

Dysfunction of the feline GI tract

Chronic GI clinical signs are common in domestic cats presenting to veterinary clinics. These include classic clinical signs like vomiting and diarrhea, but importantly, in cats, include unexplained weight loss, reduced food intake, and constipation. Diagnostic investigations are used to determine if the signs are due to extra-GI (e.g., hyperthyroidism, dental disease, renal or hepatic disease) or primary GI causes. Aging cats often present with multiple co-morbidities which may require multi-modal treatments.

Functionality of the feline GI tract declines with age. In contrast to the reduction in metabolic energy requirement (MER) seen with advancing age in adult dogs and humans, cats show a decrease in MER with maturity (age 6 to 10 years) and a subsequent

increase in MER when they reach 10 to 12 years of age[10, 11]. This correlates with the highest incidence of obesity being found in cats 7 to 12 years old, and a higher risk of underweight status in cats greater than 12 years old[12]. A study of research colony cats housed in a home-like environment found that cats lost fat and protein digestive capacities with age, with 1/3 and 1/5 of geriatric cats having reduced fat and protein digestive capacities, respectively[13]. This study also found a dramatic decreases in body weight in the last year of life regardless of cause of death. This information reinforces the importance of serial body weight measurement and adequate nutrition in aging cats, with special attention paid to amount consumed and digestibility of nutrient sources.

The two most common chronic causes of GI signs in cats are inflammatory bowel disease and small cell GI lymphoma. Much attention has been paid recently to the differentiation of IBD from SCL, however, the management approaches are broadly similar. Current understanding suggests that these two conditions may be part of a spectrum of disease[14]. For further information, readers are referred to Dr. Anne Avery's lecture. For the remainder of this lecture, the term chronic enteropathy (CE) will be used to encompass cats with *either* of these diagnosis, as well as cats fitting the clinical criteria who have not had a full workup including intestinal biopsy analysis.

Microbiome's role in GI tract function

The microbiome is an integral component of the GI tract, serving functions from pathogen exclusion to immune system 'education' to nutrient processing. Current understanding of inflammatory bowel diseases in people involves an inappropriate immune reaction against commensal microbes[15]; this has yet to be proven in cats. Like other species, the dominant phyla in the feline fecal microbiome are Actinobacteria, Bacteroidetes, Fusobacteria, Firmicutes, and Proteobacteria[16,17]. Limited data is available linking gut microbiota constituents with feline CE. Marsilio and colleagues documented reduced alpha diversity and lower prevalence of facultative anaerobes in the feces of IBD and lymphoma cats compared to healthy controls[18]. This pattern to some degree replicates those seen in canine and human chronic inflammatory intestinal diseases, with reductions in *Firmicutes* and expansions of *Enterobacteriaceae* and *Streptococcus* spp. To date, almost all investigations of the feline GI microbiome are descriptive. Future studies integrating other -omics results (e.g., transcriptomics, metabolomics, proteomics) will be critical to advance understanding of the ramifications of microbiome shifts.

While fecal samples are easily obtained, they may not represent the most physiologically relevant microbes. Analysis of the gut mucosa sheds light on more immunologically relevant microbial populations. One study used fluorescence in situ hybridization (FISH) to characterize mucosal surface bacteria in cats with IBD[19]. They found no differences in overall bacterial numbers, but significant increases in *Enterobacteriaceae*, particularly in the adherent mucus of duodenal IBD samples. The contribution of *Clostridium*, *Bacteroides*, *Streptococcus*, and *Enterobacteriaceae* made 6% of FISH (EUB-388)-positive microbes in healthy cat samples compared to 91% of these organisms in IBD cat samples. Moreover, the number of mucosal *Enterobacteriaceae, E. coli*, and *Clostridium* correlated with abnormal mucosal architecture (atrophy, villus fusion, crypt hyperplasia, epithelial cell change), proinflammatory cytokine mRNA levels (IL-1, IL-8, IL-12), and the number of clinical signs exhibited. Another study comparing the fecal microbiota of healthy cats to those with CE found an increased abundance of *Clostridium* spp., but no significant relationships between fecal bacterial populations and disease severity or histopathologic lesions[20]. Further study of mucosal bacterial populations is warranted toward the end of further unravelling of feline GI disease initiation and perpetuation.

Diet's role in GI tract function

As mentioned previously, cats have nutritional needs in line with their evolutionary history subsisting on prey animals. Indoor-only household cats likely have a dramatically different diet compared to their wilder predecessors. Dietary components are poised at the frontlines of GI tract function and dysfunction. Enteral nutrition is critical for GI tract function. Villous atrophy and increased gut permeability are well documented in dogs fed parenterally. Studies involving total parenteral nutrition (TPN) to cats exhibit the shortcomings of this feeding style; one study of 7 clinically normal cat documented vomiting, depression, anemia, and thrombocytopenia after 10 to 13 days of TPN[21]. Retrospective review of 12 client-owned cats managed with TPN documented glucose intolerance in 9/12 cats and lipid intolerance in an unspecific number of cats[22]. These findings underscore the importance of nutrient delivery to the gut mucosal surface. Early assisted feeding may increase odds of favorable outcomes and support normal immune function in critically ill cats[23,24]. Nasogastric and esophageal feeding tubes can be easily placed in most practices and have low rates of complications.

The specific foods providing nutrients to the gut mucosa and cat itself are also important. Calories can be obtained in the form of protein, fat, or carbohydrate. Cats have no intrinsic need for carbohydrates, but these make up a substantial portion of commercial feline diets (ranging from 20 to 55% metabolizable energy [ME])[25]. Cats can obtain nutrients from various carbohydrates despite their carnivorous nature[26,27,28]. Fascinatingly, some data indicates that cats have a set "ceiling" in terms of carbohydrate intake, particularly when ingesting a low protein diet[29]. This may be an ingrained behavior to prevent excessive

carbohydrate intake that would overwhelm the limited capacity for carbohydrate ingestion and promote excess proteolysis in the distal and ensuing adverse GI signs. Debate continues surrounding the appropriateness of carbohydrates as an energy source for cats[30],[31]. The author tends to aim for a carbohydrate content of <30% on a ME basis.

Evidence regarding role of microbiome & diet modification in feline chronic enteropathy
Given the clear role of the intestinal microbiome in GI health and disease, modulation of this body of organisms is of interest for prevention and management of disease.

Microbiome-directed interventions
Oral antibiotics strongly impact the gut microbiome. Oral clindamycin and amoxicillin-clavulanic acid given to healthy cats caused unsurprising dramatic shifts in fecal microbial populations including reductions in diversity[32],[33]. Many cats in these studies had substantial antibiotic-associated vomiting and/or diarrhea, which were at times ameliorated by synbiotic or probiotic administration. Antibiotics are commonly trialed to see if they improve clinical signs in cats with CE; the author appreciates a small subset of young cats with severe, refractory diarrhea that are negative for all specific etiologies with dramatic response to oral tylosin. Another unique subset of patients are those with a syndrome very similar to *E. coli*-associated granulomatous colitis[34]. It is important to highlight the significant potential adverse effects seen with metronidazole therapy in cats; reversible DNA damage in lymphocytes[35] and neurotoxicosis[36] are documented in this species. The medication also has an extremely bitter, metallic taste, which may negatively impact appetite. For these reasons, use of this drug in cats should be reserved for cases in which it is truly necessary.

Probiotics may have a role in the management of feline acute enteritis[37], tritrichomoniasis[38], and abrogating the adverse effects of oral antibiotics[32],[33]. The author also uses FortiFlora for its palatability enhancing properties.

Fecal microbiota transplantation (FMT) is a newer tool investigated for its ability to shift the gut microbiome +/- manage clinical disease. Published evidence regarding this intervention in cats is limited. A single case describes resolution of chronic diarrhea and macrophagic colitis in a 10 year old Abyssinian cat with 2 FMT procedures[39]. Well-executed, randomized, placebo-controlled studies are needed to evaluate the impact of FMT in CE cats.

Dietary modulation
Diet is another powerful mechanism of reducing CE signs. In dogs and people, change in diet has been associated with rapid shifts in gut microbial populations as different substrates become available[40]. Few studies have evaluated the impact of diet on feline gut bacterial communities using sequencing. Kathrani et. al. compared fecal bacterial populations from CE cats (10/36 with histopathologic diagnosis) before and after 6 weeks of feeding of a hydrolyzed soy protein kibble[20]. They noted reduction in the relative abundance of numerous bacterial groups post-diet, as well as differential effects on the fecal microbiome comparing responders (15/36 cats) and non-responders (18/36). Increases in the relative abundance of short-chain fatty acid producer *Bifidobacterium* was observed post-diet in responders and non-responders. Another study used 454-pyrosequencing to evaluate the impact of 3 weeks of feeding chicken-based canned gastroenteric diets on the fecal microbiome of cats with chronic diarrhea[41]. They found a greater proportion of cats achieving normal stools in one diet (47%) compared to the other (13%); cats ingesting this diet had increases in fecal *Eubacterium*, *Enterococcus* and *Streptococcus*. Additional work is needed before causality can be inferred between diet feeding, gut bacterial shifts, and clinical response.

Hydrogen breath testing, fecal short-chain fatty acid concentrations and fecal pH measurement have been applied to indirectly interrogate impact of diet on gut bacterial populations. Higher hydrogen breath area under the curve was seen in CE cats eating starch-containing diets compared to chicken meat, and CE cats had higher hydrogen breath AUC than healthy cats regardless of diet[42]. Hydrogen breath excretion may be due to undigested carbohydrate and/or protein reaching the colon or due to GI inflammation with cell desquamation and mucus production. Ingestion of the starch-containing diets did not impact fecal consistency, but fecal water content was higher in cats consuming diet with starch[42], which could benefit constipated cats[43].

Independent of microbiome investigations, evidence supports the clinical benefit of diet change to cats with CE. A retrospective study of 977 cats in the United Kingdom prescribed hydrolyzed protein diets for vomiting and/or diarrhea identified a positive response in 66% of cats[44]. Cats concurrently prescribed an antibiotic or steroid with diet had a greater likelihood of a poor response. Smaller studies have prospectively investigated the impact of diet on feline CE. In contrast to dogs, fat content does not appear to be important in management of chronic diarrhea in cats[45]. A small study of 8 CE cats documented improvement within 4 to 8 days of ingesting a soy hydrolysate-based kibble[46]. A more recent study documented the impact of two commercial chicken-based dry diets on cats presenting for chronic vomiting; at the end of the 4-week trial, 47 or 67% cats had no episodes of vomiting depending on the diet fed[47]. The diet showing a trend toward better efficacy had higher carbohydrate

(and fermentable fiber) and long-chain omega-3 fatty acid contents. Another prospective study (abstract) looked at the clinical impact of feeding a fiber-rich diets on cats with constipation or diarrhea; after 4 weeks of feeding, 17/25 cats on the control fiber blend (cracked pearled barley, ground corn, dried beet pulp, psyllium husk) and 19/19 cats eating the test fiber blend (ground corn, ground pecan shells, oats, pea fiber, flaxseed, pressed cranberries) had a positive or complete response[48].

Various options for dietary intervention exist, ranging from over the counter to therapeutic veterinary commercial to home-prepared diets. A summary of the characteristics of diets often employed for management of feline CE is displayed in **Table 1**. No reliable or accurate tests are available to determine diets or ingredients that will or will not work for an individual cat, therefore, dedicated feeding trials are paramount. Some cats may not tolerate commercial diets; home-prepared offer potential benefits of improved palatability and digestibility, in addition to the ability tailor a specific diet to the needs of a patient with multiple co-morbidities[49]. A board-certified veterinary nutritionist must be involved in the formulation of feline home-prepared diets. Feline "recipes" are readily available online but are often deficient in amino acids, choline, and/or zinc[50]. Diet can be associated with unintended mortality, as evidenced by an outbreak of pancytopenia in the United Kingdom leading to the discovery of mycotoxin contamination in various feline maintenance diets[51]. Keeping apprised of recall notices is critical for veterinary practitioners; clients should also be counseled to save pet food bags or at least take a photo of the barcode and lot number.

Future directions

Our understanding of feline GI physiology and disease pathomechanisms is far from complete. Further work is needed to flesh out the intricacies of these unique creatures. Applying current knowledge of cats' particular nutritional needs, taking a proactive approach to gut health, particularly in the geriatric patient, will improve long-term outcomes. The intestinal microbiome is clearly important, but existing studies are not able to draw causality between microbiome shifts and disease states. Diet has a central role in shaping the microbiome, and therefore cannot be overlooked as a powerful tool to change the course of disease.

diet	kcal per gm	phos (mg)	protein (gm)	carb (gm)	total dietary fiber (gm)	protein source
HYDROLYZED						
Royal Canin Ultamino	3.8	120	6.3	10.7	2	Hydrolyzed Poultry By-Products Aggregate
Hill's Prescription Diet z/d	3.7	160	8.8	10.4	1.2	hydrolyzed chicken liver
Hill's Prescription Diet z/d^	1.1	164	8.3	9.9	0.6	hydrolyzed chicken liver
Purina Pro Plan Veterinary Diets HA	3.8	300	8.2	10.7	1.5	Hydrolyzed Soy Protein Isolate
Royal Canin Hydrolyzed Protein Adult HP	3.9	170	6.3	9.4	2	hydrolyzed soy protein
NOVEL PROTEIN						
Royal Canin Selected Protein Adult PD	3.5	270	8.5	10	2.6	duck by-product meal
Royal Canin Selected Protein Adult PD^	1.1	200	9.4	3.3	2.1	duck by-product meal
Royal Canin Selected Protein Adult PR	3.5	230	8.5	10.1	2.6	rabbit meal
Royal Canin Selected Protein Adult PR^	1	170	10.3	2.9	1.4	rabbit, rabbit liver
Hill's Prescription Diet d/d duck & green pea	3.9	174	8.2	8.2	2.6	duck
Hill's Prescription Diet d/d duck^	1.1	167	8.6	4.5	2.3	duck, duck liver
HIGH FIBER						
Royal Canin Appetite Control	3.3	280	9.7	NA	5.4	chicken meal
Hill's Science Diet Adult Indoor	3.5	202	9.7	NA	4.5	chicken
Royal Canin Urinary SO Moderate Calorie	3.3	260	9.8	9.4	3.7	Chicken By-Product Meal
Purina Pro Plan Veterinary Diets NF Early Care^	1	150	9.7	9.1	3.4	Meat By-products, salmon
Royal Canin GI Fiber Response	3.7	280	8	6.4	2.9	Chicken By-Product Meal
Hill's Prescription Diet GI Biome Chicken & Veg Stew^	0.8	158	9.1	7.9	3.1	chicken broth, chicken
Hill's Prescription Diet GI Biome	3.8	183	9.3	9.1	2.7	chicken
GI-FRIENDLY DIETS						
Purina Pro Plan Veterinary Diets EN	4.2	260	12.1	5.1	1.6	soy protein isolate, poultry by-product meal
Hill's Prescription Diet i/d	4	207	8.7	8.2	1.2	chicken, corn gluten meal
Purina Pro Plan Veterinary Diets EN Savory Selects Chicken^	1	260	14.4	3.3	3.1	wheat gluten, chicken, ocean fish
Purina Pro Plan Veterinary Diets EN Savory Selects Salmon^	0.9	250	14.4	3.3	2.8	wheat gluten, chicken, salmon
Hill's Prescription Diet i/d Chicken & Vegetable Stew^	0.9	201	8.7	6.8	1.7	chicken, pork liver, wheat gluten
Royal Canin Gastrointestinal	3.9	250	7.9	6.4	2.7	chicken by-product meal, wheat gluten
Royal Canin Gastrointestinal Loaf^	1.1	260	6.4	5.2	0.6	chicken by-products, chicken, chicken liver

Table 1. Nutritional specifications of diets commonly recommended to cats with chronic enteropathies. Nutrients displayed on a metabolizable energy basis in grams per 100 kCal. ^canned diet; phos, phosphorus; prot, protein; carb, carbohydrate; NA, not available.

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Why is This Kitty Skinny? What Should I Do About It?

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Introduction

Weight loss is a problem in cats that should prompt additional investigation, with few exceptions. Here we will discuss why cats might lose weight, the most common differentials, and both pharmacologic and assisted feeding techniques. First, some definitions. In describing the amount of food consumed, an anorexic patient is consuming no food, while a hyporexic patient is consuming less food, and a dysrexic patient is a patient that's had a change in their eating habits (to include anorexia or hyporexia). Cachexia is loss of muscle mass associated with disease while sarcopenia is loss of muscle mass due to aging without disease.

Why is this important? Aside from the obvious, there is a lot of evidence that connects BCS to outcome in pets. In one study, cats diagnosed with chronic kidney disease (CKD) had lost a median 8.9% of body weight in the year prior to diagnosis, and was present up to 3 years before diagnosis.[1] Additionally, a body weight above 4.2kg at CKD diagnosis was associated with a significantly longer survival time than body weight below 4.2kg.[1] In a retrospective of 101 cats with congestive heart failure, cats with the lowest and highest body weights had the shortest survival times.[2] With regards to oncology, a retrospective of 57 cats with cancer revealed that those with BCS > 5 had a significantly longer median survival than those below five.[3] And of course, feeding can comprise a huge and important part of the human-animal bond, in addition to perception of, and actual, quality of life.

Identifying the Weight Loss

Ideally at every visit, cats should have a body weight, body condition score (BCS) on a 9pt scale, and muscle condition score (MCS) recorded. With the 9pt BCS each point over 5 corresponds to a 10% measure above ideal body weight. So a pet with a BCS of 7 is 20% overweight. Of similar importance is muscle condition scoring at every visit. Different resources recommend either using a number or narrative description: 3/3 (normal muscle mass), 2/3 (mild muscle loss), 1/3 (moderate muscle loss), and 0/3 (severe muscle loss). Muscle mass is palpated and evaluated over the scapulae, spine, skull, and wings of the ilia. In one study of this 4-pt scale evaluating repeatability and reproducibility 44 cats with variable BCS were scored by 10 vets and CVTs three times.[4] Repeatability was high for all ratings of the MCS, reproducibility was moderate for cats at either end and fair for the intermediate scores.[4] Making both MCS and BCS a part of every exam that is recorded in your medical record will help identify weight loss in your feline patients before they become that really skinny kitty.

Characterizing the Weight Loss

Once you've identified any unintentional weight loss in your patients, the first step is to find out more about appetite. Free-fed cats in multicat households can definitely make this a challenge. Depending on the owner, and the other cats, giving the cat with weight loss access to special food and a chance to eat several times a day can help make this determination. This could be food in a separate room, additional times away from the other cats, or an RFID (microchip/collar scanning) feeder. In performing the PE, take particular note of if the pet has lost muscle but not fat, the reverse, or both. Sarcopenia is not unexpected as animals (including humans!) age. The signals in the body that assist with maintenance and building of muscle wane, mobility decreases for reasons such as osteoarthritis, genetics and several other metabolic factors all play roles.[5] Cachexia on the other hand, is a loss of fat and muscle secondary to increased catabolism from inflammation caused by a primary disease process.[5] Having serial BCS, MCS and an accurate health history will help you determine sarcopenia (usually mild and slowly progressive) from cachexia. With cachexia, or weight loss due to a pathology, the goal is first to determine if the cat has *weight loss with inadequate caloric intake or adequate caloric intake* – this will drive your diagnostic plan going forward.

Weight loss with inadequate caloric intake can be secondary to a host of potential causes. Here an excellent history and PE may help drive your initial diagnostic choices. What does the cat eat, is it regularly dewormed, what are the household dynamics like, any recent stresses or changes? Evaluate for dental disease, the ability to open and close the mouth, vision, food prehension, mental status, abdominal pain or masses, in addition to a full physical examination. In the absence of specific findings, complete blood count, chemistry panel including T4, urinalysis and retroviral screening are good starts. Imaging with radiographs or ultrasound could also be considered. Comparatively, weight loss with a good appetite or adequate caloric intake has a very narrow list of differential diagnoses. Hyperthyroidism, diabetes mellitus, exocrine pancreatic insufficiency, and chronic enteropathies are the most common causes of weight loss with adequate calories in cats. Thus, for those patients

starting with a complete blood count, chemistry panel including T4, and urinalysis makes sense. If those are all normal, pursuit of measurement of cobalamin/folate/TLI and an ultrasound along with deworming and a hydrolyzed protein diet trial are appropriate next steps.

Addressing the Weight Loss

For the cat that has weight loss with a poor appetite, part of addressing the weight loss will include getting the cat eating again. Especially in cat patients, we often don't have the luxury of waiting until we get a definitive diagnosis for the cause of the weight loss, much less correct it, to try to get the cat to eat again. At home, clients can try coax feeding, changing food temperature, changing food location, changing food bowls (dish to plate, ceramic to paper, etc.), and enhancing palatability. Palatability could be enhanced with food additions such as meat, fish, baby food, or cheese. This could also be accomplished by simply trying a new food, adding other food toppers, or changing food consistency.

Pharmacologic Interventions

When addressing the hyporexic to anorexic pet it's important to consider addressing not only appetite, but any nausea the cat might be experiencing as well. Basic imaging in the form of abdominal radiographs should be performed to rule out mechanical intestinal obstruction before treating with any antiemetic or appetite stimulant drug. Additionally, remind the client that we still need to figure out why their cat's appetite changed, even if our pharmacologic intervention works; treatment of the clinical signs only without attention paid to the primary disease process is setting the cat and owner up for failure and possibly unrealistic expectations.

For appetite stimulants we're lucky to have very effective, safe options for cats available. Mirtazapine (Mirataz Transdermal) is FDA-approved to manage unintended weight loss in cats. In a multi-center, double-blinded, placebo-controlled study or 177 cats, administration of 2mg transdermally for 14 days resulted in significant weight gain (3.9% +/- 5.4%) compared to placebo (0.4% +/- 3.3%).[6] In cats that do not tolerate transdermal medications, oral mirtazapine can be used. Care should be taken when prescribing the oral formulation as accurate splitting of large (15mg or 7.5mg) pills to get the appropriate 1.88mg dose may lead to cats receiving higher doses and experiencing side effects.[7] Cats with CKD can safely receive transdermal or oral mirtazapine at a reduced dosing frequency, once every 48 hours.[8] More recent studies suggest cats with significant hepatic disease may also benefit from a longer dosing interval.[9] Of added benefit is that mirtazapine also has antiemetic properties, allowing one medication to serve dual purposes in our cats. In a study of 11 cats with stable CKD, cats randomized to receive 1.88mg mirtazapine PO q48h showed significant increases in appetite and weight, and decreases in vomiting compared to placebo cats.[10] Capromorelin (Elura) is an oral ghrelin-receptor agonist that is FDA-approved for the management of weight loss in cats with CKD. There are currently more peer-reviewed studies on the use of capromorelin in dogs, for which Entyce is FDA-approved. Capromorelin is safe for daily administration and should not be used in cats with acromegaly due to its mechanism of action whereby it leads to growth hormone secretion from the pituitary that then stimulates IGF-1 release by the liver. Given the availability of these drugs, working by different mechanisms of action and available in different dosing forms (transdermal, oral pill, oral liquid) the use of non-approved drugs should decrease. Appetite stimulants in general should be used in three scenarios: as short term support while diagnosing and treating the underlying condition, to assist in feeding after food aversion, or in chronic diagnosed illness to help maintain appetite and body condition score and muscle mass.

Antiemetics are also important to consider if the cat appears nauseated or is vomiting. As stated above mirtazapine has some antiemetic properties. Ondansetron is useful to both decrease nausea and vomiting, although the three times daily dosing may be difficult for some owners. Maropitant (Cerenia) appears to have more use in treating vomiting than decreasing nausea. In one study of cats receiving dexmedetomidine and morphine, cats treated with maropitant vomited less but did not shower fewer signs of nausea than those who received placebo.[11] Choosing a drug or drugs to administer involves a careful assessment of your patient. The response to all drugs, both for appetite and nausea/vomiting should be recorded in the medical record.

Assisted Feeding Techniques

For some cats, pharmacologic intervention alone may not be enough. We know that for many diseases, early enteral nutrition improves outcome and/or saves lives (hepatic lipidosis). In-hospital feeding tube options include naso-gastric (NG) and naso-esophageal (NE) feeding tubes – through which liquid diets may be fed. Longer duration feeding (as with hepatic lipidosis) requires a more permanent option such as an esophagostomy feeding tube (e-tube). E-tubes can also be used for delivering medications and fluid support at home. Detailed descriptions of the placement techniques for each of these tubes can be found in the references list of this document.[12]

Briefly, the major pros and cons are as follows. NG/NE tubes do not require anesthesia for placement and thus allow initiation of feeding rapidly and avoidance of dangerous side effects of anesthesia in seriously ill patients. However, NG/NE tubes are temporary and allow only the feeding of liquid diets. E-tubes do require anesthesia for placement, but provided the placing

veterinarian is proficient it can be a very fast procedure. They also allow for the feeding of blenderized diets, which provides more flexibility for formulas than the liquid diets of NG/NE tubes.

Contraindications for NG/NE tubes include patients that are comatose, laterally recumbent, lack a gag reflex, have severe esophageal dysfunction or stricture (the tube is likely to coil in front of the stricture), are coagulopathic or severely thrombocytopenic. Very aggressive patients that need heavy sedation/anesthesia for handling are also not likely good candidates. Similarly, contraindications for e-tubes include patients that are comatose, laterally recumbent, have severe esophageal dysfunction or stricture (the tube is likely to coil in front of the stricture), are coagulopathic or severely thrombocytopenic, or with intractable vomiting or regurgitation.

Drug	MOA	Dose/Frequency	Side effects
APPETITE STIMULANTS			
Mirtazapine	Nonselective serotonin blockade (5-HT3,2,1)	Cat: 1.88mg PO q24h, increase interval to q48h in renal disease Can increase dose to 3.75mg PO but not usually necessary Also available transdermally (Mirataz)	Hyperactivity, twitching, vomiting, excitability, irritability
Capromorelin	Ghrelin receptor agonist and growth hormone secretagogue	Cat: 2.0 mg/kg PO q24h	Diarrhea, vomiting, hypersalivation, not labeled for use in diabetics
ANTIEMETICS			
Maropitant	NK1 (substance P) receptor blocker	Cat: 1 mg/kg PO, SQ, or IV q24h	Pain at injection site (less if stored cold)
Mirtazapine	See above	See above	See above
Ondansetron	5-HT3 receptor blocker	Cat: 0.2-1 mg/kg IV or PO	Sedation at higher doses

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NOTES:

Let's Get Digital: How Smart Pet Tech Can Make a Big Impact on Cat Care
Sheryl Gamble, DVM, MS

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2023 CONFERENCE

The Ins and Outs of Feline Nutrition and Gastroenterology

7th WORLD FELINE VETERINARY CONFERENCE

October 12 – 15, 2023 Renasant Convention Center, Memphis, TN & Virtual

SUNDAY, OCTOBER 15, 2023

Schedule is in Central Daylight Time

TIME	SESSION TITLE		SPEAKER	ROOM	SPONSOR/ PARTNER
6:45 - 8:00 am	Breakfast			Ballroom Foyer	
7:00 - 7:50 am	*Breakfast Symposium*: Feline Constipation: Updates on Acute & Chronic Treatment Modalities	LS	Dr. Ashlie Saffire	Ballroom B	ROYAL CANIN
7:30 - 10:00 am	Cat Friendly Interactions & Handling Workshop**	IPO	Dr. Ilona Rodan	110 & 111	Ceva, ROYAL CANIN, sleepypod, TICA
8:00 - 8:50 am	Approach to the Vomiting Cat: Causes, Treatment, & Management	LS	Dr. Adam Rudinsky	Ballroom A	ROYAL CANIN
	Stem Cells in Feline GI Disease	LS	Dr. Craig Webb	Ballroom B	VetStem EveryCAT
8:55 - 9:45 am	Approach to Diarrhea in Kittens	LS	Dr. Adam Rudinsky	Ballroom A	ROYAL CANIN
	Diagnostic Dilemmas: The History, Mystery, & Bemoaning of Feline Triaditis	LS	Dr. Craig Webb	Ballroom B	IDEXX
9:45 - 10:45 am	Networking Refreshment Break			Exhibit Hall	Boehringer Ingelheim
10:45 - 11:35 am	Feline Pancreatic Disease: Familiar Friends & Missed Connections	LS	Dr. Adam Rudinsky	Ballroom A	IDEXX
	Feline Chronic Enteropathy	LS	Dr. Craig Webb	Ballroom B	ROYAL CANIN
11:40 - 12:30 pm	Approach to the Yellow Cat	LS	Dr. Adam Rudinsky	Ballroom A	IDEXX
	FMT: What's Coming Down the Pipeline	LS	Dr. Craig Webb	Ballroom B	VetStem
12:30 - 1:45 pm	Lunch			Exhibit Hall	
12:40 - 1:40 pm	*Lunch & Learn #1:* * Elevate Your Practice's Feline Wellness at Every Life Stage	IPO	Dr. Matt McGlasson	102 - 104	basepaws
12:40 - 1:40 pm	*Lunch & Learn #2:* * Cats Don't Read Textbooks: The Conundrums of Diagnosing Feline Hyperthyroidism	IPO	Dr. Kelly St. Denis	105 - 107	ZOMEDICA
12:40 - 1:40 pm	*Lunch & Learn #3:** Don't Sugar Coat It: Treatment Options for the Diabetic Cat	IPO	Dr. Cynthia Ward	113 - 115	Elanco
1:45 - 2:35 pm	Emerging or Just Ignored: Ductal Plate Malformations	LS	Dr. Adam Rudinsky	Ballroom A	Blue Buffalo Natural Veterinary Diet
	The Vomiting Cat: Probing for Answers in the Older Cat	LS	Dr. Jennifer Babineaux	Ballroom B	
2:40 - 3:30 pm	Feline Gastrointestinal Eosinophilic Sclerosing Fibroplasia	LS	Dr. Petra Cerna	Ballroom A	
	The Vomiting Cat: Probing for Answers in the Younger Cat	LS	Dr. Jennifer Babineaux	Ballroom B	
3:30 pm	Conclusion of Conference				

LS Live Streamed

IPO In-person Only

*Separate registration required. No fees associated.

**Separate registration required. Additional fees apply.

Cat Friendly Interactions & Handling Workshop

Ilona Rodan, DVM, DABVP (Feline), AdvCertFB

Introduction

Cat friendly interactions and handling reduce feline distress, thereby increasing caregiver and veterinary team safety.[1,2] Animal welfare experts, veterinarians, and cat caregivers all recognize impaired welfare in 70-89% of feline patients.[3-5] Impaired patient welfare goes beyond the appointment, starting with getting the cat into the carrier and transport, continuing throughout the veterinary visit, and after returning home for the majority of cats. The impact of client and cat stressors surrounding veterinary visits is the key major factor leading to inadequate feline healthcare. Working cooperatively with cats to promote their physical and emotional safety during veterinary visits increases team satisfaction and safety, while also completing appointments more quickly and with fewer personnel needed. This workshop provides the tools to minimize stressors and promote positive experiences surrounding veterinary visits, incorporating the 2022 AAFP/ISFM Cat Friendly Veterinary Interactions Guidelines into practice.

Clinical Presentation

Signalment and History

Optimal human-cat interactions are based on an understanding of both the species and the individual. As cats are the youngest domestic animal and also a territorial species, cats are definitely not small dogs. First and foremost, they are territorial animals who need a sense of control, safety, choice and familiarity in both the physical environment and social environment. Safe territory in the veterinary practice can be as simple as providing a safe hiding option, such as their carrier, a high-sided cat bed, or loose bedding.

Although a social species, feline sociability depends on the individual's genetics, epigenetics, and experiences.[6-8] Early experiences, especially during the first 2-7 (and up to 9 weeks) of life have a significant impact on social interaction later in life; kittens handled positively and frequently during this stage and by a diverse range of people, including children, are more amenable to handling and less fearful of people, even if unfamiliar.[9] Kittens that do not have this positive experience during this early period are more fearful during veterinary visits.[9] Although this stage is critically important to learning, kittens and cats continue to learn throughout life. An adverse experience during a veterinary visit, which results in pain or fear, can increase the cat's arousal during future visits. It is important to recognize that if a kitten was not well socialized to humans, even one negative experience can make them wary of humans, but it takes multiple positive experiences to become friendly towards people.[7,8] The history should identify previous history, including early history known to the client. Identify the individual's preferred location for and methods of interactions.

Etiology of feline behaviors

Cats use their keen senses to gather information from the environment and individuals around them. This information is interpreted by the emotional system based on the individual's genetics and previous experiences. That interpretation results in the behavioral responses observed. All emotions are important, aiding in survival and improvement of emotional health. Thus, the original names of positive and negative emotions have been changed to protective and engaging emotions as developed in the Heath model of Emotional Health.[10] Protective emotions serve to protect the individual and ensure the individual's survival. Engaging emotions lead to interactions and engagement with others and with the environment that are beneficial to the individual. They each can have different levels of intensity.

As cats are solitary survivors, it is common for them to experience self-protective emotions, such as fear-anxiety, surrounding veterinary visits, whether performed at home or in the veterinary practice. The goal of Cat Friendly interactions is to ensure that the emotions trigger a response that is appropriate and successful for the cat. Although protective emotions will still occur, we can minimize them and promote engaging emotions through carrier training and other cooperative care, providing cats hiding options, and appropriate interactions. The goal of Cat Friendly interactions is to ensure that such emotions trigger a response that is appropriate and successful for the cat, increasing feline coping and human safety.

Client education to prepare the cat for the veterinary visit

Cooperative patient care facilitates veterinary care by partnering with caregivers to prepare cats for the veterinary experience. These techniques were initially developed to facilitate care of zoo and research animals through increasing a sense of security and engaging emotions while minimizing protective emotions. More recently, it has been used with cats.

Carrier training

Classical conditioning is used to create positive emotional associations with certain experiences and operant (or instrumental) conditioning is used to encourage desired behavioral responses through positive reinforcement. For example, teaching calm behaviors (e.g., resting in a cat bed or bottom half of the carrier) and active behaviors such as sitting with neck raised for jugular collection or paw raised to facilitate nail trims. The goal is to help animals be physically and mentally comfortable with veterinary care. In addition, the concept of consent is introduced in order to give patients an element of choice and control within the interaction. This is achieved by introducing a behavioral signal from the cat, such as touching a target, to signal consent. Cooperative care enables cats to be more comfortable and relaxed during veterinary appointments and the aim is for them to calmly and comfortably accept human proximity and voluntarily co-operate with medical interventions.

Start with non-physical interactions

Interact with and handle cats in their preferred location. Cats often choose an area where they feel protected as hiding is a natural feline coping strategy in challenging situations.[11-14] Good options are the bottom half of the carrier, a high-sided cat bed, or loose towels forming a hiding place. Confident cats may choose to explore, often preferring perches or other elevated space. They may also be enticed to a location, such as a small pet scale, with treats, play, or other positive human interactions. Cat-human interactions are longer when the cat has the choice to approach a person than when a person approaches them.[15] Facilitate this initiation by getting down to the cat's level a few feet away from them and extending a relaxed, gently curved hand to invite their approach.

Starting with non-physical interactions lets cats gather information through their keen senses, impacting their emotional state and whether subsequent physical interactions will be positive or negative. Olfactory stimuli are most important to cats, and our goal is to provide positive olfactory stimuli and minimize the negative. Avoid noxious smells, such as strong chemical or perfume smells and the scent of other animals. Cats should have quiet environments, including in exam room and ward locations, away from loud auditory stimuli such as centrifuges and washers, the sounds of other animals, and loud human voices. Cats prefer human vocalization that is soft, gentle, and slow in tempo. Cats prefer a quiet environment and cat-specific music has been shown to reduce fear/anxiety at home and the veterinary practice.[16-18] Visual communication is also important, avoiding direct eye contact and approaching calmly from the side rather than towering over the cat to minimize the perception of threat. Slow blinks in the direction of the cat can increase positive feline interactions.[18] Movement around cats should be slow and predictable. During non-physical interactions, monitor body language and facial expressions to help identify the underlying emotions.

Physical interactions

Cats need a sense of control, and feline veterinary visits should be framed around providing this. The goal of protective emotions and the subsequent behavioral responses is for the cat to feel safe and secure. It is therefore the responsibility of the veterinary clinic to facilitate this, allowing the cat to respond to protective emotions through appropriate behavioral responses when they occur. More positive interactions occur if the cat has the choice to sit, stand, lay down, and move body parts during physical interactions.[21]The goal of Cat Friendly veterinary interactions is to enhance patient welfare, enable cats to cope, and improve the success of future appointments. In double-blinded studies with cats as their own controls, minimal handling was compared to full-body restraint, scruffing, and clipnosis. All restraint methods led to behavioral responses that indicated fear and aversion when compared with minimal handling.[19] Clients also resist restraint methods used on their cats.[20] Even short restraint impairs feline welfare and should never be used during veterinary visits.[15,,19] Examples of restraint equipment which is not recommended include cat bags, gauntlets or gloves, muzzles of any kind, Elizabethan-collars of any kind, anesthetic induction boxes, pillow cases, mesh cat 'nabbers', and air muzzles or any other device placed over the cat's head, and rabies poles.

Start physical interactions by petting over the cats' preferred areas of touch, the facial gland areas which produce the facial pheromones that are used in facial rubbing and marking.[20,21] Pet or massage over these areas in the direction of the fur. Avoid touch over the least preferred areas of touch, the base of the tail and belly.[21] One hand can massage over the facial glands, while examining the cat with the other.

Use of pre vet visit medications

Pre-appointment anxiolytics do not replace the need for a Cat Friendly environment and Cat friendly veterinary interactions and should be used in conjunction with these steps. Anxiolytics are most effective when administered before patient arousal and therefore it's best to administer in the home environment prior to the visit. They can be used prior to anesthesia, with fasting times shortened to 3 hours prior to anesthesia.[26] Medication should not be forced, but rather given in treats or otherwise so that they are not directly involved in the administration to further reduce anxiety and optimize the efficacy of the anxiolytic.

Gabapentin reduces distress during transport and examination.[27-30] It also has been shown to improve performance of a complete examination by reducing feline fear-associated behaviors.[27] A single dose of oral gabapentin can minimize fear-associated behaviors and associated injuries.[27] The lowest stress score occurs 2-3 hours after gabapentin administration[27-30] and recommended doses in the literature have included 20mg/kg[28-30] or 100-200mg/cat.[27]

Gabapentin is 100% renally excreted,[29] and significantly higher levels of serum gabapentin were measured in cats with IRIS stages 2 and 3 chronic kidney disease as compared to cats without renal disease.[31] It is therefore suggested to reduce the dose by 50% in cats with reduced renal function.[31] Gabapentin is safe to use in cats with systemic illness, including hyperthyroidism.[30] It has minimal cardiovascular effects and can enhance ability to perform procedures such as blood pressure measurement and phelobtomy.[30,31] Caregivers should be warned that cats may be ataxic after receiving gabapentin and this effect can last for several hours after the cat is discharged. Caregivers should be informed that it may be necessary to prevent access to high perches/stairs to avoid falls and if cats usually have access to the outdoors, they should be kept indoors for at least 8 hours.

Pregabalin has been reported as a safe alternative to Gabapentin and a commercial veterinary oral solution has been licensed for alleviation of acute anxiety and fear associated with transportation and veterinary visits in cats in Europe (https://www.ema.europa.eu/en/medicines/veterinary/EPAR/bonqat).

Maropitant has been shown to eliminate signs of motion sickness such as lip-licking, drooling, or vomiting, when given 4 hours prior to travel.[32] There are no contraindications to its use with anxiolytics.

Periodontal pain and degenerative joint disease (DJD), which includes osteoarthritis (OA) and spondylosis are common in cats[33,34] and are associated with chronic pain. Short-acting analgesics administered at home prior to the veterinary visit can reduce pain and prevent exacerbation of protective emotions during travel and examination. Advice about ongoing management of chronic pain is also important in these cases.

Principles of Cat friendly veterinary interactions for the veterinary consult

- All team members should be educated to understand the feline species as well as individuals, how they respond emotionally and behaviorally, and how to best interact with them. Only team members that have been educated about the species and individual cats should work with awake cats. Share guidelines or webinars on veterinary interactions to enhance team member education.
- Develop a plan prior to the appointment based on the individual's history and preferences to minimize negative experiences and protective emotions.
- Feline veterinary visits should take place in a quiet and enclosed space. The exam room is the most appropriate location for examination and procedures in order to reduce sensory arousal, avoid separation from caregivers, and increase accuracy of certain diagnostic tests.[33]
- Prepare the exam room in advance to minimize feline sensory arousal.
- Give cats the option to hide by providing suitable locations, such as beds or bottom of carriers, thereby enabling them to successfully select an avoidance response.
- Allow the cat to remain in its preferred location and position and to change positions so that they are most comfortable. More positive interactions occur if the cat has the choice to sit, stand, lay down, and move body parts during physical interactions.[14]
- Give the cat the option to initiate interactions. Come down to their level and slow blink, but avoid direct eye contact. Extend a soft hand in their direction to invite them to approach and rub on you.
- Massage gently over the preferred areas of touch, the facial glands and other areas that individual may prefer.
- If the cat shows repelling behavior, use chemical restraint if the patient is unwell or the appointment must occur today. Other options are to give the client the option to resume the appointment after one or more hours with the goal of reducing the cat's intense emotional motivation, or to reschedule the appointment allowing sufficient time to prepare the cat at home (e.g., carrier train) and administer an anxiolytic prior to the next appointment.
- Recognize that cats displaying inhibition are responding to protective emotions and alter approach to meet their needs.
- Give consideration to pre-visit preparation and cooperative care.
- Use minimal handling, with no scruffing, clipnosis, or full body restraint as they can trigger protective emotions.

Minimizing stress in hospitalized and boarding patients

In addition to considering appropriate interactions in the consultation it is important to consider cats that are spending time in the veterinary environment due to hospitalization or boarding. In relation to hospitalization the first consideration is whether cats need to be kept in the hospital setting. While some surgical procedures and certain illnesses do necessitate this approach it is helpful to assess the benefits of hospitalization for ill cats versus the benefits of home management or recheck examinations on a daily or every other day basis. This will depend on many factors including caregiver ability but in many cases where intravenous therapy and/or frequent patient monitoring are not indicated, it can be beneficial to manage the medical condition with the cat remaining in the home. When patients do need to be hospitalized or boarded the aim is to ensure that the environment meets the needs of the patient from an emotional as well as a physical health perspective. For example, providing cats with accommodation which enables them to respond effectively to their protective emotions, through hiding. Reducing patient distress has been shown to expedite recovery, reduce pain, and encourage voluntary food intake.[19] Information about how to optimize the veterinary environment is available in the ISFM/AAFP Cat Friendly Environment Guidelines.

Minimizing interactions and transitions from one location to another is an important aim and it is helpful to perform assessments, procedures, and treatments at the same time (for example, all done once in the morning and once in the evening) and to carry these out within the cage where possible. Consistency in terms of the schedule of activity within the hospital ward can also minimize frustration of cats desiring attention. If analgesia is needed it is important to schedule interactions with the patient when the analgesic is at maximum effect. Topical anesthetic cream or gel applied 30 minutes in advance to sites for intravenous catheterization and venipunctures can help to reduce pain and other protective emotions.[34,35] When patients require multiple medications it can be helpful to combine them into a small gel capsule to avoid the need for multiple administrations. Interactions such as rechecks, procedures and administration of medication should not be carried out in front of other cats and screens can be used to ensure this. Where appropriate, interactions that trigger the individual's positive emotional responses, such as treats, play, or grooming can be used to improve the hospitalization experience but the level of emotional arousal should be kept to a minimum. For some patients it is appropriate to invite caregivers to visit but each cases needs to be considered individually.

Conclusion

Cat Friendly Veterinary Interactions take into consideration the emotional cognitive and physical health of patients. They are based on an understanding of the natural behavior of the species and the individual nature of every cat. In addition, they consider the importance of the cat's experiences before as well as during the veterinary visits and encourage a partnership between caregivers and veterinary team. When a cat friendly approach is used for all interactions it will enhance feline and human safety, and reduce stressors for cats, caregivers and veterinary teams.

References available upon request

NOTES:

Feline Constipation: Updates on Acute & Chronic Treatment Modalities

Ashlie Saffire, DVM, DABVP (Feline)

Constipation is a common presenting medical condition in cats. Defined as absent, infrequent, or difficult defecation with retention of feces in the colon and rectum. Left untreated, constipation can progress to obstipation which is the development of a severe impaction and complete inability to defecate[1]. There are many causes of constipation in cats[2,3] (see Box 1). It is important to note that in many patients, several compounding causes of constipation may occur simultaneously. For example, comorbidities that can lead to dehydration such as chronic kidney disease (CKD), diabetes mellitus, and hyperthyroidism can lead to chronically desiccated stool and subsequent constipation[4].

In a recent retrospective study, it was found that older age, overweight body condition, history of constipation, and CKD were the most common causes of cats presenting to the emergency room with constipation[2]. Other known risk factors for constipation include pelvic fractures or pelvic stenosis, neuropathies (as with feline dysautonomia syndrome), sacral spinal cord disease or injury, megacolon (both idiopathic and secondary), and the use of certain medications such as anticonvulsants, calcium channel blockers, diuretics, antihistamines, and iron[2,5].

Acute management of obstipation in cats can be challenging in some cases. Medical therapy typically involves the use of enemas, oral laxatives/stool softeners, and manual dis-impaction, under heavy sedation or general anesthetic, by manipulation of the feces rectally or via abdominal palpation[6]. These medical therapies can be painful, stressful, ineffective, and result in extended hospital stays for feline patients. In some severe cases, surgery may be necessary to manually break down the fecal impaction and/or to perform a subtotal colectomy in cats diagnosed with megacolon[1,7].

An alternative method to treat acute constipation or obstipation is the administration of an oral polyethylene glycol (PEG) 3350 solution. The osmotic laxative effect of PEG 3350 is hydrophilic, binding water molecules to reduce the movement of water out of the colon, and consequently both softening and bulking its contents[8]. Administration of this solution (also known as GoLytely, CoLyte, and GaviLyte-G) can be facilitated via placement of a nasoesophageal (NE) tube. Placement of an NE tube is a quick, non-invasive procedure that can be easily performed under a combination of light sedation and topical local anesthesia[9]. Once placed, the PEG-3350 solution can then be administered as a CRI at a rate of 6-10 ml/kg/hour. The patient may be discharged as soon as they start defecating on their own and do not need to remain hospitalized until all fecal matter has passed. In one study, the median total dose of PEG 3350 administered to constipated cats was 80 ml/kg (range 40-156 ml/kg), with a median time to defecation occurring at 8 hours (range 5 to 24 hrs)[10]. No adverse effects were reported. This method can be performed easily in general practice and ultimately reduces pain and stress for the feline patient since enemas and manual dis-impaction are generally not required. It is important to note that prior to starting any treatment for acute constipation, the patient should be properly rehydrated with IV fluids and potassium supplementation in addition to receiving antiemetics and appropriate analgesia. Considering the ease and effectiveness of this treatment modality, oral PEG-3350 CRIs should be considered a first-choice treatment in constipated feline patients.

Long term medical management of chronic constipation commonly involves the use of oral laxatives (e.g. osmotic agents, bulk forming substances, emollients) and prokinetic agents in addition to the use of intermittent enemas. The osmotic laxative PEG-3350 (discussed previously) is also readily available in powder form and has been shown to have good palatability and safe stool softening effects in cats when used daily for long-term treatment of constipation[11]. Although one pilot study of PEG-3350 in 6 cats did not reveal any adverse effects when used daily, there was development of mild, non-clinical hyperkalemia, therefore, rechecking serum electrolytes and monitoring hydration status while on therapy is recommended[11]. The author recommends starting PEG3350 at an initial low dose of 1/8-1/4 tsp of powder per cat q 12-24 hours. The powder can be easily mixed with food for administration.

Lactulose is another commonly used osmotic laxative for treatment of constipation[6,12]. It is a non-absorbable disaccharide that is fermented by colonic bacteria and results in fecal volume expansion which in turn relieves constipation[12]. Although human studies have shown that lactulose is efficacious and safe, it can cause bloating and flatulence and is not very palatable to cats[13]. The author recommends administering lactulose at an initial dose of 2 ml/cat PO q 8-12 hours with any increases in dose performed slowly as it can take several days to see an effect[6]. Overdosage of lactulose can result in diarrhea therefore close monitoring is recommended.

Prokinetic agents may be required in some cases of chronic constipation, especially those cats with concern of dysmotility issues or megacolon. Prokinetic agents should only be initiated when there is no longer evidence of impacted stool in the colon. Cisapride is a benzamide prokinetic drug that requires compounding as it was withdrawn from the human market following reports of serious and fatal cardiac toxicity in people. This adverse effect has not been reported in feline patients and the drug appears to stimulate colonic motility in cats with megacolon[14]. A published dose recommendation of cisapride in cats is 0.5mg/kg PO q 12h; however anecdotally, doses of 2.5-7.5 mg/cat PO q12h are used without noted side effects.

A known sequalae to chronic constipation is the development of megacolon, therefore appropriate long-term management and prevention of this end-stage condition is essential. Megacolon can be defined as persistent increased colonic diameter & dilation, hypomotility and poor to no response to medical management[1,6]. Megacolon can be idiopathic or secondary to chronic colonic distension[3]. The diagnosis of megacolon requires a combination of evidence including clinic presentation, repeated radiographic evidence of impacted stool, and a history of chronic constipation. Additionally, measuring the colon on abdominal radiographs and determining the ratio of the colon width to the length of the vertebral body of L5 can be helpful in identifying megacolon. In normal cats, this ratio is usually <1.28 whereas cats with megacolon are more likely to have a ratio > 1.48[15]. Subtotal colectomy may be required in cases of end-stage megacolon when the patient is no longer responsive to medial or dietary management, to improve quality of life and extend survival times[16,17].

Nutrition is another important part of the management of constipated cats. Incorporation of dietary fiber (soluble and/or insoluble) into the diet of constipated cats is well known to have a beneficial effect[18]. Insoluble/low soluble fibers are usually not fermentable. Examples include cellulose, lignin, husks, and oat/wheat bran. These fibers draw water into the lumen of the GI tract to soften stool but also act as a bulk-forming laxative and can increase intestinal motility. As the colon wall is distended, contraction is stimulated. Care should be taken not to over-supplement with this fiber-type however, as high levels of insoluble fibers, can lead to lower fecal moisture content and in some cases cause a worsening of constipation[19]. Highly soluble fiber including psyllium, guar gum, and pectin (e.g. carrots, fruits), and canned pumpkin are usually more fermentable. As they absorb water, they delay gastric emptying due to a highly viscous consistency and in turn, slow GI transit. Additionally, they produce short-chain fatty acids which act as food for colonic microbes leading to a prokinetic effect on colonic smooth muscle[18,20,21]. However, just as with insoluble fibers, high amounts can lead to negative effects including development of liquid stools (diarrhea), flatulence, bloating and decreased nutrient digestibility[19].

Psyllium is a commonly chosen fiber supplement. It is considered a soluble fiber with low/partial fermentability[23]. Psyllium's water absorbing abilities along with development of a viscous gel (from the husk) provides lubrication and increased fecal bulk[22]. Lubrication created by the psyllium gel stimulates peristalsis resulting in propulsion and elimination of fecal material through the colon. In summary, psyllium slows gastric emptying (which assists in proper digestion of proteins), it treats diarrhea by regulating intestinal chyme and stool in the colon, and it reduces constipation by facilitating the elimination of stool[24,25], therefore acting as an excellent choice for patients experiencing gastrointestinal disease of different causes. Psyllium can be easily added to wet food diets as supplementation (1-2 tsp/meal)[22] but may affect palatability of the food.

A commercially available fiber-supplemented food for cats has been developed by Royal Canin (Royal Canin Veterinary Diet Feline Gastrointestinal Fiber Response). This highly digestible, dry-extruded diet contains a moderate level of psyllium and appears to be beneficial to constipated cats. In two field trials, this diet was found to be palatable, reduced the need for supplemental medication (including cisapride and lactulose) and induced clinical remission in most cats[22]. Future randomized controlled clinical trials are still needed to prove a clinical benefit, however anecdotal experience using this diet has shown positive results in most cats. In the author's experience, cats that are transitioned to this diet experience excellent control of chronic constipation with reduced need for supplemental oral medications (e.g. lactulose, cisapride) which is a benefit to both the feline patient and their caregiver!

Highly digestible, low residue intestinal diets have also been commercialized and help to reduce the volume of fecal material reaching the colon. This type of diet can be beneficial for cats that cannot tolerate extra fecal volume, such as those with structural or mechanical causes of constipation.

Lastly maintaining adequate hydration is essential for GI health and prevention of constipation. Multiple water sources should be readily available and easily accessible in the home environment. Although no difference was found in the amount of water consumed when water bowls were compared to fountains, some cats may have preference for different types of water bowls such as those that are wide and shallow[26]. Other methods to increase hydration may be feeding wet diets, administration of subcutaneous fluids, the use of supplements to promote hydration, and the addition of zucchini to dry food[27].

Box 1: Causes of constipation in cats

Nutritional/Dietary factors	• Obesity • Inadequate fiber, high residue diet • Inadequate daily water intake
Mechanical/Structural obstruction	• Extraluminal: pelvic fractures, neoplasia/masses within adjacent abdominal organs • Intraluminal: foreign material, neoplasia, perineal hernia, strictures • Intramural: neoplasia
Neuromuscular dysfunction	• Colonic smooth muscle disorder: megacolon (idiopathic or secondary) • Diseases of the spinal cord: sacral spinal cord deformities (Manx cat), lumbosacral disease, cauda equina syndrome • Hypogastric or pelvic nerve disorders: trauma, neoplasia, dysautonomia • Submucosal or myenteric plexus neuropathy: dysautonomia, normal aging/degeneration
Chronic Pain/Inflammation	• Degenerative joint disease, perianal fistula, anal sac abscess, anorectal foreign bodies, perianal bite wounds
Metabolic/Endocrine/Systemic disease	• Metabolic: dehydration, hypokalemia, hypercalcemia, hypomagnesemia • Endocrine: hypothyroidism (spontaneous or iatrogenic), nutritional secondary hyperparathyroidism • Diabetes mellitus, IBD/lymphoma, chronic kidney disease
Pharmacological	• Opioid agonists, general anesthesia, cholinergic antagonists, diuretics, phenothiazines, anticonvulsants, calcium channel blockers, antihistamines, antidepressants, aluminum hydroxide and iron
Environmental and Behavioral	• Litter box aversions, prolonged inactivity, confinement (hospitalization or boarding), change in environment, intercat issues/conflict

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NOTES:

Approach to the Vomiting Cat: Causes, Treatment, & Management

Adam Rudinsky, DVM, MS, DACVIM

Introduction

The focus of this lecture hour will be on understanding how prevalent, concerning, and important chronic vomiting is in our feline patient population. This condition is defined as vomiting that lasts 2 weeks or greater in duration and does not respond adequately to symptomatic therapy.[1-2] Amongst feline patients it is reported as a very common problem, with estimates of prevalence reaching nearly 5% of all cats in one study involving 8000 cats presenting to primary care clinics.[1] In addition to the high prevalence of this clinical problem in the feline population presenting to primary care clinics, what is additionally concerning is the fact that vomiting is considered 'normal' cat behavior by many and the 5% estimate may be underestimating the true prevalence within the general population. This is the result of this myth of 'normal vomiting' in the cat being perpetuated by many sources, including many sites on the internet, all with no evidence to support this claim that vomiting is normal. Thus, as clinicians interacting with clients and feline patients, it is imperative to be aware of the high prevalence of this problem and screen every feline patient for its presence.

If you ask many owners about their cat 'periodically vomiting' you will hear that they are not bothered by it or simply that they feel it's a normal amount of vomiting for a cat. This is a very hard perception of normalcy to break down in people's mind once it is engrained. However, it is important to remember that vomiting is a 3-phase physiologic response to irritation or insult to the stomach and proximal small intestine. In other words, it does not occur under normal circumstances and is occurring in response to something with the end conclusion being that if vomiting is reported in a patient, it is a clinical problem. Phase one of vomiting in the cat is typically denoted by signs of nausea, phase two is characterized by retching, and the final phase involves coordinated contractions between the abdominal muscles, stomach, and diaphragm with simultaneous relaxation of the lower esophageal sphincter to allow for the expulsion of gastric contents.[2] This is a neurologically mediated reflex after stimulation of the emetic center by various inputs.[1] Of particular interest is that the domestic cat lacks a well-defined emetic center, and the neurons involved in this process are distributed more diffusely throughout the central nervous system, once again another attribute separating this species in a novel manner.[3] This unique anatomy affects how central and peripheral stimuli for vomiting are conveyed and may dictate a species effect of some anti-emetic therapies (ex. metoclopramide).

For the above reasons, it is prudent to inquire about vomiting behaviors in all feline patients regardless of reason for presentation to the clinic. During this historical interview with the client, in addition to normal, comprehensive historical questions, special emphasis should be put on educating the client that 'normal vomiting' is not a normal behavior in cats! If vomiting is reported, it should be first differentiated from regurgitation. Although an uncommon problem in the feline species, regurgitation can be confused with vomiting by the owner.[4] Once vomiting has been confirmed as a primary problem, specific questioning should be directed at the frequency, duration and severity of vomiting, as well as concurrent clinical signs, the contents of the vomitus, and the overall status/health of the patient. This should dove-tail nicely with the physical examination which may range from unremarkable findings to in some cases where it may indicate a specific cause of the vomiting (ex. thyroid slip). Based on this initial clinical information, you can then consider the gastrointestinal and non-gastrointestinal causes of vomiting and order them in terms of what is most likely for that patient. A general list of differentials and categories for disease for feline vomiting are outlined in Table 1:

Gastrointestinal Differentials	Non-Gastrointestinal Differentials
Inflammatory (IBD, Food Intolerance, Food Allergy)	Hepatobiliary Disease (Cholangitis, Cholangiohepatitis, Hepatitis)
Neoplasia (Lymphoma, etc..)	Pancreatic Disease (Pancreatitis, EPI)
Structural Disease (Foreign Body, Ulcerations, Strictures, etc.)	Endocrinopathies (Hyperthyroidism)
Anomalous Disease (IBS/FIC, Eosinophilic Sclerosing Fibroplasia)	Renal Disease (Uremia)

Functional Disease (Motility Disorders)	Neurologic Disease
Infectious Disease Parasitic (Ollulanus tricuspis, Physaloptera, Ancylostoma tubaeforme, Toxocara cati, Toxascaris leonine) Bacterial (Helicobacter spp.) Viral (FIP, FIV, FeLV) Fungal (Pythium insidiosum, Histoplasma capsulatum) Protozoal (Toxoplasma gondii)	Heartworm Disease

In each individual patient, there must be a recommendation to investigate the underlying cause of vomiting. The recommendation on how aggressively to pursue this work-up in each individual patient will vary, and be dependent on both the client's goals as well as the over health status of the patient (severity of vomiting, frequency of vomiting, concurrent clinical signs, etc…). This once again emphasizing the importance that this patient specific information is acquired during the history and physical examination. From this information, a recommendation can be made and the client can then decide what the best approach/decision is for their individual animal.

In general, the traditional work-up includes a minimum database (complete blood count), biochemistry profile, urinalysis), T4 (for cats 7 years of age or older), fecal floatation, and abdominal imaging (abdominal radiographs and/or ultrasound). However, each of these diagnostics have greater or lesser importance depending on the individual patient. For example, the older the cat, the more likely a biochemistry profile, T4 and abdominal ultrasound are to provide useful information. In contrast, there is an argument that could be made that fecal floatation, infectious disease testing and abdominal radiographs are most important in young patients. The most important consideration, in every case, still being the individual patient, as these are general rules based on general population dynamics. In individual situations, they all have the potential to be very useful or in others rarely provide diagnostic information. Advance diagnostics including *Tritrichomonas feotus* testing, other targeted infectious disease testing, gastrointestinal panels (Cobalamin, Folate, PLI, TLI), fine needle aspiration, and/or histopathology should be performed following the initial diagnostics. Rarely are fecal cultures, direct fecal smears, and fecal PCR panels indicated during routine diagnostic work-ups.

In the lecture portion, we will discuss how to incorporate this clinical information into making the best, targeted diagnostic plan and empirical, therapeutic plan. The ultimate goal being a comprehensive review on identifying our secret feline vomiters as well as understanding the best approach diagnostically and therapeutically in a patient specific context.

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NOTES:

Approach to Diarrhea in Kittens

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Introduction

Diarrhea in kittens is one of the most common and frustrating problems in feline medicine. This syndrome has a large range of clinical severity, responsiveness to treatment, as well as etiologies. In order to properly manage these patients, understanding the most common causes of diarrhea in kittens is vital for developing targeted diagnostic and therapeutic plans. While there is a large number of different etiologies, clinicians should pay particular importance to infectious causes. These are likely the most common culprits in many of these cases, and particularly refractory cases.

Key Pathogens

Tritrichomonas foetus – T. foetus is a protozoal pathogen in cats which is often found infecting the colon in cats. Infected cats are typically younger in age (3 months to 13 years of age (median 9 months)). To date, this is likely still an underdiagnosed pathogen and some studies have shown a prevalence (cat show) was 31%. Concurrent infection with Giardia spp. was also frequently identified, and likely explains the frequency of misdiagnosis of Giardia spp. in many T. foetus cases. Affected cats may be non-clinical, may show signs of colitis (increased mucus, tenesmus, occasional hematochezia, and increased frequency), as well as

Cryptosporidium spp. – Coccidia are protozoan parasites that replicate in the microvillous borders of intestinal and respiratory epithelium of cats. Infection, particularly in kittens and immunosuppressed patients, can cause a variety of clinical syndromes. The range of clinical severity spans from asymptomatic cats, cats with minimal clinical signs, and some animals affected with a life-threatening malabsorption syndrome.

Giardia spp. – Giardiasis is a diarrheal disease caused the parasite *Giardia duodenalis*. Once a cat is infected with *Giardia*, the parasite lives in the intestines and is passed in feces. Once outside the body of the cat, *Giardia* can sometimes survive for weeks or even months in the environment. *Giardia* also has a worldwide distribution and is endemic in the United States. Young kittens have a higher risk of illness than adult cats. General prevalence of Giardia spp. infection in cats in North America has been reported at about 4%. However, higher prevalence has been reported in kittens and shelter cats. *Giardia* infections in adult are typically mild or non-clinical; however, kittens are more likely to have significant acute diarrhea early in the infection.

Feline enteric coronavirus - This virus infects enterocytes at the tips of the villi. Infected cats may be asymptomatic or develop mild, transient diarrhea and fever.

Feline panleukopenia (FP) - This viral disease can result in fever, depression, anorexia, vomiting, and diarrhea. Currently, it is an uncommon disease due to vaccination; however in unvaccinated animals (e.g. some catteries, feral populations) this still remains clinically relevant.

Potential Pathogens

There is also a range of pathogens which are either routinely diagnosed or in some cases less likely to cause disease. These should always be considered during a diarrhea kitten evaluation:

Hookworms - *Ancylostoma tubaeforme, Ancylostoma braziliense, Uncinaria stenocephala*, and less commonly, the canine hookworm, *Ancylostoma caninum*
Coccidia spp - *Isospora rivolta* and *Isospora felis*
Whip worms – *T. vulpis*
Round Worms - *Toxocara cati* and *Toxascaris leonine*
Enteropathogenic bacteria

Diagnosis and Empirical Management

Managing a diarrhea kitten is typically a combination of targeted diagnostics and empirical trials. In lecture we will discuss a strategic approach to utilizing diagnostics in identifying causes of kitten diarrhea. This will be combined with a strategic approach to using empirical trials to build confidence in eliminating infectious disease differentials.

Commonly used diagnostics include the following:

- CBC
- FeLV/FIV
- Direct fecal smears/rectal scrape cytology
- Fecal flotation-centrifugation
- *Giardia* fecal antigen
- *T. foetus* testing
- Fecal culture
- *Cryptosporidium* testing
- Fecal PCR panels

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NOTES:

Feline Pancreatic Disease: Familiar Friends & Missed Connections

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Introduction

Exocrine pancreatic insufficiency (EPI) is a uncommon disease while at the same time under-recognized in our feline patients. This disease occurs when the exocrine pancreas function (synthesis and secretion of pancreatic digestive enzymes) is inadequate to maintain normal digestive functions. In the mid 1990's, feline EPI diagnosis was advanced drastically with the development of a readily available (feline trypsin-like immunoreactivity (fTLI)). More recently, as the broad spectrum of clinical presentations has been established in recent literature, awareness of this disease has broadened and further increased diagnosis. [1-3]

Etiology and Physiology

The exact mechanism of EPI is unknown in cats. However, one long standing theory is that cats with EPI results from the effects of chronic pancreatitis.[4] Different mechanisms have been documented in human EPI including pancreatic aplasia, pancreatic hypoplasia, pancreatic acinar atrophy, pressure atrophy due to pancreatic duct obstruction, and pancreatic destruction due to pancreatic inflammation. However, these have not been definitively characterized in cats. Regardless of mechanism, when nearly all of the exocrine reserve (>90%) is lost, clinical signs develop from maldigestion. The clinical presentations which cats develop are a notable difference from other species. For comparison, only 30% of cats with EPI will present with the classic phenotype associated with the disease. Beyond maldigestion, erum cobalamin (vitamin B_{12}) deficiency and serum folate deficiency are common in EPI cats. Even vitamin K responsive coagulopathy have been reported secondary to EPI in cats.

Clinical Signs

Exocrine pancreatic insufficiency in cats has a distinct presentation and due to the age range at time of diagnosis (median age 7.7 years (interquartile range - 5.5, 11.4; range - 3 months to 18.8 years). The 'classic' constellation of clinical signs associated with EPI (polyphagia, weight loss, and loose stools) are reported in approximately 30% of cats. Importantly, even in these 'classic' cats, these clinical signs are not pathognomic and must be differentiated from other differentials with similar clinical pictures (e.g. inflammatory bowel disease). Interestingly, in many other cats clinical signs are even more vague and in isolation (e.g. weight loss). Thus, the practitioner must be aware of the nonspecific clinical signs in EPI cats and weight the benefit of testing. In the largest study of EPI in cats, clinical signs included weight loss (91%), unformed feces (62%), poor hair coat (50%), anorexia (45%), increased appetite (42%), lethargy (40%), watery diarrhea (28%), and vomiting (19%).[1] As such, any of these signs should prompt consideration for EPI is more common diseases have been eliminated. Lastly, this study also documented 58% of cats had concurrent disease, which may also impact the clinical presentation.

Diagnosis

Diagnosis of EPI is relatively straight forward as long as clinical suspicion is present. The diagnostic assay for feline trypsin-like immunoreactivity (fTLI) concentration is commercially available (reference range is 12.0–82.0 µg/L, with values of ≤ 8 µg/L being considered diagnostic for EPI).[5] The assay measures serum trypsinogen. The two main clinical conundrums with the assay include grey zone results, at which point re-testing should occur in the future. And also understanding that decreased renal function has an effect on serum fTLI. As such, CKD cats or other kidney disease may falsely increased serum fTLI concentrations resulting in false negatives.

Treatment

The foundation of treatment is the supplementation of pancreatic enzymes in the diet. Although the use of fresh pancreas is possible, dried extracts of porcine pancreas are the most commonly utilized in most cases. (e.g., Viokase® or Pancrezyme®). Powdered formulations are thought to be the most successful and in attempt to avoid taste aversions are best mixed in cats or pate foods. A response to therapy is usually seen within the first week of therapy. Vitamin (cobalamin, folate) supplementation is advised in most cases. If bleeding tendency is noted, vitamin K supplementation is advised. Anecdotal evidence has also indicated that proton pump inhibitors and some antibiotics (e.g. tylosin) can be used in refractory cases.[2]

Prognosis

The majority of cats diagnosed will respond well to appropriate EPI therapy with pancreas enzyme supplementation. Recent research has also documented that cobalamin supplementation appears to be beneficial in obtaining a good response.

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NOTES:

Approach to the Yellow Cat

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Introduction

Yellow cats are a frequent occurrence in feline emergency rooms and clinics. Jaundice is the yellow discoloration of the skin, mucous membranes and sclera which makes our feline friend glow, and is caused by an increased concentration of bilirubin in serum and tissues. Standard convention dictates that this change is visible when serum bilirubin concentration exceeds around 2 mg/dl. Jaundice correlates with hyperbilirubinemia and represents a specific marker of acute hemolysis (prehepatic), hepatobiliary disease (intrahepatic), or extrahepatic biliary disease (extrahepatic). Hepatobiliary disease is very common in cats seen in clinical practice and is frequently diagnosed at a higher frequency than prehepatic diseases.

Cholangitis, hepatic lipidosis, and neoplastic processes are the most common hepatobiliary diseases in the cat. While bile sludge and choleliths, associated with cholangitis, cholecystitis and impaired contractility of the gallbladder, have been implicated as the most common causes of extrahepatic bile duct obstruction (EHBDO). Other causes intrahepatic and extrahepatic yellow cats may include infectious disease, pancreatitis, biliary neoplasia, foreign bodies, biliary mucoceles, gastrointestinal disease as well as other uncommon differentials.

The key concept when approaching a yellow cat is to rule out prehepatic causes of the jaundice, and the utilize diagnostics or clinical reasoning to establish either a definitive or presumptive diagnosis in each patient. Importantly, as many cases are either unable to have extensive diagnostic work-ups for financial, personal, and patient stability reasons, understanding population dynamics, disease characteristics, and population distributions are vital for presumptive diagnoses.

Diagnostic Examination

Clinical Presentation

It may be simple identifying that a patient is icteric from either clinical examination or laboratory screening. However, the clinical signs of the myriad diseases which cause icterus are relatively non-specific. They most commonly include abdominal pain/discomfort, vomiting, dehydration, nausea, anorexia, weight loss, lethargy, pyrexia, icterus, diarrhea and polyuria/ polydipsia, but this will not typically provide a diagnosis.

Initial Screening Laboratory Testing

Laboratory investigation is the typical first line of diagnostics used for either confirming or establishing a patient is icteric. In this manner, the biggest goal of a minimum database (complete blood count, biochemical profile, urinalysis) is attempting to rule hepatic disease in or out in a particular patient. At the same time, there may be a bonus of either assessing the functional impact of disease on the liver and determining whether hepatic disease is a primary or secondary problem.

The complete blood count and urinalysis provide supporting clinical information (e.g. bilirubinuria), but rarely provide a diagnosis in a intrahepatic or posthepatic cat (presuming the complete blood count has already determined a hemolytic process is not present). The biochemical profile is the foundation of the preliminary assessment with the initial focus on hepatic enzymology. Enzyme patterns allows for determination as to whether disease is active in hepatocytes, the biliary system, or both (hepatocellular pattern, e.g. ALT and AST; cholestatic pattern, e.g. ALP and GGT). The enzymes do not correlate with distribution or severity of disease. The second component evaluated on the biochemical profile is synthetic parameters, including bilirubin, glucose, albumin, globulin, and urea.

Coagulation Testing

The liver is also responsible for the production of the majority of cats clotting factors. As such, assessment of bleeding tendency is important with coagulation testing, particularly when invasive procedures (e.g. surgery, feeding tubes, sampling catheters) are considered. At minimum, coagulation testing (e.g. PT, PTT) and a manual platelet count is recommended. However, recent work has also characterized cats by more advanced means (thromboelastrography, TEG). In the most recent study, cholestatic cats even after treatment with vitamin K displayed multiple different coagulation profiles. In comparison to traditional methods, the presence of a prolonged PT and aPTT was associated with a hypocoagulable and/or hyperfibrinolytic state by TEG. There was also a rough correlation with elevated serum ALP activity and a hypocoagulable state.[1]

Additional Laboratory Testing

Paired pre- and post-prandial serum bile acids are the most commonly recommended test of hepatobiliary function in cats.[2,]

Post-prandial bile acids is reported to have the highest sensitivity of all single tests in cats with hepatic lipidosis, portosystemic vascular anomaly, or cholestasis; and ALT enzyme activity or post-prandial bile acids had the highest sensitivity for cats with hepatic necrosis.[3] Pre-prandial and postprandial bile acids also had improved specificity, however the utility of the test for specificity is dependent on the clinician's suspicion of disease at the time of testing. In many cases, since the disease suspicion is already high, additional bile acid testing provides minimal clinical benefit. The other frequently recommended specific laboratory test is fasting ammonia. However, due to handling requirements, this is less frequently performed unless in house analysis is possible. And lastly, recent literature has documented other laboratory abnormalities in cholestatic cats (e.g. hypovitaminosis D in cats with chronic liver disease) but the clinical utility of these tests in clinical patients is currently unknown.[4]

Hepatobiliary Imaging

A variety of hepatobiliary imaging modalities exist for feline patients. For those appropriately trained, abdominal ultrasound can be beneficial and is widely available compared to other advanced modalities (e.g. CT scan). On ultrasound, a normal feline liver has a uniform echogenicity and appears similar to the spleen and renal cortex. There is individual variation between cats which can account for some variability in echogenicity between tissues. Ultrasounds biggest assess is in assessing structural and obstructive pathologies in the hepatobiliary system and aiding in hepatobiliary sampling (e.g. bile aspirate). Otherwise, the ultrasound of the hepatic parenchyma is nonspecific. The ultrasonographer can report different types of lesions (diffuse, focal and multifocal) and whether they alter liver size, shape and echogenicity. However amongst these changes there is significant overlap in appearance limiting the diagnostic ability of ultrasound. For example, differentials for a diffusely hyperechoic liver include hepatic lipidosis, chronic hepatitis/cholangio-hepatitis, fibrosis and lymphoma. Diffusely hypoechoic liver differentials include acute suppurative hepatitis, passive congestion, lymphoma, mast cell neoplasia and amyloidosis. Differentials for a diffusely mixed echogenicity include hepatic lipidosis in association with benign nodular hyperplasia, extramedullary hematopoiesis, cholangitis/cholangiohepatitis, toxic hepatopathy, hepatic necrosis and cirrhosis, lymphoma, mast cell neoplasia, metastatic disease and amyloidosis. As you can see from these differential lists, there is significant overlap and leaves the clinician unable to discriminate between different diseases of the liver.[5]

Hepatobiliary Sampling:

The main options for hepatobiliary sampling include liver aspirates, bile aspirates, tru-cut liver biopsy, and surgical liver biopsy (laparoscopic or open). Aspirate cytology provides small sample without associated tissue architecture which can limit the diagnostic utility of the technique (e.g. inflammatory liver disease). However, this can also provide specific diagnoses (e.g. lymphoma, bactibilia) in other instances. It can also provide samples for aerobic and anaerobic culture. In one study on the accuracy of FNA of the liver of cats, histopathology and cytology agreed in 51.2% of cats.[6] And in a separate study, it was further documented that secondary lesions (e.g. hepatic lipidosis) could obscure the underlying primary diagnosis found on biopsy (e.g. inflammatory or neoplastic disease).[7, 8]

Tru-cut needles will provide a larger tissue biopsy and may be a more representative sample for diagnosis. However, this isn't a guarantee as lesions can be unevenly distributed throughout the liver. This in turn can lead to missed diagnoses even with larger biopsy samples. As a general rule of thumb – Size matters– smaller biopsies (e.g. tru-cut) have been shown in some studies to not be as accurate as larger biopsies (e.g. wedge biopsy) for definitive diagnosis.[7, 9]

Importantly, as biopsies are larger and more invasive they also have a higher risk of complications (e.g. hemorrhage, bile peritonitis, abscessation, pneumothorax and death). These concerns should be discussed with clients prior to performing a sampling technique and monitored for before, during, and after a procedure. In one large study, cats with a coagulation disturbance (e.g. prolonged activated partial thromboplastin time (aPTT), or marked thrombocytopenia), were at an increased risk of complications compared to cats with normal coagulation values.[10] As a final note, it should be noted that the use of an automatic Tru-cut biopsy gun has been linked to fatal complications in cats. This is not seen with semi-automatic devices.[11] The complication is attributed vagal response from the pressure wave from the biopsy device.

Differential Diagnosis

Metabolic Disorders

Feline Hepatic Lipidosis (HL)

HL is the most common hepatobiliary disorder recognized in cats. It is a metabolic disorder that revolves around abnormal fat metabolism. The most important initial decision you have as a clinician is to determine if you believe you have a primary hepatic lipidosis or a hepatic lipidosis secondary to another disease process. The classic primary clinical picture of an HL cat is a middle aged or older, obese cat that goes through a period of anorexia. The key is identifying why the cats stopped eating. If no cause is identified, HL is treated as a primary condition. If a cause is identified, you must treat both the HL and the underlying disorder.

When a cat has prolonged inappetence, peripheral fat is mobilized, which ultimately results in hepatic lipid accumulation. Fatty acid metabolism is deranged in obligate carnivores under a state of malnutrition/anorexia. Metabolic consequences stem from these base changes. Cytolgoy and biopsy both demonstrate the severe vacuolization of hepatocytes (>50% of acinar unit involved) without the presence of inflammation and necrosis in primary cases.

Stressful events, concurrent disease, and anorexia are frequently reported at presentation. Cats will be icteric and may have signs of HE. The initial work---up should include a minimum database and a cholestatic pattern is classic but not specific for HL. However, relatively unique to primary HL, serum GGT is often normal which should raise suspicion for this disease as a primary process. Electrolyte abnormalities are common with the most important to monitor for being the development of hypophosphatemia or hypokalemia.

Clinically, diagnosis is made from clinical picture, minimum database, imaging (ultrasound – hyperechoic parenchyma and the absence of other clinically significant findings) and cytology of the liver. The ultrasound is mainly important for eliminating concurrent disease. Definitive diagnosis requires histopath and is rarely performed as it is high risk and often not needed. Typically, I will treat for art least 5 days with no improvement prior to proceeding with liver biopsy. The main goal of the biopsy at that point is to determine if I am missing an underlying disease, which is compromising therapy.

The most important therapy is feeding the patient. This will often require placement of a feeding tube. I typically start with a nasogastric tube for the first few days while the patient is stabilized. Once stable for anesthesia, I then place a temporary feeding tube (e-tube) that the patient can leave the hospital with intact. Higher protein diets are ideal in mobilizing hepatic fat stores and resolving disease. However, if signs of HE are present protein should be adjusted to moderate levels. During feeding, each day small increments should be made in feeding volume. I typically start at 20% RER and workup in increments from there. You should also monitor for refeeding syndrome. Refeeding syndrome is when with the reintroduction of food, insulin release promotes intracellular movement of phosphate, potassium and magnesium. These should be monitored and supplemented as needed. This is a rare but potentially serious complication.

The constellation of medications that I have my 'typical' patient on include: ondansetron 0.2 mg/kg IV T-BID, Vitamin K 1 mg/kg SQ BID for a minimum of 3 doses, Denamarin, and cobalamin 250 mcg. Other medications are used depending on the specific case including carnitine, taurine, vitamin E and maropitant.

Prognosis is dictated by the underlying disease present or not but overall with time and commitment most animals will do well (85% of cases), especially with primary HL. Metabolic abnormalities will take weeks to resolve and the owner should be aware that outpatient care will be required. Cats with primary disease have been shown to be significantly younger, had significantly higher ALP activity and bilirubin concentration, and had a slightly better survival rate than cats with secondary lipidosis. Low PCV, hypokalemia, and an older age were significantly related to nonsurvival.

Amyloidosis

Hepatic amyloidosis occurs in cats with a much higher risk in Abyssinian, Oriental and Siamese cat breeds. In addition, cats have developed amyloidosis secondary to vitamin A toxicity. Amyloid deposition can be easily demonstrated on routine histopathology staining. Most animals will have signs consistent with chronic progressive hepatopathies. However, a less common presentation is for hepatic rupture to occur with acute intrabdominal hemorrhage. Laboratory findings are dependent on the clinical status of the patient. Treatment is primary supportive in nature. Some individuals have tried dimethyl sulfoxide and/or colchicine but evidence for these treatments is not available. Long-term prognosis is guarded.

Intrahepatic Biliary Disorders

Cholangitis

The cholangitis/cholangiohepatitis complex represents the second-most common hepatic disease in cats and the most common feline inflammatory liver disease.[12, 13] The four classic types of cholangitis (i.e. what you would receive on a histology report) include neutrophilic cholangitis (NC), lymphocytic cholangitis (LC), chronic cholangitis (associated with liver flukes), and destructive cholangitis (DC).

Feline Cholangitis – Neutrophilic/Suppurative

On your liver biopsy, neutrophilic inflammation centered in the lumen or epithelial lining of the bile ducts is characteristic of this type of cholangitis. Varying degrees of histopathologic severity are common and a full spectrum of clinical presentations (acute to chronic) may occur. Currently, it is still unknown as to why this happens in cats. The most common theory is that it results from an ascending infection (from the gut) due to the unique anatomy of the biliary and pancreatic ducts in this species. Interestingly, when this was investigated bacteria were able to be implicated in the majority of cases (100% of acute and 60% of chronic cases) when culture and fluorescent in situ hydbridization were used simultaneously. However, not all cases have a bacterial component indicating that there is likely a more complex/multi-factorial etiology present. This

syndrome is seen as a solitary disease process and may also be seen with some frequency concurrently with inflammatory bowel disease and/or pancreatitis. Potentially one of these is the initiating inflammatory event and this spreads to adjacent organs. This disease can also be so severe that is results in extra-hepatic bile duct obstruction (EHBDO). If EHBDO is suspected surgical intervention is the main recommendation.

Most cats with cholangitis have similar presentations, regardless of the type. This can occur in any breed, age, or gender of cat. Clinical signs are vague and nonspecific with variable duration. Common clinical features included hyporexia (82%), hyperbilirubinemia (80%), lethargy (80%), vomiting (80%), jaundice (67%), weight loss (54%), and hypoalbuminemia (50%). Comorbidities included extrahepatic bile duct obstruction (53%), cholelithiasis (42%), cholecystitis (40%), and ductal plate malformation (44%) as well as biopsy-confirmed inflammatory bowel disease (60/68 [88%]) and pancreatitis (41/44 [93%]).[14] Icterus is a frequent finding on physical examination and up to 40% of cats with this disease may be febrile. Hepatomegaly and abdominal pain are less commonly reported.

Diagnosis requires histopathologic confirmation on biopsy (cytology is inconsistent and lacks strong agreement) and the other tests that are typically run are used to rule out other differentials and provide supportive evidence. A nonregenerative anemia and inflammatory leukogram (including left shift) may be seen on complete blood count. All liver enzyme activities and cholesterol may be increased, although not always. Bilirubin is commonly increased. Imaging appearance on radiographs and ultrasound can be highly variable and is nonspecific. Gall bladder distention and bile duct distention may be seen in obstructed and non-obstructed cases. Bile cytology may be useful to support NC diagnosis. All cats should have samples submitted for aerobic and anaerobic culture (gall bladder bile is preferable to hepatic parenchyma). And recent literature indicates combination samples (bile, hepatic tissue, crushed choleliths) may increase culture yields.[14] Although the emphasis of this paragraph is on obtaining a liver biopsy, this also may not be in the best interest of the patient. As the clinician, you must decide whether the cat is clinically stable enough to undergo various diagnostics.

Perfect treatment recommendations are unknown at this time. Antibiotics are the mainstay of most treatment regimens, and ideally chosen on results of culture and sensitivity testing. If cultures are unavailable and there is a high suspicion, it is typically to use either single agent or a combination of a penicillin (amoxicillin or clavamox), a flouroquinolone (pradofloxacin) or metronidazole. This treatment will likely continue for 4-6 weeks. These antibiotic decisions are driven by knowledge of the most commonly isolated pathogens (E coli, Entercoccus spp, Clostridium spp, and others).[14] However, further work needs to be done to determine ideal regimens and treatment durations.

In addition to antibiotics, supportive care should be implemented including hepatoprotectant medications (SAMe, ursodiol, carnitine, +/- others) and appropriate nutritional support. Importantly, as you all likely know the joys of pilling cats, minimizing medications to those, which are absolutely necessary is preferred. In fact, in many patients it may be prudent to only start antibiotics and nutritional management to increase compliance and minimize patient stress. If poor response is noted, at that time it would be reasonable to consider other medications and expand treatment. Including the possibility that there is an immune mediated component and immunomodulatory drugs are needed. If at all possible, it is ideal to see antibiotics therapies outcome with no response (less time if patient is deteriorating) before starting immunomodulatory drugs. If immunomodualtory drugs are needed, they should be weaned to the lowest controllable dose possible.

Surgery should be reserved for those animals who are stable enough to obtain a definitive diagnosis or those with EHBDO. Multiple surgical options exist for the EHBDO cat. These include options for biliary stenting and biliary diversion. There are significant perioperative and intraoperative risks with these procedures that require extensive knowledge and expertise. However, recent work has shown that surgically correctable morbidities (ie, cholecystitis, cholecystocholelithiasis) can provide a survival advantage.[14]

Overall, the prognosis with NC is reasonably good. A median survival time of approximately 3 years has been reported and to date no specific clinical variables have been identified to assist in prognosis. For those requiring surgery, the perioperative period is most critical for survival.

Lymphocytic Cholangitis

This is typically a more slowly progressive, chronic disease marked by lymphoplasmacytic inflammation. Bile duct fibrosis and hyperplasia are associated with the portal areas. Immune mediated and infectious causes are the proposed reasons for this disease. Genetics may also play a role as there are some over-represented breeds (e.g. Persians). Similar to NC, inflammatory bowel disease and pancreatitis may occur concurrently, although this does not have to occur. Clinical presentation, although typically more subtle and chronic in nature, is similar to NC. Likewise, the clinical picture is highly variable and share many similarities with other feline hepatobiliary diseases.

Diagnosis and supportive information is similar to NC and requires a biopsy. For your pathologist, it can be difficult to

distinguish between LC and well-differentiated lymphoma. Treatment is also similar to NC. The most notable exception is that I only treat with antibiotics while I await my culture results in clinically ill cats. If it is positive (less than 20% of cases) I will continue based on those results. If it is negative, I will discontinue and solely treat with immunomodulation. Typically, prednisolone between 1---2 mg/kg/day is started and then tapered gradually on an every 3---4 week basis depending on level of control until a lowest controllable dose is reached. Chlorambucil is my second line immunomodulatory drug for this disease. Nutritional management is still paramount. Additional medications (hepatoprotectants) should be used at the discretion of your clinical judgement.

Chronic Cholangitis
Trematode parasites (e.g. Platynosomum, Dicrocoeliidae and Opisthorchiidae) can inhabit the gall bladder of cats with worldwide distribution. Light infection may be nonclinical and go unnoticed. Although other cats may present with the full spectrum of hepatobiliary clinical signs and occasionally EHBDO. Fecal analysis with the Formalin-Ether technique is most reliable for identification, although eggs and adults may be seen on bile cytology or liver biopsy. Praziquantal at 15 mg/kg PO for three consecutive days is the recommended treatment. As re-infection is possible, some clinicians recommended retreatment every 3---4 months. Prognosis can be good to grave.[15]

Destructive/Sclerosing Cholangitis
Cats less commonly get destructive cholangitis but when it does occur it is marked by a ductopenia (loss of bile ducts) and people have proposed that it is secondary to a drug reaction, viral infections and other causes. Clinical picture is similar to other cholestatic disease in cats and liver biopsy is required for diagnosis. Liver enzyme activity and bilirubin are usually markedly increased. There is no good basis for therapeutic recommendations however, I suggest that dogs should have current medications discontinued, as well as immunomodulatory medications, SAMe, and ursodiol begun. Unfortunately, prognosis appears to be very poor with this disease compared to other cholangitis subtypes.

Extrahepatic Biliary Disorders
Gall Bladder Mucocele
This is primarily a problem of dogs, but is increasingly recognized and overlooked in cats. The gall bladder is filled with inspisated bile mucus. These can be clinically silent, associated with abdominal disease, rupture and cause bile peritonitis, or be associated with chronic vague clinical syndromes in other species. However, there has been little characterization in cats. The exact cause of mucoceles is unknown.

Mucoceles are most commonly diagnosed on abdominal ultrasound where they exhibit their classic 'kiwi' appearance. This is different than 'sludge' in the gall bladder, which has debatable clinical significance in the cat. Treatment is usually by cholecystectomy. However, medical management may be attempted with a fat restricted diet and ursodiol. Once again, there is limited data on this disorder in cats, and the clinical course is poorly documented and optimal therapy unknown.[16]

Gall Stones
These are most commonly incidentally identified and rarely cause problems. When clinical they are typically associated with cholecystitis or EHBDO. Stones can be composed of bilirubin, cholesterol or mixed type, but feline gall stones are most commonly calcium carbonate or mixed type. These can be identified on both plain radiographs and ultrasound. Treatment for these is typically benign neglect and monitoring if the patient is otherwise well. The most clinical significance of choleliths arises from obstructive pathology or when they act as a nidus of infection.

Management
Principles of management of feline cholestatic liver disease include symptomatic control of clinical signs, nutritional support, medical therapy, and in some instances surgical treatment. The specific therapeutic approaches are highly dependent on the specific underlying etiology. This accents the importance of establishing a definitive diagnosis or if not possible utilizing clinical information to establish a high pre-test probability of the top differential(s).

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Emerging or Just Ignored: Ductal Plate Malformations

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Introduction

Development of the ductal plate is an important component of the biliary epithelium and ultimately the bile ducts. This is an intricate process and when dysregulated for any reason can result in ductal plate malformations (DPM), other structural abnormalities, and functional consequences for the affected animal. These commonly result in varying degrees of extracellular matrix deposition, and in the worst-case scenario hepatic fibrosis and portal hypertension. A group led by Dr. Sharon Center at Cornell University has been examining dogs and cats affected with DPM and have proposed the following classification system including 6 DPM subtypes:

1. Simple Biliary Cysts
2. von Meyenberg Complexes
3. Biliary Cystadenoma
4. Choledochal Cysts
5. Caroli's Syndrome (with or without Congenital Hepatic Fibrosis)
6. Proliferative-like DPM (with or without Congenital Hepatic Fibrosis)

They are not new abnormalities in feline hepatobiliary disease, and some of these disorders (e.g. biliary cystadenoma) have previously been characterized in the veterinary medical literature. However, these disorders have largely been missed and are now more frequently recognized due to advancements in hepatic histopathology and increased frequency of liver biopsies.

Clinical Presentation

Some of the frequently encountered DPM's are clinically silent. These include simple biliary cysts, von Meyenberg complexes, and biliary cystadenomas. In some instances, these can create a space occupying effect that require drainage or removal to resolved associated clinical signs.

The other classifications include choledochal cysts, Caroli's syndrome, and prolferative-like DPM, which all result in a higher incidence of hepatobiliary bacterial infections. So while there is no know specific treatment for the developmental abnormalities, the presence of these abnormalities may alter how we manage patients. For example, the duration antimicrobial courses and the duration of hepatoprotectants required will often be prolonged compared to normal courses used in feline hepatobiliary disease. In the lecture, we will discuss how these specific abnormalities may be managed and approached in clinical practice.

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Feline Gastrointestinal Eosinophilic Sclerosing Fibroplasia

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Introduction

Feline gastrointestinal eosinophilic sclerosing fibroplasia (FGESF) is a recently described disease in cats that presents as eosinophilic mass(es) that are associated with the gastrointestinal tract and associated abdominal lymph nodes, most commonly near the pylorus or ileocolic junction (1, 2).

Clinical Presentation

Signalment and History

This disease is most commonly seen in middle aged and male cats of all breeds, with Ragdolls being overrepresented in previous studies, and Maine Coons, Persians, Exotic Shorthairs, Bengal and Scottish fold cats also being reported (1-5).

The most common presenting signs of cats with FGESF (Figure 1) are weight loss, hyporexia, chronic vomiting and/or diarrhea, and lethargy; less commonly an acute onset of vomiting and/or diarrhea has been reported (1, 2, 6). A palpable intestinal mass has been reported in 85-100% of cases, with abdominal pain and pyrexia being less common (1, 2).

Clinical sign	% of cats
Weight loss	60
Hyporexia/anorexia	55
Chronic (>2 weeks) vomiting	37
Lethargy	35
Chronic diarrhea	27
Acute (<2 weeks) vomiting	13
Acute diarrhea	10
Constipation	10
Tenesmus	8
Polyphagia	7
Hematochezia	7
Decreased grooming	5
Melena	2
Excessive grooming	2

Table 1: Presenting clinical signs of cats with feline gastrointestinal eosinophilic sclerosing fibroplasia in Černá *et al. 2023.*

Etiology

The pathogenesis of FGESF is still poorly understood; however, an aberrant immune response to antigens from bacteria or parasites has been proposed (1). With some breeds, such as Ragdolls, being overrepresented, a genetic predisposition could be considered. However, more studies are needed to evaluate the role of infectious agents in this disease.

Diagnostic Examination

The most common bloodwork abnormality in cats with FGESF is usually peripheral eosinophilia, which is present in about 50% of the cats (1, 2, 6) and anemia was present in almost third of the cats in a recent study (6). On serum biochemistry, hypoalbuminemia and hyperglobulinemia were the most common abnormalities, occurring in 27-45% and 14-67% of cats (2, 6).

Large studies evaluating abdominal ultrasonography findings of cats with FGESF are lacking to date; however, one study reported 5 cats that had solitary mass with mural thickening and loss of layering in the stomach, duodenum, jejunum and colon (7). In a recent study, the majority of the masses originated from the stomach or intestines (Figure 2) and were associated with loss of the intestinal layering and circumferential thickening in most cases, although in 20% there was alteration of the layering rather than loss of it (6). Enlarged local lymph nodes were present in 90% of the cases, and peritoneal changes in 73%, of which 36% had a peritoneal effusion; however, none of the lesions showed ultrasonographic findings compatible with gastrointestinal perforation (6).

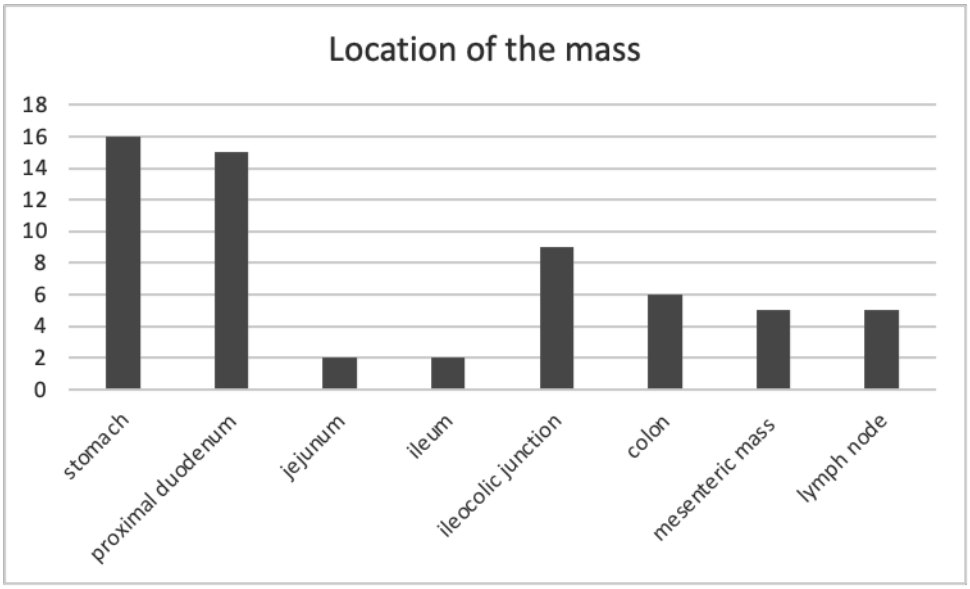

Figure 2: Common locations of the masses found in cats with feline gastrointestinal sclerosing fibroplasia in Černá *et al. 2023.*

Management

Surgical removal of the mass has been performed in most cases with FGESF; however, several studies have also reported medical management with corticosteroids, and/or cyclosporine or mycophenolate (2, 8-10). A mass in a second location has been reported to develop in some of the cases, after surgical removal of the initial one (6, 7, 11).

Corticosteroids appear to be important in the treatment of cats with FGESF and cats being treated with surgery alone had a significantly shorter survival time than those cats treated with surgery and corticosteroids in one study (1) and improved survival time was reported when prednisolone was included in the therapeutic regimen in another study, regardless of whether or not they also had surgery (2). Re-occurrence of masses has been previously reported when surgery was not followed by corticosteroids (6, 7, 11).

Prognosis

The prognosis for cats with FGESF has been reported as variable in previous publications, varying from guarded, to cats living for several years (1, 2, 7). Linton *et al.* reported that most cats surviving the perioperative period remained well for several years (2) and the mean survival was reported 937 days in a retrospective study on 60 cats with FGESF (6).

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Stem Cells in Feline GI Disease

Craig Webb, PhD, DVM, DACVIM

Introduction

This discussion will focus on adipose-derived mesenchymal stem cells (MSC); what they are, where they come from, what they can do in theory, and what they can and might be able to do in dogs and cats.

Defined

The International Society for Cellular Therapy defines mesenchymal stem cells as plastic-adherent under standard culture conditions, expressing a number of specific markers on their cell membrane (e.g. CD 44 and CD105, CD90), not expressing other markers (e.g. MHC II, CD4, CD 18), and being able to differentiate into osteoblasts, adipocytes, and chondroblasts *in vitro*. These are adult stem cells and therefore have limited self-renewal and differentiation capabilities, in contrast to Embryonic Stem Cells that are immortal and pluripotent. Mesencymal stem cells can be allogeneic (from the same species), autologous (from the individual in whom they are then transplanted), or even xenogeneic (across species).

Although they can be cultivated from a variety of different tissues, most commonly they are isolated and cultured out of adipose tissue. For example, in our clinical trials we isolate them from adipose collected from Specific Pathogen Free research cats during their ovariectomy surgery. The adipose goes through a number of processes, the result of which is isolated MSCs. The initial number of MSCs acquired in this way is relatively small, but they continue dividing to confluence in the original flask, at which time they are "cultivated" and split amongst a number of new flasks – a process called a "passage". With each passage the number of MSCs is increased exponentially, to a point, as these cells are not immortal.

Mesenchymal stem cells are not to be confused with other regenerative therapies such as the stromal vascular fraction or platelet-rich plasma, each of which has strengths and weaknesses.

Impact

MSCs exert their impact in a variety of ways, one of the most important being that they seem to be able to hone in and migrate to an area of need. In contrast to the classic route of injecting stem cells directly into a joint in the hopes of rebuilding or repairing damaged connective tissue, it may well be that MSCs administered IV can find their way to an inflamed gastrointestinal tract, for example. MSCs communicate and influence their surroundings through direct cell-to-cell contact, the release of mediators and messengers such as cytokines, as well as the production and release of exosomes, or secretomes - small "packages" of active molecules. In general, the sum-total of this MSC effort is immunomodulatory and anti-inflammatory. MSCs influence both the innate and acquired immune systems, and "talk" to most every cell associated with an immune/inflammatory response: T-cells, B-cells, NK cells, macrophages and neutrophils, T-regs and dendritic cells, etc. It is likely that MSCs also help regulate important cellular processes such as apoptosis, cell adhesion, oxidative stress, and cell differentiation. Not surprisingly these inherent properties make adipose-derived feline mesenchymal stem cells (fMSCs) seemingly an ideal therapy for a wide variety of inflammatory and immune-mediated feline diseases. To date the majority of the work in this arena has focused on chronic gingivostomatitis Arzi et al. UC-Davis), feline asthma (Trzil et al. Univ. of Missouri), chronic enteropathy (and specifically inflammatory bowel disease)(Webb & Webb, CSU), and kidney disease (Quimby et al. CSU & The Ohio State University). Results have ranged from mixed to remarkable.

Results, Briefly:

Feline chronic gingivostomatitis was one of the first, and visually most impressive uses of fMSC. This disease in it's most severe form is simply not compatible with life and often leads to full-mouth extractions and repeated rounds of antibiotics, steroids, and pain medications. And yet frequently the end result is still euthanasia. The underlying etiology has not been identified and is certainly multifactorial, with inflammation dominated by T-cells. The numbers of treated cats remains small and select (usually the worst, refractory cases), and yet the results in some number (not all) of cats is absolutely stunning (see Figure 2 of the Quimby reference below).

Feline asthma requires lifelong therapy with corticosteroids and bronchodilators and in spite of that, may continue to progress. This condition also highlights the potential for Translational Research – looking for treatments and cures in veterinary patients that may well "translate" to humans. Because fMSC administered IV travel first through the lungs (and often get stuck there) it would appear to be an ideal target for this therapy – and it works well in mice. In a feline model of acute asthma there was a

decrease in airway eosinophila, diminished hyper-responsiveness, and decreased airway remodeling. The results were less impressive, although not negligible, in a model of chronic feline asthma.

In our own studies of fMSCs in cats with chronic enteropathy, and then biopsy-confirmed IBD, our protocol (two IV injections separated by 2 weeks) was shown to be well-tolerated, very safe, and at least as effective as the traditional therapy utilizing prednisolone – these were owner-blinded, randomized, placebo-controlled studies, although with very small numbers of cats. But these results are consistent with a number of studies looking at a similar protocol in dogs, and along with chronic gingivostomatitis, may be one of the most promising areas of impact, especially considering the prevalence of this disease in the feline population.

Unfortunately, the attempts to improve AKI and CKD using fMSCs in cats have been somewhat disappointing, especially compared to the responses seen in rodent models. This is disappointing, again, considering the prevalence of this condition in cats, but "hope springs eternal" and there will undoubtedly be future studies aimed at this complex condition.

NOTE: The following description undoubtedly does not represent a complete listing of available products and services, and **IN NO WAY** should this be interpreted as any sort of endorsement. I have no experience with any of these companies, but it is highly likely that an increasing number of clients will become aware of this technology and begin to make inquiries.

In the United States there are several companies that provide regenerative medicine products intended for use in veterinary patients. VetStem (https://vetstem.com/company.php) advertises therapy for arthritis in dogs and cats – "VetStem is a regenerative medicine company that isolates autologous stem cells for you from your patient's own fat sample. The cells are returned, via FedEx overnight, for you to inject back into the patient. Our current clinical uses are osteoarthritis and soft tissue orthopedic injuries." They offer a free RACE approved 3 CE credit course for DVMs and they state that they are evaluating the use of stem cells for treatment of IBD, kidney disease, immune-mediated diseases, back pain, and gingivostomatitis.

MediVet Biologics (https://animotionanimalrehab.com/regenerative/medivet-biologics.php), apparently associated with "Animotion, Animal Rehabilitation Center in MA, advertises a similar process (mail in fat, process autologous cells, return for injection) for the treatment of orthpedic cases "world wide". They also claim to be seeing "exciting results" with degenerative myelopathy, feline gingivitis, end-stage renal disease, liver and kidney failure, allergy, auto-immune, inflammatory bowel disease, pulmonary fibrosis, IMHA, atopy, and spine trauma.

VCA Animal Hospitals seemingly offer it as a treatment option for their clients, although it is unclear which "specialized laboratory" they utilize (https://vcahospitals.com/know-your-pet/stem-cell-therapy). The description from their website:

1. The first involves the collection of fat from your dog, cat, or horse. This procedure is typically performed while the patient is under anesthesia. Fat cells are most often taken from a small incision in the groin or shoulder region.
2. The fat cells are then transferred to a specialized laboratory, where stem cells are obtained and concentrated.
3. The final stage of treatment is injection of stem cells into the affected area, such as a hip, elbow, or knee joint. This step also generally requires some form of anesthesia for your pet

Gallant even offers Stem Cell Banking for pets (as seen on "Shark Tank", who knew!), the idea being that fat is collected during a spay or neuter, sent in, processed and stored for later use in that pet, as needed in the future (gallant.com).

"Working in tandem with you and your veterinarian, we will collect and store these powerful cells now, so down the road we can help to alleviate the most common health problems your pet may face. We will also update you on new and potentially life-changing treatments as they become available."

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Diagnostic Dilemmas: The History, Mystery, & Bemoaning of Feline Triaditis

Craig Webb, PhD, DVM, DACVIM

Introduction

Occam's Razor or Hickam's Dictum

It is often statistically more likely that a patient has several common diseases, rather than having a single rarer disease which explains their myriad symptoms. Also, independently of statistical likelihood, some patients do in fact turn out to have multiple diseases, which by common sense nullifies the approach of insisting to explain any given collection of symptoms with one disease.

"The 4 most important therapeutic considerations that must be incorporated in caring for every patient, especially those that are older, are optimizing hydration, nutrition, comfort through analgesia, and ensuring that the environmental needs are met so they can perform normal behaviors." (Scherck, VCNA 2020)

Triaditis can be broken down into the component parts; in the original research it was felt that the predominant signs of triaditis were the result of the cholangitis, with pancreatitis and IBD being secondary complications. More recently, with an increased awareness of pancreatitis in cats, and the long-standing popularity of the diagnosis of IBD, rank-ordering the importance of the individual diseases or determining the actual prevalence of the various possible combinations has become problematic.

Feline Cholangtitis

A yellow tinge on the inner aspect of the pinna is rarely what signals to a cat owner that it's time to seek veterinary care, but it does serve as a very bright and visible signal to that veterinarian that this is a case that will demand some time and attention, effort and expense.

First Things First

Bilirubin (or a small child with access to both the cat and finger paints) is the substance that has turned the cat yellow, so the question is why and where did the bilirubin come from? In addition to a complete History and Physical Examination, a KEY diagnostic test in the original work-up of a yellow cat is something as simple as a "crit tube" with its PCV/TP. A marked disparity between a significantly low PCV and normal TP points us down the Pre-hepatic diagnostic road of RBC lysis and brings the Complete Blood Count and a particularly observant Clinical Pathologist to the forefront of our diagnostic efforts.

When the Liver Turns a Cat Yellow

If the PCV/TP and CBC suggest that RBC lysis is not the source of bilirubin, our attention is turned towards the liver and gallbladder (Hepatic and Post-hepatic) as the cause of the cats yellow discoloration. This also draws our diagnostic attention to the biochemical profile, where predictably there will be an elevation in total bilirubin (usually greater than 2.5-3.0 mg/dl when the outside of the cat is turning yellow). It might be suggested that the degree of hyperbilirubinemia is indicative of the underlying disorder, with pre-hepatic causes, FIP, and pancreatitis resulting in a mild-to-moderate elevation and hepatic lipidosis and post-hepatic obstruction resulting in much greater elevations. Use caution (of course) when drawing generalities because the timing and severity of the disease will also impact the elevation, and because we are dealing with cats. My colleague at CSU, Dr. David Twedt, reviewed 180 cases of cats with hyperbilirubinemia. Those cats that were clinically icteric (bilirubin> 3.0 mg/dl) without evidence of RBC lysis most often had primary hepatobiliary disease. Cats that were not obviously icteric (bilirubin ranging from 0.5 to 2.9 mg/dl) often had non-hepatic disorders, with the liver being secondarily affected (reactive hepatopathy). Non-hepatic inflammatory disease, such as pyothorax, abscesses or fat necrosis were included in this group. Dr. Twedt also found the higher the bilirubin, the poorer the survival rate. Those having only mild increases in bilirubin tended to have a better prognosis; however, that prognosis was influenced by the underlying primary liver disease.

From the biochemical profile, in contrast to the dog where ALT is a specific indicator of liver disease, in cats the ALP is an indicator of significant primary liver disease. ALP in cats has a short half-life (6 hours), is in short supply, and is not induced by steroids, so a much smaller elevation of ALP in a cat should raise a much bigger red flag than it would in a dog. Gamma-glutamyl transpeptidase (GGT) is a similarly informative enzyme in cats, particularly in cases of feline inflammatory liver disease, as this enzyme is concentrated in bile ducts. Ironically, in one of the most famous feline liver conditions, idiopathic hepatic lipidosis, there's a marked mismatch between the two enzymes, ALP elevation usually being marked while the change

in GGT is minimal. In the cat, elevations in ALT by itself is often indicative of non-hepatic disease. As in dogs, an elevation in bile acids in the non-icteric cat is indicative of a loss of liver function, including but not exclusively portosystemic shunts.

Liver Disease Differentials

The large-category rule-outs for liver disease in cats at CSU include hepatic lipidosis (30%, idiopathic and secondary), cholangitis (29%), neoplasia (23%), and reactive (18%).

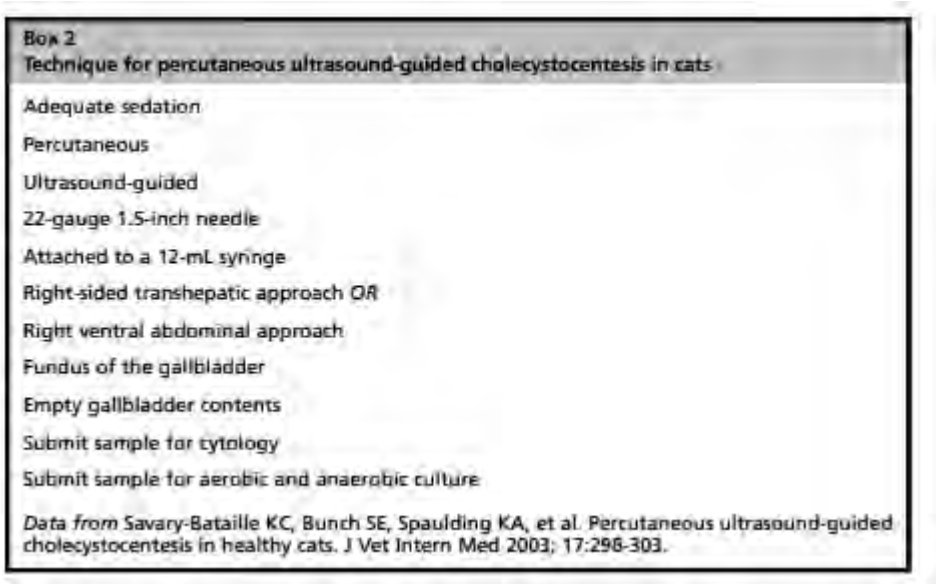
Cholangitis is the most common primary hepatic disease of cats (hepatic lipidosis is more common, but secondary to another concurrent condition and anorexia in the vast majority of cases). There are 3 distinct forms of cholangitis in cats: Neutrophilic (bacterial, acute and chronic), Lymphocytic, and Chronic cholangitis associated with liver fluke infection.

Although clinical signs can be non-specific (anorexia, weight loss, lethargy, vomiting, diarrhea, fever), variable, and overlap extensively, Table 1 attempts to summarize the nomenclature and clinical characteristics of Neutrophilic and Lymphocytic cholangitis.

Neutrophilic (N) acute and chronic	Lymphocytic (L)
Younger males	Older, chronic, progressive (European breeds)
Acute, febrile, icteric, lethargic, abd pain	Variable appetite, vomiting, weight loss
+/- Vomiting or Diarrhea	Icteric, ascites
Extra-hepatic biliary obstruction, lipidosis	↑Globulins
↑ALT (although can be normal)	Total bilirubin, ALT, ALP, GGT are all variable
total bilirubin, ALP, GGT are all variable	Bile duct distention, hepatomegaly, mixed echogenicity
CBC shows left shift w/toxic neutrophils	Bile cytology (toxoplasmosis, *Helicobacter*)*
US reveals thickened GB wall	Bile culture (E.coli, other enterics)
Bile cytology (toxoplasmosis, bacteria)*	Liver touch-prep cytology for bacteria
Bile culture (*E.coli*, other enterics)	Histopathology for definitive diagnosis

Abd = abdominal; GB = gallbladder; CBC = complete blood count; US = ultrasound
* 22 gauge 1.5 inch spinal needle in a trans-hepatic approach (decreased leakage)

From: Webb CB. Evidence-based medicine: Ultrasound-guided percutaneous cholecystocentesis in the cat. VCNA 2020;50:1123-1134.



Box 2
Technique for percutaneous ultrasound-guided cholecystocentesis in cats

Adequate sedation
Percutaneous
Ultrasound-guided
22-gauge 1.5-inch needle
Attached to a 12-mL syringe
Right-sided transhepatic approach *OR*
Right ventral abdominal approach
Fundus of the gallbladder
Empty gallbladder contents
Submit sample for cytology
Submit sample for aerobic and anaerobic culture

Data from Savary-Bataille KC, Bunch SE, Spaulding KA, et al. Percutaneous ultrasound-guided cholecystocentesis in healthy cats. J Vet Intern Med 2003; 17:298-303.

Although the prevailing opinion is that ultrasound cannot distinguish between lymphocytic and neutrophilic cholangitis in cats, maximal GB wall thickness and irregularity might be predictive of a positive culture result. Smith and colleagues provided the most direct and quantitative answer, with the most powerful result being the negative predictive value of a normal GB on ultrasound; in those cases it was highly unlikely that PUC would provide a sample that produced a positive bacterial culture

result. Contrary to these finding, several reviews conclude that feline cholangitis (not divided into neutrophilic or lymphocytic) may occur, even frequently, in the absence of notable changes on abdominal ultrasound.

Treatment	Information	Dose
Fluids & Electrolytes	Oral (voluntary), IV, subQ	40-60 Kcal/kg/day
Nutrition	Oral (voluntary), E-tube	40-60 Kcal/kg/day
Maropitant	Antiemetic	1 mg/kg SQ
Cobalamin (vit B_{12})	Taper after 6 weeks	250ug Inj & Oral available
Pain management	Buprenorphine	0.01 mg/kg sublingual
(N) Antibiotics	Pradofloxacin, Ampicillin, Clavimox*	3-6 months
(L&N) Metronidazole	Immunomodulatory & Antibiotic	7.5 mg/kg BID
(L) Prednisolone	Immunomodulation	1-4 mg/kg/day, taper q2wks
(L) Chlorambucil	Chemotherapeutic	Std dosing or Pulse dosing
Ursodiol	Choleretic, “silver bullet”	10-15 mg/kg q24hr, long term
SAMe	Liver protectant, antioxidant	200 mg q24hr
vit K_1	Dose prior to E-tube placement	5 mg/cat q1-2 days SQ
Lactulose	HE, ptyalism	0.5-1.0 ml/kg PO TID
Neomycin	HE, acts within GI tract	20 mg/kg q8–12hr PO
Methotrexate	Confirmed cases of bridging fibrosis	0.4 mg/day divided, q7-10 days

E-tube = esophagostomy feeding tube; cobalamin = DOSE; BID = twice daily; TID = 3 times daily; HE = hepatic encephalopathy
* Avoid chloramphenicol, clindamycin, erythromycin, lincomycin, streptomycin, sulfonamides, trimethoprim- sulfas, tetracyclines

Pancreatitis

Feline pancreatitis may occur as one of two forms, or an overlap of the two: Acute Necrotizing (ANP) is the more rare presentation, with acute or chronic Lymphoplasmacytic appearing to be more common. There is no age, sex, or breed predisposition, although some reports find Siamese to be over-represented. The clinical signs can be indistinguishable and include lethargy, anorexia, and dehydration, with icterus, abdominal pain, and hypothermia appearing in the more severe ANP form. Abnormalities on the biochemical profile can include elevations in liver enzyme activity, total bilirubin, and blood glucose. The cats are often azotemic with electrolyte abnormalities, including hypokalemia. Low ionized calcium is a poor prognostic indicator. CBC can reveal a nonregenerative anemia and a leukocytosis is more common than leukopenia. The feline PLI (Texas AM GI Lab) or the SpecfPL (IDEXX), run on a serum sample from a fasted cat, are excellent blood tests for the ANP form (100% sensitivity), while they perform with a bit less sensitivity in cases of mild or chronic feline pancreatitis (60-85% sensitivity). At CSU we have removed amylase and lipase from our biochemical profiles entirely. Abdominal radiographs could be normal or show a loss of serosal detail, a mass effect, or dilated fluid or gas-filled duodenum. Abdominal ultrasound could also be normal, or reveal a hypoechoic pancreas, hyperechoic surrounding mesentery, a mass effect, or dilated common bile duct. Definitive diagnosis is histopathology, obtained either through laparotomy or laparoscopy, but with the caveat that pancreatic disease can be focal and non-uniform.

Summary of the treatment options for the various forms of feline pancreatitis

Acute Necrotizing Pancreatitis (ANP)		
Fluids	Crystalloids & Colloids	Consider Hetastarch, Dextran
Nutrition	NE-tube, E-tube	Crucial for the Cat
Antiemetics	Maropitant	1.0 mg/kg q24 hours
	Ondansetron	0.1-1.0 mg/kg q12-24 hours
Pain management	Buprenorphine	0.005–0.01 mg/kg lingual q 4–8 hours
	Meperidine	1–2 mg/kg IM q 2–4 hours
	Butorphanol	0.2–0.4 mg/kg IM q2–4 hours
	Ketamine or Lidocaine	CRI
Acidity	Pantoprazole	0.5–1 mg/kg IV over 15 minutes q12h
Antibiotics	Controversial, Cefotaxime	50 mg/kg IM q8 hours
Plasma	Controversial	20 ml/kg IV
Chronic Pancreatitis		

Fluid support	Oral, subQ, E-tube	Hydration
Nutrition (fat not the issue)	Highly digestible	Feed the Beast
Cobalamin (vit B_{12})	Taper after 6 weeks	250–500 µg SC once per week
Pain management	Buprenorphine	0.01 mg/kg lingual q4–8 hours
Antiemetic	Maropitant	1.0 mg/kg q24 hours
Choloretic	Ursodiol	10 - 15 mg/kg q24hours
Antioxidant	SAMe	200 mg/day
Probiotic	Proviable, FortiFlora	As directed by package insert
Omega-3 FA	Various formulas	2000 mg/day
Steroids	Human Autoimmune dz	5 mg/cat/day
Antibiotics (rarely appropriate)	Broad spectrum	Cover *E. coli*

Suggested Reading

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Feline Chronic Enteropathy

Craig Webb, PhD, DVM, DACVIM

Introduction

Feline Chronic Enteropathy (CE) is really just the latest in a long list of umbrella terms that attempt to organize our approach to cats experiencing persistent vomiting and/or diarrhea. You don't have to be Aristotle to define Feline (cat) Chronic (as in 'not acute') Enteropathy ('a disease of the intestine' – Oxford Dictionary), but you've seemingly got to be a genius to fi.gure out what's actually causing this condition in any given cat, and how to effectively treat the problem. Underneath the chronic enteropathy umbrella, we have categories that are based on the treatment modality that garners the best result – so Food Responsive, Antibiotic Responsive, Steroid Responsive, or Not Responsive. This might suggest that we simply need to employ a series of trial treatments and hope we land on one that helps, done deal. That might be an OK strategy if we were dealing with the lesser species, dogs, for whom this nomenclature was developed; but cats are much more sophisticated than that. For example, the category called Antibiotic Responsive has been even further defined in dogs as Tylosin-Responsive diarrhea, whereas in cat, this is a tenuous diagnosis at best.

Idiopathic, our saving grace.

Fortunately, 'Idiopathic' is a perfectly acceptable differential for most any clinical condition in feline medicine. In fact, Idiopathic is often found at the top of the list of differentials for feline GI cases. Using the term is a great way to bamboozle a caregiver into thinking we actually know what we are talking about, when in fact, we have no idea. Dr. Grant Guilford was one of the first of us to decide that if Idiopathic was going to continue to find its way onto our rank-ordered list of rule-outs we ought to figure out how best to treat it. Not surprisingly, dietary intervention turns out to be both critical and sufficient in a fair percentage of cats with chronic vomiting/diarrhea. It was also Dr. Guilford that saved us from the fate faced by our dermatology colleagues, for whom a "food trial" to rule-out food allergies as a cause of skin problems requires at least 2, often 3 months of strict adherence to a special, and expensive diet, before the dermatologist can say much of anything intelligent about the patient's itch. As it turns out, to answer the question "Is this cat's chronic enteropathy going to respond to a change in diet?" takes about 2 weeks – if the vomiting/diarrhea has not improved significantly in that timeframe, it is time to move on. That does not necessarily mean giving up on diet as therapy – if we only need 2-weeks of effort we could repeat the test using a different diet (hypoallergenic to hydrolyzed to low-fat to high protein to easily digestible to high-fiber to the can that jumps off the shelf at us) some number of times before moving further down our list of differentials. Notice that a diet trial is being used as a powerful and irreplaceable diagnostic test, which has a very impressive sensitivity and specificity. We must remain cognizant of the fact that the term Food Responsive GI signs include a true food allergy (immunologic response to antigenic stimulation, usually a protein), a food intolerance (a non-immune mediated response to a single ingredient or additive) and food intoxication (mold, mildew, and other toxic chemicals or byproducts). Point of emphasis: a 2-week hypoallergenic or hydrolyzed diet trial (one study suggests these are equivalent, so pick something the cat wants to eat) is a critical diagnostic test and should be used in young to young-adult to adult otherwise relatively healthy chronic enteropathy cats.

Diet

It was so much easier back-in-the-day when cats were still just small dogs, and therefore we could feed them small dog kibble. These days I need a Nutrition Consult just to figure out what to feed my perfectly healthy indoor-only domestic shorthair. And because many of the cats who present for signs of chronic enteropathy are older adults, there's almost certainly a comorbidity to consider. Hence the recent appearance of diets designed for a pair of problems, which is actually quite clever. Then there's the recognition of the critical role that the microbiome plays in health and disease, and so not surprisingly, there are now diets that specifically target the microbiome. Undoubtedly a number of cats with chronic GI signs suffer from inflammatory bowel disease (IBD), a condition where we have a handle on the use of hypoallergenic/hydrolyzed diet, but working with Anne Avery's lab at CSU, we've figured out that a sizable percentage of CE cats actually have GI lymphoma, so what do you feed to a cancer? What's more, many cats appear to have IBD in one area of their intestinal tract and GI lymphoma in another part, so what do you put on the plate when you've got both guests coming to dinner? Yet to be determined. As if that's not complicated enough, dietary intervention has evolved to include innumerable supplements, additions, additives, prebiotics, post-biotics, symbiotics, fiber, vitamins, nutraceuticals, even essential amino acids. True believers might still consider an antibiotic trial (tylosin 10 mg/kg PO TID). Clearly the relationship between diet, the microbiome, and the clinical signs of the cat are unclear – "it's complicated".

Hairballs, a classic case
A common chronic enteropathy that's been with us since about the beginning of time…or is it? There are those who thinks it's normal behavior, there are those that think it's behavioral (excessive grooming), and there are those that think its reason-enough for full-thickness biopsies covering the GI tract stem to stern. It turns out there's a lot more thinking then there is studying, and attempting to address this ancient presentation with evidence-based medicine is a challenge. But there are a myriad of choices! (Where can I pick up some sugar cane fiber?)

Dysbiosis, now you can put a number to it.
The Texas A&M GI Lab (https://vetmed.tamu.edu/gilab/) now offers a feline fecal Dysbiosis index as a way to quantify the degree of dysbiosis in the feces coming out of individual patients. This panel represents the contribution of a relatively small number of bacterial groups that evidence would suggest play an important role in the microbiome as it pertains to clinical signs of chronic enteropathy: total bacteria, *Faecalibacterium*, *Turicibacter*, *Escherichia coli*, *Streptococcus*, *Blautia*, *Fusobacterium*, *Bifidobacter*, and *Clostridium hiranonis*. A negative number is considered normal, an index between 0-2 is the "grey zone", and anything above 2 is considered dysbiosis. The clinical use and utility of this assay is still being determined as there are cases where the dysbiosis index contradicts the clinical presentation, i.e. normal index in a case of persistent diarrhea or abnormal index in a cat with no signs of GI dysfunction. The index is one tool for assessing the presence of *C. hiranonis*, a critical microbe for the metabolism of bile acids within the GI tract. A decrease in this particular component means a decrease in secondary bile acid production, which appears to induce an increase in intestinal inflammation.

The Feline Boxer-wannabes
Although rare, there are several reports of what appears to be antibiotic-responsive colitis in a cat. Just like it's Boxer counterpart, this condition appears to be responsive, and in fact require treatment with, an fluoroquinolone (Pradofloxacin would be our first choice, several weeks pending response of clinical signs, those being persistent large bowel diarrhea that reads out as neutrophilic on histopathology.

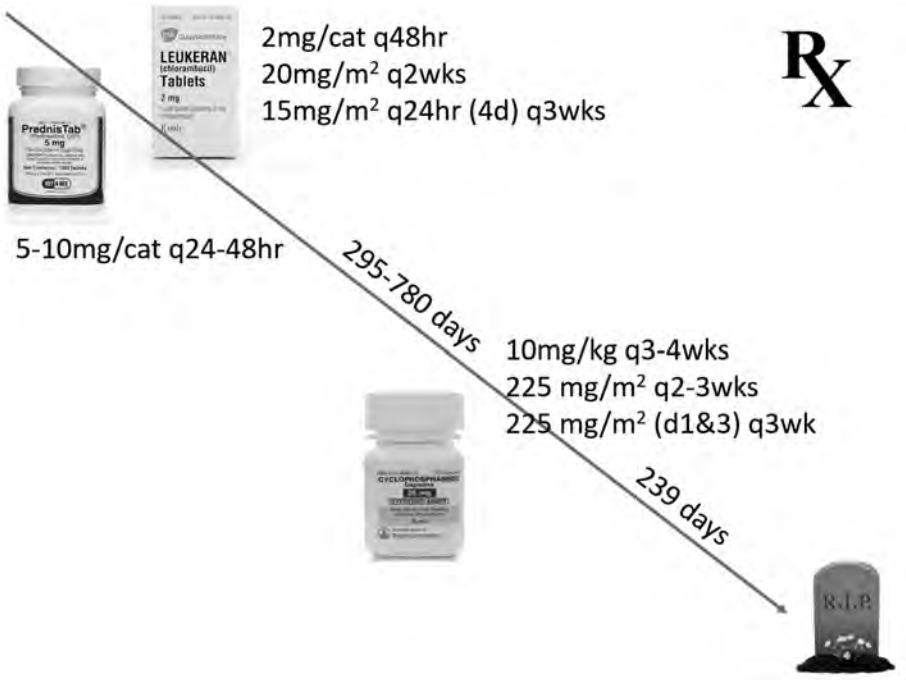
Inflammatory Bowel Disease (IBD) or Low-grade alimentary lymphoma (LGAL)
The lead into the diagnostic conundrum of IBD vs. LGAL should include ruling out secondary GI causes of chronic vomiting/diarrhea, so the standard CBC, chemistry panel, urinalysis, thyroid testing, GI panel including TLI & cobalamin, some version of a test of pancreatic lipase, and often imaging, particularly abdominal ultrasound, although that is best used to rule-out other issues vs. rule-in or distinguish between the two major players (don't forget a fecal exam and diet trial in the appropriate patients).

By definition, IBD is a histopathologic diagnosis. In recent years it has become apparent that histopathology, formerly considered the 'gold standard' for diagnosing chronic GI disease, is simply not sufficient for discriminating between IBD and GI lymphoma. For starters, histopathology comes from pathologists, and even agreement amongst pathologists is not consistent or guaranteed. Hence the development and utilization of immunohistochemistry (marking B and T cells) and molecular clonality testing (PARR, PCR for antigen receptor rearrangement). Working with Anne Avery and Emily Rout at Colorado State University, we have confirmed that cats can have IBD in one portion of the small intestine and LGAL in a different part of the small intestine. We have, in fact, gone one step further and found that with the same cat's GI tract you can find LGAL arising from one population of clonal T-cells in the duodenum, and LGAL arising from a different population of clonal T-cells in the ileum. It is now generally accepted (although difficult to prove) that IBD and LGAL represent two points on the same line – the progression of a chronic inflammatory condition to a cancerous one. The inflammation of IBD likely results from an over-exuberant immune response to environmental (including cytokine signaling), dietary, and bacterial stimuli in a genetically susceptible cat (e.g. NOD2 mutations in dogs). The clonality that define LGAL may share some of these triggers in that persistent inflammation is thought to predispose one to the development of cancer, and a at least one genetic mutations has in cats (STAT5B) with GI lymphoma that is shared with a certain class of human IBD patients.

Standard treatment for IBD includes a hypoallergenic or hydrolyzed diet, cobalamin supplementation as indicated, and prednisolone (1-2 mg/kg/day) or budesonide (0.5-2mg/cat/day) tapered to the lowest effective dose. Prebiotics, probiotics, and fiber may be added, but those that have a base of intact protein for flavor (e.g. chicken) should be avoided, as that defeats the purpose of the dietary intervention. Chlorambucil (featured in the treatment of LGAL) has become popular as the next addition in cases where the cat's response to the traditional regimen is not adequate.
There is an unacceptable paucity of research on what the optimal treatment is for cats with LGAL; several retrospective studies from over a decade ago found that the combination of prednisolone and chlorambucil (either the resulted in an average survival of 700+ days (Figure 1), but without a control group or comparative population it's impossible to say how that result

compares to no treatment, or single-agent treatment. Then there's the question of diet, as mentioned earlier, what do you feed a GI tract that contains both inflammatory antigen-responsive tissue as well as cancer containing mucosa?

Figure 1. Summary slide of retrospective treatment recommendations for LGAL.



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FMT: What's Coming Down the Pipeline

Craig Webb, PhD, DVM, DACVIM

Introduction

If our patients were cows instead of cats the use of Fecal Transplantation would be a no-brainer. Known as Rumen Transfaunation in bovine, the cud from a healthy donor cow is used to treat a sick cow, based on the assumption that changes in the intestinal microbial population could be associated with GI disease (indigestion), abnormal rumen function post-surgery (left-displaced abomasum), and manifestations of toxin exposure. Rumen Transfaunation is considered an effective, practical, and easy method to treat simple indigestion of ruminants. In humans Fecal Microbiota Transplantation (FMT) is the transfer of stool from a healthy donor into the GI tract of a patient whose disease is, again, presumed to either cause or result from an altered microbiome. FMT is best studied and most frequently and effectively used for humans with recurrent *Clostridium difficile* (CDI) infection. The potential therapeutic benefit of FMT may extend beyond CDI in people, particularly in conditions of GI dysbiosis and immune dysfunction. As of April, 2023, searching PubMed for "fecal microbiota transplantation" AND "canine" produced over 20 publications, from Parvovirus to IBD. From the same date, searching PubMed for "fecal microbiota transplantation" AND "feline" produced 3 publications…but one of them is entitled "On the threshold of a revolution…"!

The Importance of an Altered Microbiota: Dysbiosis

The fecal Microbiota (actual organisms) and Microbiome (genetic material) are essential to the normal development and function of most every system in the body, although most often highlighted with regards to the gastrointestinal tract [these terms are often used interchangeably]. Although the microbiota includes all organisms (fungal, viral, protozoa, and bacteria) the bacterial population has dominated GI research and attempted therapies thus far. We (and cats and dogs) have 10 times more bacterial DNA than human genetic information inside us. The GI tract also houses the largest collection of immune cells anywhere in the body, so it is not surprising that the microbiota has a critical impact on immune function, and FMT might act as "immunotherapy".

Dysbiosis is a disruption or imbalance in the normal GI microbiota. Dysbiosis may result from an increase or decrease in some number of commensal bacteria, may involve the introduction of pathogenic organisms, or the proliferation of opportunistic bacteria. Because the microbiota is a metabolically active "organ", dysbiosis may also impact the production of beneficial nutrients or metabolites, such as short-chain fatty acids or secondary bile acids.

Significant dysbiosis is found in cases of acute diarrhea (infectious, non-infectious, and hemorrhagic), chronic diarrhea (food or antibiotic responsive and IBD), GI motility disorders, EPI, and with the use of antibiotics and gastric acid reducers. Although the research is very limited, dysbiosis appears to be a significant component of feline and canine diarrhea, both acute and chronic. Changes in GI bacterial groups results in changes in the microbiota metabolism of many compounds, including fatty acids, biotin, tryptophan, ascorbate, and glycosphingolipids.

FMT: The Ultimate Probiotic

Probiotics are given to patients with GI disease in an effort to correct dysbiosis (measured or assumed) and return the microbiota to a normal, healthy state. According to the World Health Organization, probiotics are living organisms (not just bacteria) that when administered in adequate amounts (the more the better) confer a health benefit on the host. Probiotics are available in droves OTC, and are not currently regulated by the FDA, so it is often, and unfortunately, a "crap shoot" as far as what is actually inside the bottle you are buying. In fact, several studies (Weese et al. 2011 & 2003) have demonstrated that the majority of OTC probiotics simply do not live up to label claims – including labels where the advertised components are misspelled! But there are a number of veterinary studies that, despite some challenges and faults, at least suggest that probiotic administration may be helpful in some number of cases of canine and feline, acute and chronic GI disease. Some of the likely limitations include our lack of understanding as to which "bugs" are best for which diseases, and the enormity in terms of numbers and diversity found in a healthy microbiota – that simply cannot be reconstituted in a commercial product. So how could a clinician replicate that complexity and those numbers? Of course, produce the product as it comes straight out of a healthy GI tract!

FMT: The Logistics

Screening a Donor: Patient Preparation

Even in our human counterparts, there is a lack of standardization when it comes to donor selection for FMT. Although it is

unclear what makes for an optimal donor, common sense helps us with our exclusion criteria. Insufficient feces production, for instance; my long-haired Chihuahua has not entered the ranks of fecal donor at CSU. Poor doers, obese pets, unvaccinated animals, current clinical signs or history of relevant disease, recent (past 3 months) antibiotic use, or atopic or food allergic pets (Table). The patient (recipient) should be off antibiotics for at least 48-72 hours and off prebiotics, probiotics, and supplements, as is practical. The patient should undergo standard bowel preparation – so at a minimum a 12-hour fast and enemas, but more extensive if administering FMT by colonoscopy. In some human protocols the recipient is pre-treated with Imodium, but I am not aware of this being done in veterinary patients, and a number of post-procedure side-effects (constipation, bloat, flatulence) are likely due to the use of this drug. (Ideal Donor Adapted from Ziga Gerbec Thesis)

Ideal Donor
No Hx GI disease or clinical signs
No systemic antibiotic use
Naturally born, fed by mother
No immune disorder
No immunosuppressive therapy
No cancer or allergic diseases
Matched diet (e.g. hypoallergenic)
Not obese, no behavioral issues
Diverse, species rich microbiome
Dysbiosis Index (Bile Acid Metabolism)

Poop Preparation

And that's just the pet – now the poop. Obviously the goal is a clean, disease-free sample, where enteropathogens have been ruled out (Table). For both screening the donor and the feces the word "Ideal" is used as there is no agreed upon selection criteria, in either humans or veterinary patients, and these lists may well be longer or shorter in practice.

Ideal Fecal Screening
Screen for species specific parasites & pathogens
Fecal Floatation
Fecal Culture – *Salmonella* & *Campylobacter*
Giardia & *Cryptosporidium* IFA
Clostridium & *Yersinia enterocolitica*
Formed & Fresh (6-8 hours maximum)

Administration

There are many different protocols with varying amounts and dilutions; there is no evidence, as of yet, as to what constitutes an optimal FMT protocol. (the following was developed by Dr. Manchester, CSU PhD & Fellowship)

Fecal Preparation & Administration
Use approximately 2 gram feces/kg body weight
5-7 mL Ringer's solution:1 gram feces
Blend to a liquid slurry
Filter through a metal tea strainer
Load 50 mL syringes
10 mL Slurry/kg body weight
Given as a retention enema
Sedation as necessary
Pretreatment with maropitant (1 mg/kg SubQ)
Retention for 30 minutes if possible

Human patients are warned of potential side-effects that may occur in the first 24-48 hours following FMT: a low-grade fever, diarrhea, constipation, gas, bloating, and flatulence. Obviously these are possible in veterinary patients as well, although we find they are rarely reported by owners after FMT at CSU.

Putting Poop in its Place

1. We have a lot to learn and a long way to go.
2. Screen the donor and their feces: At first do no harm.
3. To augment, not replace, appropriate work-up and targeted therapies.

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The Vomiting Cat: Probing for Answers in the Older Cat

Jennifer Babineaux, MBA, DVM, DABVP (Feline)

Introduction

Determining the cause of vomiting in older cats can be challenging for several reasons. Owners often believe that vomiting is normal in their cats, and cats can vomit for a wide variety of reasons. Additionally, cats with chronic vomiting often have an unremarkable minimum data base (physical exam, serum chemistries and CBC, and abdominal radiographs). Ultrasound is one of the best, most readily available diagnostic tools for determining the cause of vomiting in cats.

In older cats, chronic enteropathies can be represented by a constellation of clinical signs, including vomiting, diarrhea, anorexia and even polyphagia. The most commonly reported clinical sign is weight loss, which is found in 80% - 90% of all cases. Large cell lymphoma should be on the differential list for older cats presenting with more acute signs of gastrointestinal disease and rapid weight loss.

Abdominal ultrasound is generally superior to radiographs for identifying the underlying cause of vomiting in older cats, because it can identify subtle changes in parenchyma in all the organs in the abdomen, including layering of bowel, enlarged lymph nodes and changes to the mesentery.

For success in performing ultrasound in cats, patient preparation is important. Ideally, cats should be fasted for 8-12 hours prior to ultrasound. However, cats have faster gastric emptying time than dogs, and several hours of fasting may be adequate. Shaving the abdomen for every ultrasound will significantly improve visualization of organs, and high frequency probes are also very useful for scanning cats.

Normal Feline Gastrointestinal Tract

The stomach is in the midline of the abdomen, immediately caudal to the liver. The stomach is best visualized by ultrasound when empty. The presence of gas or ingesta creates acoustic shadows, which interfere with the ability to visualize the entire stomach. In cats, an empty stomach often has a clearly defined spoke and wheel shape created by a layer of hyperechoic submucosal fat that can be observed from a ventral approach. If there is gas or ingesta present, using a left lateral approach may enhance visualization of gastric walls.

The entire stomach should be surveyed by sweeping from left (fundus) to right (pyloric antrum) in both sagittal and transverse planes to assess wall thickness and layering. The entire gastrointestinal tract has five distinct layers: mucosal surface, mucosa, submucosa, muscularis and serosa. The mucosa and muscularis are hypoechoic on ultrasound, while the other three layers are hyperechoic. Normal gastric wall thickness in the cat ranges from 2 mm in interrugal areas to 4.4 mm for rugal folds.

The duodenum is next scanned and is found on the right side of the abdomen, where it is in close proximity to the right kidney. The duodenum is generally superficial to the jejunum and follows a relatively straight course down the right lateral abdomen. The feline duodenum typically has slightly thicker walls than the jejunum, with normal wall measurement of 1.8 mm to 2.7 mm. Normal feline jejunum is also between 1.8 mm and 2.7 mm on ultrasound. The mucosal and submucosal layers should be thicker than the muscularis layer. The ileum is the thickest layer of feline bowel, with normal thickness ranging from 2.5 mm to 3.6 mm. The ileum typically is medial to the right kidney (although location can vary) and can be identified by a “wagon wheel” or “button” appearance in transverse plane. It is normal in the cat for the muscularis layer to be appear thicker in the ileum than in other segments of the small intestine. The colon is the thinnest layer of bowel, with normal wall thickness ranging between 1.5 mm to 2.5 mm and the colon can therefore be differentiated from the small bowel by its relatively thin walls. It can be difficult to visualize the entire colon due to gas shadowing from feces.

Normal feline lymph nodes have an elongated or spindle shape (also called fusiform) and a homogeneous echotexture comparable to splenic parenchyma; they are slightly hypoechoic compared to mesenteric fat. The most common lymph nodes to observe in a healthy cat are the jejunal and ileocecal lymph nodes. Typical size for jejunal lymph nodes is approximately 5 mm x 20 mm. Ileocecal lymph nodes are smaller than jejunal lymph nodes (5 mm x 10 mm) and have a more ovoid shape.

Feline Chronic Enteropathies

Chronic enteropathies primarily include inflammatory bowel disease (lymphoplasmacytic enteritis) and small cell lymphoma

(low-grade intestinal T-cell lymphoma). Both diseases may result in segmental or diffuse thickening of the bowel with retention of normal wall detail and/or selective thickening of the muscularis layer of the small intestine. Ultrasound cannot be used to distinguish between them due to the substantial overlap in the appearance of both diseases on ultrasound. An abnormal ultrasound may be used to help confirm the presence of gastrointestinal disease in cats with compatible clinical signs, but it cannot be used to rule-out intestinal disease (ultrasound is fairly specific, but not sensitive).

In the absence of wall thickening, other abnormal findings on ultrasound that are suspicious for a chronic enteropathy include gastric distension with ingesta despite fasting, or diffusely chyme-filled, hypermotile small intestines, which may be indicative of malabsorption. It is also common identify mildly to moderately enlarged jejunal lymph nodes that still retain a normal fusiform shape.

Gastrointestinal Large Cell Lymphoma

Large cell lymphoma (high-grade alimentary lymphoma) is the most common form of gastrointestinal neoplasia in cats, may be focal or diffuse, and may arise from any part of the gastrointestinal tract. Gastric large cell lymphoma can result in hypoechoic focal thickening and effacement of the gastric wall to profound circumferential thickening. Large cell lymphoma affecting the small intestine similarly results in a hypoechoic, circumferential mass lesion that destroys normal wall architecture and can also range from small mass lesions to very large lesions.

Feline mesenteric lymph nodes can have a wide range of abnormal findings on ultrasound, including enlargement, irregular shape, heterogeneity, cystic changes, and target lesions. Ultrasound cannot be relied on to differentiate between reactive and neoplastic lymph nodes, although severely enlarged, hypoechoic and rounded lymph nodes are more typically associated with neoplasia than smaller nodes retaining a more normal shape. There is also a higher probability of neoplasia with increased number of abnormal lymph nodes and hyperechoic peri-nodal fat.

Intestinal masses caused by lymphosarcoma may be confused with severely enlarged lymph nodes on ultrasound – to confirm that the mass is arising from the small intestine, the sonographer should search for a hyperechoic lumen with the presence of gas shadowing, which confirms the mass is intestinal in origin.

Other Causes of Gastrointestinal Masses

Adenocarcinoma is the second most common intestinal neoplasia in cats. Feline gastrointestinal eosinophilic sclerosing fibroplasia (FGESF) is also a differential for intestinal masses in cats. FGESF is a non-neoplastic cause of mass lesions in cats that most frequently appears near the pylorus or ileocecal junction in middle-aged cats. Both adenocarcinoma and FGESF have similar appearances on ultrasound: complex heterogeneous masses that efface normal wall detail. In addition, both of these masses can result in mechanical obstruction of the gastrointestinal tract, and both may be difficult to diagnose with fine needle aspirates.

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The Vomiting Cat: Probing for Answers in the Younger Cat

Jennifer Babineaux, MBA, DVM, DABVP (Feline)

Introduction

Determining the cause of vomiting in younger cats can be challenging for several reasons. Owners often believe that vomiting is normal in their cats, and cats can vomit for a wide variety of reasons. Additionally, cats with chronic vomiting often have an unremarkable minimum data base (physical exam, serum chemistries and CBC, and abdominal radiographs). Ultrasound is one of the best, most readily available diagnostic tools for determining the cause of vomiting in cats.

Vomiting in younger cats can be due to a wide variety of causes, including food allergies or intolerance, foreign bodies, gastroenteritis and acute pancreatitis. A careful patient history may provide clues to the cause of vomiting in younger cats. Younger cats with chronic vomiting that are not acting sick are more likely to have a food allergy or intolerance. Younger cats with acute onset of vomiting that have other signs of illness (e.g. anorexia, lethargy, hiding behavior) are more likely to have a mechanical obstruction, pancreatitis or gastroenteritis. The nature of vomiting may also provide hints – projectile vomiting may be associated with a mechanical obstruction, while vomiting undigested food shortly after eating may be associated with a food allergy.

Ultrasound is a better diagnostic tool than radiographs for differentiating causes of vomiting in cats. Ultrasound has greater accuracy, fewer equivocal results and provides greater confidence for diagnosing mechanical obstructions in vomiting animals compared with radiography.

Using Ultrasound to Diagnose Gastrointestinal Foreign Bodies and Intestinal Obstructions

Ultrasound can be utilized to identify gastrointestinal foreign bodies in vomiting cats. Care should be taken in scanning cats with suspected gastrointestinal foreign bodies since performing the study in dorsal recumbency and utilizing firm transducer pressure may induce vomiting and possible aspiration.

It is important to understand the appearance of shadows on ultrasound. Gas trapped within a lumen creates a “dirty” acoustic shadow caused by reverberation artifact. Gas will be hyperechoic and irregular at the interface with the ultrasound beam, with wavy, moving distal shadowing. In contrast, foreign bodies create a sharp intraluminal hyperechoic interface on ultrasound with strong distal acoustic shadow. The hyperechoic interface may be curvilinear with foreign bodies such as balls, toys or fruit pits.

The stomach is a challenging area to evaluate with ultrasound due to the presence of intraluminal gas. The stomach frequently has swallowed gas creating a “dirty” acoustic shadow at the non-dependent wall, and a gastric foreign body may not be visible if it is not obstructing the pylorus. Survey radiographs may be preferred, especially if the foreign body is radio-opaque. If a gastric foreign body can be observed on ultrasound, it will create a hyperechoic interface with sharp distal acoustic shadowing. Gastric foreign bodies resulting in pyloric outflow obstructions are more easily identified on ultrasound since they result in moderate to severe fluid dilation of stomach, and gastric fluid may outline the foreign body. Gastric motility will frequently be increased, which is in contrast to ileus, which results in hypomotility or atony.

Non-linear foreign bodies cause dilation of the stomach and small intestine proximal to the foreign body, while bowel distal to the obstruction has a normal, non-dilated appearance. Intestinal foreign bodies are characterized by an intraluminal hyperechoic interface with sharp distal acoustic shadow. Mesentery surrounding the obstructed intestine may be hyperechoic due to inflammation. Intestinal perforation results in more significant mesenteric inflammation and echogenic free fluid, which can range from mild and focal to severe. Linear foreign bodies are the most common foreign body in cats and are readily identified using ultrasound. Linear foreign bodies are often anchored in the mouth or stomach and cause severe plication of the duodenum and/or jejunum around a hyperechoic linear striation within the lumen of the bowel. Depending on the length of the foreign body, plication may be focal or multi-focal.

Intussusception is another cause of mechanical obstruction that is readily identified with ultrasound. It occurs in both younger and older cats (bimodal age distribution), and is caused by a portion of the gastrointestinal tract invaginating into part of the tract that precedes it or follows it. Jejuno-jejunal intussusception is most common, but any part of the intestinal tract may be affected. Predisposing factors may include intestinal foreign body, inflammatory bowel disease, neoplasia, or parasitism, but

many cases are idiopathic. Clinical signs include anorexia, weight loss, lethargy and vomiting. Diarrhea is less frequently reported in cats than in dogs. On physical exam, patients are often dehydrated and in poor body condition with a palpable abdominal mass Abdominal ultrasound is much more likely to provide a specific diagnosis of intussusception than survey radiographs as the cause of obstruction. Intussusceptions have a unique ultrasound appearance: in the transverse plane, they create a circular, target-like lesion with multiple hyperechoic and hypoechoic concentric rings.

Gastrointestinal Functional Ileus

Functional ileus/gastroenteritis is typically characterized by mild diffuse intestinal dilation and mild corrugation. A functional ileus can therefore mimic mechanical obstruction on ultrasound with the finding of dilated bowel. However, with functional ileus, the entire intestinal tract is typically uniformly affected: stomach, duodenum, jejunum, colon. In addition, the degree of intestinal distension is not as severe with functional ileus as with mechanical obstruction.

With functional ileus, the intestinal walls may appear normal or thickened. This appearance may be observed with pancreatitis, small intestinal bacterial overgrowth, dietary indiscretion and post laparotomy. With enteritis, mesentery may be normal to mildly to moderately inflamed (hyperechoic), and lymph nodes are frequently mildly enlarged.

Pancreatitis

The pancreas in the cat is somewhat easier to identify than in the dog. In cats, the left pancreatic limb is most visible, and it lies medial to the spleen, cranial to the left kidney and lateral to the greater curvature of the stomach. The left pancreatic limb is best visualized by turning the probe to a transverse plane and fanning cranially and caudally to identify the pancreatic duct, which has hyperechoic walls and no flow on color flow Doppler. The normal size for the left pancreatic limb is 5 to 9 mm in thickness. The right pancreatic lobe is found along the craniomedial aspect of the duodenum, and normal thickness is 3 to 6 mm. The pancreatic duct should have a thickness of 0.8 mm to 2.5 mm. It is common for the pancreatic duct in older cats to appear more dilated than in younger cats. A normal pancreas should have smooth and homogenous parenchyma.

Acute pancreatitis has a varying appearance on ultrasound in cats. It is more common to observe ultrasonographic changes in the left lobe in cats than in the right lobe. The sensitivity of diagnosing pancreatitis in cats using ultrasound increases with the severity of the disease, the quality of ultrasound equipment and experience of the ultrasonographer. In mild cases, no changes may be observed. Common ultrasound abnormalities observed in acute pancreatitis include hypoechoic pancreatic parenchyma, pancreatic enlargement, irregular shape, dilated pancreatic duct, hyperechoic peri-pancreatic mesentery and mild effusion. Peri-pancreatic mesenteric inflammation is the most specific ultrasound marker for pancreatitis. If the right limb is more affected, severe pancreatitis may cause duodenal corrugation, gastric ileus and obstruction of the common bile duct. The pancreaticoduodenal lymph node is also frequently enlarged. In very severe cases, changes observed on ultrasound may be very similar to pancreatic neoplasia.

Typhlitis

Typhlitis (inflammation of the distal ileum and cecum) is a frequent ultrasound finding in cats with a history of vomiting, anorexia and/or diarrhea. It is most commonly diagnosed in young to middle-aged cats. Cats may be painful on abdominal palpation. On ultrasound, the mesentery surrounding the ileocecal junction will appear hyperechoic, forming a halo effect, and ileocecal lymph nodes are frequently mildly enlarged. The walls of the distal ileum and cecum may also be mildly thickened, hypoechoic (normal cecal wall thickness is 1.7 mm to 3.6 mm) and may have blurred mural detail.

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Elevate Your Practice's Feline Wellness at Every Life Stage

Matt McGlasson, DVM, CVPM

Introduction

Cat ownership in the United States is at an all-time high and the largest cat owning demographic group is now Millennials. By better understanding the wants and needs of today's modern cat parents, veterinary healthcare providers can elevate the wellness experience for our feline patients and their pet parents at every life stage. In this presentation, we will discuss 5 key opportunities for veterinary professionals to provide a wellness experience that will lead to healthier and happier feline patients and a stronger human animal bond with their families.

First Kitten Visit

The first time a client brings in their new kitten offers us an amazing opportunity to build rapport and trust. Every effort should be made to make the patient and pet parent as comfortable as possible and minimize fear, anxiety, and stress. Never minimize the importance of this visit. Your team should be celebrating this new family member and take every effort to set up the new cat parent for success. Utilize your team members to ensure the topics of wellness plans, pet insurance, litter box training, diet, and oral care are discussed.

Wellness Plans

If your practice isn't providing wellness plans for your feline patients, you are missing out on a huge opportunity to elevate the wellness care and compliance of your clients. Wellness plans are very attractive for Millennial cat parents for a number of reasons. They are used to subscription models for services. Wellness plans allow for them to budget for their pet's wellness care (cost of 12 months of Revolution Plus), cost of a spay, cost of annual metabolic lab work. Besides the financial benefit, wellness plans provide an easy-to-follow formula for wellness care. This streamlines the visit for pet parents and your staff. For example, in our practice when a 2-year-old cat checks in for his annual wellness visit the veterinary technicians know that the visit will include a complete blood count, chemistry panel, Intestinal parasite screening, Physical Exam, Vaccinations, and a refill of Revolution Plus. There is no need for a discussion of prices, which tests are most important, etc. The wellness plan covers it all. The client doesn't even have to get out their credit card.

Pet Insurance

At the time of this presentation, approximately 4.9 million dogs and cats are insured in the US. 80% of these are dogs, while only about 20% are cats. We know as veterinary professionals that pets with insurance are more likely to approve emergency medical and surgical care. It is our duty to make sure our cat parents consider pet insurance and that they know about the benefits. Having these discussions when the patients are young and healthy is important, before health concerns arise.

Genetic Testing

New Genetic Testing platforms are available to veterinarians that can provide a wealth of information. A simple cheek swab performed during a kitten wellness exam will provide you with information related to risk factors for many serious conditions. If a patient shows elevated risk for cardiomyopathy or renal diseases, this gives us the opportunity to investigate further and potentially address conditions before clinical signs are evident. In addition to the breed and health data, the oral microbiome test provides information about the risk of dental diseases that can significantly affect a cat's quality of life, but can be managed effectively if diagnosed early.

Periodic Lab Work

Starting when the patient is young (typically prior to spay or neuter surgery), a CBC and Blood chemistries should be performed annually. This allows us to spot trends early and gives us time to intervene if needed. It is of vital importance to explain the benefit of "normal" lab work to your pet parents so they are keenly aware of the value to their cat's health and wellness. As discussed previously, the incorporation of wellness plans can dramatically improve client compliance in this area.

Utilization of AAFP's life stage guideline can help guide us on what lab tests are most appropriate for each stage. The ability to spot trends becomes extremely important as our feline patients age.

Client Communication

As veterinary professionals, we have a very limited time to evaluate our feline patients. A typical wellness exam will offer us 10-15 minutes of time with this patient and that may be the only chance we have to connect with the patient and pet parent

for an entire year. Cats do not exhibit the same behaviors in a veterinary clinic that they do at home. Make sure you are giving your cat parents an opportunity to bring up behavior concerns, even if they seem trivial. It is up to us to ask the right questions. Signs of pain (OA specifically) may not be recognized as such by cat parents until we ask the appropriate questions.

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Cats Don't Read Textbooks: The Conundrums of Diagnosing Feline Hyperthyroidism

Kelly St. Denis, MSc, DVM, DABVP (Feline)

We all know that cat. The total T4 is a little bit high, but there are no clinical signs. Or maybe the TT4 is normal, but the clinical picture fits with feline hyperthyroidism. Perhaps there are comorbidities which are complicating the diagnosis. Sometimes a diagnosis of feline hyperthyroidism can be straight forward, but at times we are left with 'that cat', trying to sort out what to do next. In this seminar, we will explore diagnostic dilemmas with feline hyperthyroidism including how to use additional testing to navigate our way through the diagnostic maze. We will also look at case management, with or without comorbidities.

The thyroid glands play a significant role in homeostasis by regulating metabolism. Respiratory rate, heart rate, nervous system function and digestion rates are all impacted. Regulation is via feedback loops through the hypothalamus and pituitary gland. Dysregulation of the thyroid most commonly occurs in the feline species as an elevation in thyroid activity often related to adenomatous growth of the thyroid tissue, with carcinoma changes being significantly less common.[1] Hypothyroidism as a primary disease is rare, most often presenting as a congenital issue, with secondary hypothyroidism occurring primarily as an iatrogenic problem.[2]

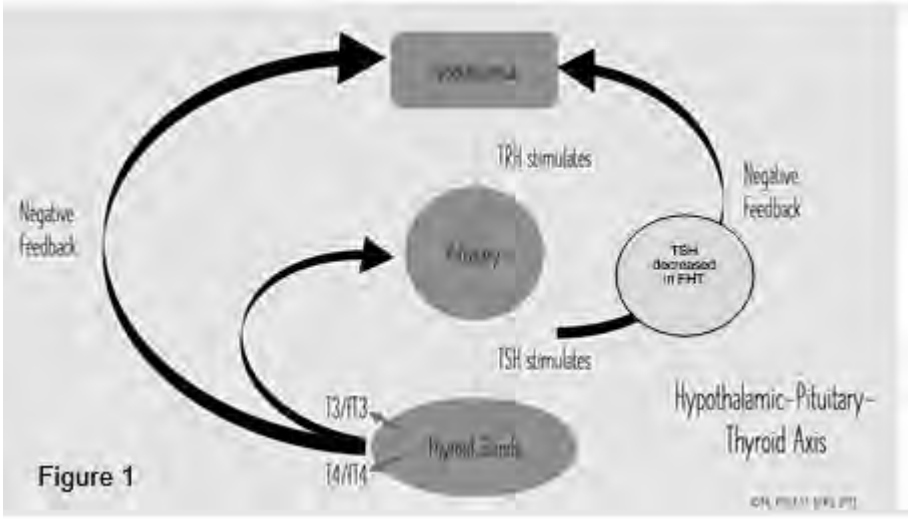

Figure 1

Risk Factors for feline hyperthyroidism (FHT) include mature age and indoor lifestyle. Genetic factors such as mutations in the TSH receptor might be at play, while environmental goitrogens such as iodine have been suspected in the past.[1] No single **clinical sign** is pathognomic for FHT, however a grouping of specific signs (Figure 2) combined with mature age will increase clinical suspicion dramatically. Many **differential diagnoses** have overlapping clinical signs including diabetes mellitus, gastrointestinal disease (malabsorption, maldigestion, inflammatory bowel disease, neoplasia), chronic kidney disease (CKD) and parasitism.

CLINICAL SIGNS

Figure 2

- Weight loss
- Polyphagia
- Polyuria
- Polydipsia
- Increased vocalization
- Agitation, increased activity
- Tachypnea, tachycardia
- Vomiting, diarrhea
- Unkempt hair coat
- Apathy, inappetence, lethargy

Testing

The 2021 AAFP Guidelines for Senior Care Task Force recommends a minimum database for senior care include physical examination, clinical chemistry, CBC, total thyroid (TT4), urinalysis and blood pressure series.[3] Where applicable risks exist, retrovirus testing should be completed annually.[4] With increased care and frequency of testing in the ageing cat, examination of the TT4 can be pursued as a trend in values. Ageing cats will often have TT4 values in the lower range of the reference limit. Cats with gradually increasing TT4 values over time, albeit in the reference range should be considered at risk for FHT. Thyroid testing may also be initiated when a patient presents with related clinical signs. As a sole measurement, the TT4 can be diagnostic for hyperthyroidism if the value is elevated and the patient has associated clinical signs. At other times, the TT4 may not reflect what is observed in the patient. Diagnosis of FHT can be challenging in these situations. While we may choose to measure other values such as T3, free T4 or thyroid stimulating hormone (TSH), or perform a T3 suppression test, ambiguities and challenges with these tests and their results also exist. These are discussed in more detail elsewhere.[5]

Figure 3
Adapted from Carney et al, 2016†

As noted in Figure 1, the TSH value should be decreased in a hyperthyroid state, as the feedback loop of excessT4 and T3 hormones suppress pituitary activity. If available, 99Tc scintigraphy for iodine uptake is valuable to confirm the diagnosis.5 In the past, measurement of feline TSH (fTSH) was not available and the canine TSH (cTSH) assay was sometimes used for testing. Unfortunately reference intervals for fTSH fall below the sensitivity of the cTSH (Figure 4), making it difficult to discern a decrease in a cat's TSH. More recently measuring the fTSH Truforma assay has become an in-house testing option that can discern true decreases in the TSH (Figure 4). The assay is also useful for detecting elevations in TSH for confirmation of hypothyroidism.

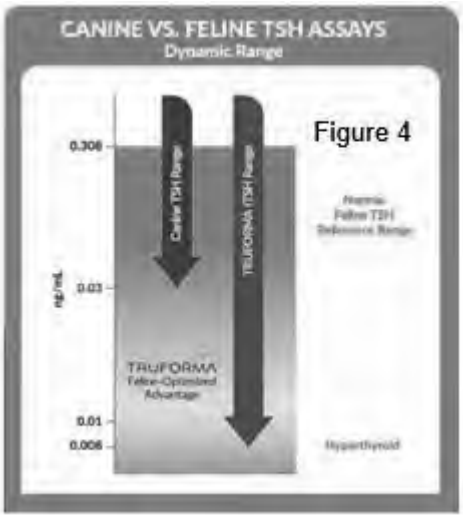

Figure 4

For veterinarians that do not yet have access to fTSH through Truforma, another option is to trend T4 values by retesting TT4 in 1-3 months (depending on patient status). A cat with an upward increasing value and persistent (possibly worsening) clinical signs should be treated as hyperthyroid in the absence of any other diagnoses. Treatment options include oral medication (ex.methimazole) to suppress excessive thyroid gland activity, surgical removal of the affected thyroid gland(s), radioactive iodine ablation of active thyroid tissue or dietary restriction of iodine intake. Each of these treatments comes with risks to the patient, has varying ease of use and variable cost to the caregivers.[1] The goal of therapy is to restore euthyroidism and minimize side effects of treatment. Regular patient re-evaluation is recommended to ensure the treatment is successful, that benefits of selected treatment outweigh the risks, and that caregivers are still comfortable with the therapeutic choice.

Due to the likelihood of comorbidities in the ageing feline species, concurrent conditions should be considered in the patient with FHT. These include CKD, cardiac disease, hypertension, retinopathies, GI disease and insulin resistance. Management of comorbidities alongside FHT management, in particular, FHT and CKD, can present unique challenges.[6] An intimate relationship exists between thyroid and kidney function. Increased thyroid hormones elevate glomerular filtration rate (GFR), potentially masking pre-existing kidney disease. While lowering of GFR during FHT treatment may contribute to azotemia and decreased survival time, micromanagement of TT4 values during treatment of FHT can result in iatrogenic hypothyroidism may contribute to azotemia and decreased survival time.

FHT is a common feline endocrinopathy. Diagnosis can be challenging when changes are subtle and comorbidities can complicate both diagnosis and management. Newer testing formats provide additional power to diagnose and monitor FHT.

Additional Resources

1. 2016 AAFP Guidelines for the Management of Feline Hyperthyroidism
2. Client Brochure: Feline Hyperthyroidism
3. Client Handout: Advantages and Disadvantages of Feline Hyperthyroidism Treatments

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Don't Sugar Coat It: Treatment Options for the Diabetic Cat

Cynthia Ward, VMD, PhD, DACVIM

Introduction

Feline diabetes mellitus (FDM) is a metabolic disorder characterized by chronic hyperglycemia in cats. It is a significant health concern in veterinary medicine, with increasing prevalence observed in recent years. FDM shares similarities with human diabetes, making it an important model for understanding the pathogenesis and exploring treatment options. The prevalence of FDM varies in different populations, with reported ranges between 0.2% and 1.5%[1,2] Certain factors, such as obesity and advancing age, have been associated with a higher risk of developing FDM.

Clinical Presentation

Signalment and History

FDM can affect cats of various ages, breeds, and genders. Although the disease can occur in cats of any age, it is more commonly observed in middle-aged and older cats. The median age of cats diagnosed with FDM is 12 years, with a range of 2 to 22 years. Additionally, certain breeds, such as the Burmese and Norwegian Forest cats, have been identified as having a higher predisposition to developing FDM.[1,2]

Obesity has also been strongly associated with the development of FDM. Overweight and obese cats are at an increased risk of developing insulin resistance, a key factor in the pathogenesis of FDM. Weight gain, sedentary lifestyle, and high-calorie diets contribute to the development of obesity and subsequent insulin resistance.[3,4]

When evaluating a cat suspected of having FDM, a thorough history is essential. Common clinical signs of FDM include polyuria (excessive urination), polydipsia (increased thirst), polyphagia (excessive hunger), weight loss despite an increased appetite, and lethargy. The owner's observations regarding changes in water intake, litter box habits, and appetite can provide valuable diagnostic clues. Additionally, a history of previous illness, medications, and any recent changes in diet or lifestyle should be noted, as these factors can influence the development and progression of FDM.

Etiology

The etiology of FDM is multifactorial, involving a complex interplay between genetic predisposition, environmental factors, and lifestyle influences. Genetic factors play a significant role in FDM, as certain breeds exhibit a higher prevalence of the disease. For example, the Burmese breed has been associated with a higher risk of developing FDM. Environmental factors such as obesity, sedentary lifestyle, and dietary factors also contribute to the development of FDM. Obesity, in particular, is a significant risk factor for FDM, as excess body fat leads to insulin resistance and impaired glucose metabolism. Furthermore, chronic low-grade inflammation and altered adipokine profiles in obese cats contribute to the pathogenesis of insulin resistance and beta-cell dysfunction. Other environmental factors, such as stress and pancreatic diseases, can also influence the development of FDM. Understanding the multifactorial etiology of FDM is crucial for implementing effective preventive and therapeutic strategies.

Concurrent Conditions

FDM is often associated with the development of concurrent medical conditions that can complicate the management and prognosis of affected cats. One common concurrent condition observed in cats with FDM is diabetic ketoacidosis (DKA), a potentially life-threatening metabolic derangement characterized by hyperglycemia, ketosis, and metabolic acidosis. DKA can occur as a result of insulin deficiency and is more commonly seen in newly diagnosed or poorly regulated diabetic cats. [5] Prompt recognition and treatment of DKA are critical to stabilize the cat's condition and restore metabolic balance.

Furthermore, cats with FDM are predisposed to other comorbidities, including urinary tract infections (UTIs) and pancreatitis. UTIs are more prevalent in diabetic cats due to factors such as glucosuria (excretion of glucose in urine), which provides a suitable environment for bacterial growth. Pancreatitis, an inflammatory condition of the pancreas, has been reported to occur more frequently in cats with FDM.[6] The underlying mechanisms linking FDM and pancreatitis are not fully understood, but inflammation and dysregulation of pancreatic function may contribute to the development of both conditions.

The presence of concurrent conditions highlights the importance of comprehensive medical management in cats with FDM. Regular monitoring, early detection, and appropriate treatment of these comorbidities are crucial for optimizing the health and well-being of affected cats.

Differential Diagnosis

When evaluating a cat with clinical signs suggestive of diabetes mellitus, it is important to consider other potential differential diagnoses to ensure accurate diagnosis and appropriate management. Some conditions that can mimic the clinical presentation of feline diabetes mellitus (FDM) include hyperthyroidism, chronic kidney disease (CKD), and pancreatitis. Hyperthyroidism, a common endocrine disorder in older cats, can cause weight loss, increased appetite, and polyuria/polydipsia, similar to FDM. Additionally, CKD can lead to increased drinking, urination, and weight loss, which can overlap with FDM clinical signs. Pancreatitis, characterized by inflammation of the pancreas, can cause vomiting, anorexia, and weight loss, sometimes mimicking the clinical picture of FDM.

To differentiate FDM from these conditions, comprehensive diagnostic tests are necessary, including blood glucose measurement, thyroid hormone levels, renal function evaluation, and pancreatic enzyme assays. Additional tests, such as imaging studies or further laboratory investigations, may be required to rule out other underlying causes. Accurate differential diagnosis is crucial for implementing appropriate treatment and management strategies tailored to the specific condition.

Diagnostic Examination

When evaluating cats suspected of having FDM, a comprehensive diagnostic approach is essential to confirm the diagnosis and assess the overall health status of the cat. The diagnostic workup typically involves a combination of clinical, laboratory, and imaging tests.

Measurement of blood glucose concentration is a fundamental component of FDM diagnosis. Persistent hyperglycemia, especially when accompanied by glucosuria, is indicative of impaired glucose regulation. Additionally, a thorough physical examination should be performed to assess the cat's general condition, body weight, hydration status, and presence of any concurrent medical issues.

Laboratory tests commonly employed in the diagnostic evaluation of FDM include a complete blood count (CBC), serum biochemistry profile, thyroid hormone measurement, and urinalysis. The CBC can provide valuable information about the presence of concurrent diseases or underlying conditions. The serum biochemistry profile helps evaluate kidney and liver function, electrolyte balance, and presence of ketones. Urinalysis aids in the detection of glucosuria, which is a hallmark of FDM. Thyroid status should be evaluated and hyperthyroidism treated appropriately. A urine culture should be submitted if urinalysis results are suspicious of UTI.

Furthermore, imaging studies, such as abdominal ultrasound, may be recommended to evaluate the pancreas and surrounding structures for any abnormalities. Imaging can assist in identifying pancreatitis or other potential causes or sequelae of FDM.

A comprehensive diagnostic examination helps confirm the diagnosis of FDM, rule out other conditions, and guide appropriate treatment decisions.

Management

Effective management of FDM involves a multimodal approach aimed at addressing insulin resistance, promoting weight loss, and maintaining glycemic control. The primary treatment goal is to achieve and maintain euglycemia, thereby minimizing the risk of complications and improving the cat's quality of life.

1. Dietary Modifications:
   - Feeding a well-balanced, calorie-controlled diet is crucial for weight management and glycemic control in diabetic cats.
   - A high-protein, low-carbohydrate diet has been shown to improve glycemic control and facilitate weight loss in cats with type 2 diabetes. [7,8]
   - Consultation with a veterinary nutritionist can help tailor a dietary plan specific to the individual cat's needs.

2. Weight Management:
   - Obesity is a significant risk factor for the development and progression of FDM.
   - Achieving and maintaining an ideal body weight through caloric restriction and increased physical activity is essential for managing insulin resistance and improving glycemic control.

- Regular monitoring of body weight and adjustments to the dietary and exercise regimen are necessary to ensure steady weight loss and prevent weight regain.

3. Insulin Therapy:
- Insulin therapy is a cornerstone of managing FDM.[9]
- Exogenous insulin administration helps compensate for the insulin deficiency and improves glucose utilization.
- Several types of insulin formulations are available for feline patients and have shown success in diabetic control including: PZI (ProZinc^{R}), Glargine, Glargine U-300 (Tujeo^{R}), Detemir^{R}, and Vetsulin^{R}. Dosing should start at 0.25-0.5 U/kg or 1-3 U/cat, but must be closely tailored to the individual.
- Close monitoring of blood glucose levels, serum fructosamine levels, and periodic adjustments of the insulin dosage are essential to achieve optimal glycemic control. Continuous glucose monitoring is helpful to obtain accurate glucose curves to help with insulin dosing in difficult-to-control cats.

4. SGLT2 Inhibitors (SGLT2i):
- SGLT2i are a new class of antidiabetic medications that work by inhibiting the reabsorption of glucose in the kidneys, leading to increased urinary glucose excretion.
- Belagliflozin (Bexacat^{R}) has been FDA approved in cats and is currently available for clinical use.[10]
- Patients must be screened carefully before SGLT2i therapy is initiated
- SGLT2i have the advantage of being a once daily oral medication, removing the need for twice-daily treatment and injections.
- Glucose curves are not needed as frequently (or at all) to monitor SGLT2i therapy.
- Ketones, preferably serum or whole blood beta-hydroxy butyrate (BHB) must be closely measured especially in the first month of treatment
- Euglycemia diabetic ketoacidosis (eDKA) is an uncommon but potentially fatal adverse event with SGLT2i. Practitioners may fail to recognize this condition as blood glucose is usually normal, although serum (and urine) ketones are present.

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The additional CE Sessions below will be available on-demand through the Virtual Platform at catvets.com/conference2023. Both in-person and virtual attendees will have access to these CE Sessions.

Virtual-only Sessions

SESSION TITLE	SPEAKER	SPONSOR/PARTNER
Feline GI Pain: Underappreciated & Over-Represented	Dr. Jennifer Slovak	IVAPM
Nutritional Support for Cats with Cancer	Dr. Catherine Ruggiero	Hill's Transforming Lives
The Cat is Losing Weight: Is it GI or FHT, or Both?	Dr. Kelly St. Denis	ZOMEDICA
Using Ultrasound to Collect Fine Needle Aspirates	Dr. Jennifer Babineaux	

Virtual-only Session Abstracts

Feline GI Pain: Underappreciated & Over-Represented, *Dr. Jennifer Slovak*
Veterinary medicine has evolved in recent years regarding the recognition and appreciation of osteoarthritis and peri-surgical pain in our companion animals, especially cats. Unfortunately, there is a commonly under-appreciated aspect of feline discomfort—abdominal/GI pain. Generally, abdominal pain is felt below the ribs and extends to the pelvis, an area largely encompassing the gastrointestinal tract and its associated organs such as the pancreas and hepatobiliary system. Visceral nociceptors within the mesentery or serosal surfaces and within the mucosal walls of hollow organs respond to chemical or mechanical stimuli. Unfortunately, visceral pain can be diffuse and poorly localized due to sparse afferent innervation relative to somatic innervation, making GI pain challenging to detect in our feline patients. This is relevant in clinical medicine as many diseases involving the GI tract occur in cats such as: chronic enteropathies (inflammatory and lymphoma), cholangiohepatitis, constipation, and pancreatitis. With continued diligent patient assessment and evolution of pain scales and analgesia options, we can improve our patients' quality of life.

Nutritional Support for Cats with Cancer, *Dr. Catherine Ruggiero*
Neoplasia is prevalent in the feline population and can have a significant impact on nutritional status. There is risk of malnutrition from cancer, especially when the neoplastic process interferes with prehension, chewing, and/or swallowing. Additionally, some cancer therapies can contribute to malnutrition. To help mitigate this risk, certain food features should be prioritized when feeding cats with cancer, including taste. A new food, Hill's Prescription Diet ONC Care, can benefit feline patients with neoplasia.

The Cat is Losing Weight: Is it GI or FHT, or Both?, *Dr. Kelly St. Denis*
Unexplained weight loss can be a challenge in the aging feline species. A minimum database, including total T4 can be enlightening, but what if the results are equivocal? If the results seem clear, how do we rule out other contributing comorbidities? In this seminar we will review the ins and outs of diagnosis, management, and monitoring these two common feline health issues.

Using Ultrasound to Collect Fine Needle Aspirates, *Dr. Jennifer Babineaux*
Percutaneous ultrasound-guided aspiration is a safe procedure that improves medical diagnoses, is minimally invasive, and may help avoid more costly procedures such as laparoscopic or surgical biopsies. This lecture will discuss the approach to percutaneous ultrasound-guided fine needle aspirates (FNA) for the general practitioner, including risks and benefits, case selection, and how to perform the procedure safely.

Feline GI Pain: Underappreciated & Over-Represented

Jennifer Slovak, DVM, MS, DACVIM

Historically, pain has been described as an unpleasant sensation or experience, but we now know it is much more complicated and is estimated to be significantly under reported in both humans and animals.[1-5] Although nearly every veterinarian thinks they are adept in pain identification and treatment, few of us have been adequately trained and possess these skills.[6]

Prior to the development of validated veterinary pain scales [7-9] many veterinarians relied on palpation as the sole means to identify pain which only measures one dimension; intensity. Current pain scales are a composite of many human models of pain assessment, especially scales used in pediatric patients.[2,3, 7-10] Based on the current literature, in order to evaluate a patient for pain, a holistic approach is necessary including assessment of patient behavior, reaction to touch, and physiologic parameters.[1,5,7-10] Patient pain interpretation can be impacted by many variables such as experience of the observer, comfort in handling the affected/examined species, the behavior and stress level of the patient, the type of pain assessed (acute versus chronic or adaptive versus maladaptive or visceral versus somatic) and the underlying disease process or co-morbid conditions.

Veterinary medicine has evolved in recent years regarding the recognition and appreciation of osteoarthritis (somatic pain) and peri-surgical pain in our companion animals- especially cats. We have several validated pain scales[1-3] though most are geared towards identifying acute pain. Unfortunately, there is a commonly under-appreciated aspect of feline discomfort- abdominal and gastrointestinal (GI) pain. Generally, abdominal pain is felt below the ribs and extends to the pelvis, an area largely encompassing the gastrointestinal tract and its associated organs such as the pancreas and hepatobiliary system. Many common feline GI-related conditions cause chronic pain, though identifying and treating this discomfort can be clinically challenging.

Unfortunately, visceral pain can be diffuse and poorly localized due to sparse afferent innervation relative to somatic innervation, making GI pain challenging to detect in our feline patients. Visceral pain can occur in the absence of evident tissue damage, especially in functional or idiopathic disorders.[11] This is relevant in feline clinical medicine as many diseases involving the GI tract occur in cats; chronic enteropathies (inflammatory and lymphoma), cholangiohepatitis, constipation and pancreatitis.

Abdominal pain is one of the main reasons human patients seek medical attention.[12] Treating chronic visceral pain in humans poses multiple clinical challenges such as limited effective therapies, poor side-effects, addiction, constipation, nausea and fatigue.[12] This is not dissimilar to trying to manage abdominal discomfort in our feline patients.

Visceral nociceptors within the mesentery or serosal surfaces and within the mucosal walls of hollow organs respond to chemical or mechanical stimuli.[11-14] Inflammation can impact an affected organ due to immune mediators released at the site of injury, it can increase epithelial permeability, and can also shift commensal microbiota populations within the GI tract.[12] Research into alternative non-pharmaceutical therapies for patient pain management has been pursued in human medicine due to the association of the gut – brain axis.[13]

The gut-brain axis refers to bidirectional communication between the GI tract and the brain via integrated immunological, neural and hormonal signals.[14] An unhealthy gut microbiota has been intimately linked to various GI conditions and may have a role in the pathogenesis of visceral pain in conditions such as IBD, food allergies and irritable bowel syndrome.[14] Microbiota refers to the ecological community of micro-organisms hosted by a multicellular organism. This bacterial community is variable between individuals and is shaped by genetics, environment, medications and diet.[13]

Recently, clinical studies indicate, that targeting the gut-microbiota in human patients may be a promising strategy for visceral pain management in patients with GI disorders.[11,14] Chronic pain management strategies include; minimizing pro-inflammatory antigens in the diet, as well as encouraging a diversified gut microbiota with use of pre and/or probiotics, and even implementation of fecal transplants. Pain in patients has been shown to be mitigated by minimizing noxious stimuli, eliminating gas formation and reducing sensitization of visceral nociceptors.[11-14]

Thus far, in veterinary medicine we implement these strategies in our patients on a case-by-case basis, but there is a paucity of literature investigating their use in managing feline GI discomfort. Currently, opioids, NSAIDs, frunevetmab, and gabapentin

are the predominant pharmaceuticals used by veterinarians for pain management. Unfortunately, these medications may be difficult to administer, or obtain, or be inappropriate for use for certain patients, or may be inadequate in alleviating patient discomfort.

Due to the inadequacy of traditional medications in feline chronic GI-related pain management, alternative therapies and strategies should be further investigated for use. A conscious goal for all veterinarians is to consider the pain that may be present in our patients and do our best to minimize it. The ability to adequately control chronic GI related pain, combined with the ease of administration to the patient, and the cost of the therapies are exquisitely important considerations in feline practice. With continued diligent patient assessment, evolution of pain scales, and research and development into therapeutic options, we can improve our patients' quality of life.

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Nutritional Support for Cats with Cancer

Catherine Ruggiero, MS, DVM, DACVIM (Nutrition)

Introduction

Cancer is common in pets and may result in metabolic changes that can lead to malnutrition.[1] As cancer progresses, signs may include decreased appetite, lethargy and weight loss, and in advanced stages, there can be a loss of body fat and lean muscle mass. Recovery or remission is associated with improved clinical status; however, metabolic alterations may persist. The metabolic changes and accompanying malnutrition can decrease quality of life and impair response to treatment.

Food Acceptance

The 2016 AAHA Oncology Guidelines for Dogs and Cats state that "the most important dietary consideration for canine and feline oncology patients is that the ration is palatable and eaten, otherwise it has no benefit".[2] For pet parents, seeing a decreased appetite can indicate a poor quality of life, and they may choose to have their pets euthanized at this point.

Food acceptance by pets is driven by the sensory properties of food such as aroma, texture and flavor. Pets may be initially attracted to a food primarily based on its scent; however, texture plays as crucial a role as ingredients regarding influence on taste perception. Most palatability research is proprietary; however, there is an extensive body of work evaluating factors that influence acceptance of foods by pets. Shape, texture, density, aroma, taste enhancers, processing techniques and other technical aspects of producing food can be used to develop and manufacture highly palatable foods.

Energy Balance (Caloric Intake)

In adult cats, the prominent clinical feature of cachexia is weight loss, which is associated with decreased quality of life and poor prognosis.[3] Studies have shown that weight loss and being underweight negatively affects survival in cats and dogs with cancer.[4-6] The cause of weight loss may be multifaceted, ranging from inappetence, increased metabolic rate attributable to cancer burden, changes in taste preference, negative effects of cancer treatment or alterations in host metabolism that impair utilization of key nutrients.

It is vitally important to maintain a positive energy balance via adequate caloric intake in pets with cancer so they do not begin to utilize glycogen stores, adipose tissue and dietary protein to compensate. The simplest way to increase the energy density of the food, and thus calories, is to add fat. It has been suggested that fat be 25-40% of the dry matter content of the food in pets with cancer.[1] An exception is pets with known fat sensitivities, such as hyperlipidemia, who should be managed with lower-fat foods.

Protein and L-Carnitine

Because cats do not have storage reserves of protein, any physiological state that results in a negative nitrogen balance causes a loss of normal functions performed by protein. Protein malnutrition may negatively affect the immune system, gastrointestinal (GI) function and other protein-dependent processes. Loss of lean mass, a late sign of protein malnutrition, usually is attributed to increased turnover of protein induced by cancer cells. However, other nutrient deficiencies can contribute to decreased muscle mass. One such nutrient is carnitine, which has been shown to be deficient in people with advanced cancer.[7]

Offering food with increased amounts of highly digestible protein is a logical choice for pets with cancer.[8] This provides amino acids that may be utilized to help blunt nitrogen losses attributable to metabolism changes induced by cancer and its management. Recommended levels of protein in cats with cancer are 35-45% (dry matter) for cats, except for pets with kidney disease and some liver diseases.[9] In addition to the absolute amount of amino acids available in the food, the correct balance is also needed to promote efficient protein synthesis. Other nutrients, such as L-carnitine, may help to spare lean muscle mass by promoting fat metabolism and reducing protein turnover.[10] Finally, in order for adequate amounts of high-quality protein and balanced amino acids to support muscle mass, a positive energy balance must be maintained. Therefore, ensuring adequate caloric intake is still the most important aspect of nutritional support for pets with cancer.

Carbohydrates

Because of metabolic alterations in cancer patients (e.g., increased lactate, insulin resistance), it has been suggested that foods for pets with cancer should contain less than 25% digestible carbohydrates.[1,9] This is based on data from dogs with specific

cancers and treatment regimens, and the assumption that the Warburg Effect (where cancer cells consume glucose and produce lactate) is present, which is not true for all tumor types.[11] Furthermore, it has been difficult to prove that limiting dietary carbohydrates slows tumor growth even in those cancers that display the Warburg Effect.

Because no ideal carbohydrate level has been established, and the potential for insulin resistance exists, it seems reasonable that a moderate level of carbohydrates (20-30% of dry matter for cats) would be acceptable in a food supporting pets with cancer. Because pets with cancer may have difficulty digesting key nutrients (due to cancer or cancer treatments), providing foods with highly digestible macronutrients (including carbohydrates) may be helpful.

Omega-3 Fatty Acids

Potential beneficial effects of long-chain omega-3 fatty acids such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in pets with cancer include preserving lean muscle and helping decrease inflammation that occurs as part of the pathogenesis of cancer.[1,12] The limited studies in pets with cancer suggest a positive benefit to feeding long-chain omega-3 fatty acids.

Based on available information, it seems reasonable to include omega-3 fatty acids (EPA, DHA) in foods for pets with cancer. This can be accomplished by using marine oils and other ingredients at a moderate ratio of omega-6 to omega-3 (ranging from 3:1 to 5:1).

Prebiotics

Pets with cancer may develop GI signs (e.g., diarrhea or constipation) that result from the cancer, its treatment or the lack of appropriate nutrient support for the microbes in the lower GI tract. Cancer and its treatment in people and dogs has been shown to cause gut dysbiosis.[13-14]

While there are no consensus recommendations for the amount or type of prebiotic fibers to provide to pets with cancer, recent research has identified prebiotics that are beneficial and can help manage diarrhea in pets.[15] For cancer, it seems reasonable that a mix of soluble (fermentable) and insoluble (non-fermentable) fibers in moderate levels may provide the necessary variety needed by the complex ecosystem within the GI tract to help promote a healthy microflora and optimize stool quality.

Evaluation of Cancer Patients

A nutritional assessment should be performed as a baseline at the initial diagnosis of cancer and at each visit to detect changes in the pet's condition and the need for adjustments in the nutritional plan. The whole process can be done very quickly, and much of the information can be collected by the veterinary technician or nurse prior to evaluation by the veterinarian. Engaging with pet parents about nutrition helps build relationships between them and the veterinary healthcare team. There are excellent online resources that include descriptions of a nutritional assessment, practical tips and checklists for having nutritional conversations with pet parents, and how to make a specific nutritional recommendation.[16,17]

Providing Nutritional Guidance for Pet Parents

People with pets who have cancer are usually engaged and motivated to do what's best for their pet. Even though they often consult many resources to learn and understand the options for their pet, they highly value advice and guidance from the veterinary healthcare team. In one survey of people whose pets had cancer, 96% said they trusted their veterinarian's advice regarding their pet's healthcare and 79% indicated the same trust regarding nutritional advice.[18] In the same survey, 100% believed nutrition played an important role in their pet's health and 85% said they would purchase a conventional pet food that met their pet's medical needs.[18]

Because of the interest of pet parents and the importance of proper nutrition for pets with cancer, the veterinary healthcare team is in an ideal position to proactively engage in a nutrition conversation with pet parents at the time of a cancer diagnosis. This is an opportunity to discuss/understand their goals (which almost always relate to quality and length of life), answer their questions, inform them about credible online sources of information and make a specific nutritional recommendation. Each nutrition support plan should be developed with specific goals in mind and tailored to meet the needs of each pet. General nutritional goals for pets with cancer include preserving lean muscle, minimizing metabolic and GI intolerance to food, and optimizing quality of life.[9] It is recommended to begin nutritional support at the time of a cancer diagnosis and continue past remission for at least 6 to 9 months or longer.[9] The reasoning is that residual alterations in nutrient metabolism associated with the presence of cancer cells persist for a varying period past treatment.

Conclusions

To increase the likelihood of food acceptance and long-term consumption, it is important to recommend a complete and balanced food with exceptional taste that meets the nutritional needs of each pet with cancer. Veterinary therapeutic foods have been recommended for pets with cancer instead of over-the-counter foods because therapeutic foods have more accessible nutrient information for the veterinary healthcare team, the digestibility of key nutrients is usually higher, they may be appropriate for GI issues resulting from cancer treatment or concurrent diseases, and some contain specific nutrients or functional ingredients that may be beneficial, such as EPA, DHA and fiber.[19]

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Using Ultrasound to Collect Fine Needle Aspirates

Jennifer Babineaux, MBA, DVM, DABVP (Feline)

Introduction

Percutaneous ultrasound guided aspiration is a safe procedure that improves medical diagnoses, is minimally invasive and may help avoid more costly procedures such as laparoscopic or surgical biopsies. This lecture will discuss fine needle aspirates (FNA) for the general practitioner.

In choosing to perform FNA, the practitioner should ensure there is minimal risk of hemorrhage associated with the procedure: adequate platelets, no suspicion of coagulopathy and minimally vascular target organ (or major vessels can be avoided). Color flow Doppler is very helpful in identifying vessels. The target lesion should have a reasonable probability of yielding a cellular and diagnostic sample – e.g. there is good target visibility on ultrasound with a safe needle trajectory and the target is of adequate size for aspiration.

Conversely, contraindications to FNA include significant risk of hemorrhage from the procedure (e.g. severe thrombocytopenia, highly vascular target or major vessels in needle trajectory), a low probability of obtaining a diagnostic sample or adding cost/risk with minimal patient benefit, such as when a surgical biopsy may be both curative and diagnostic.

The author prefers the following supplies: 22 G 1 ½" standard hypodermic needles, 3 mL luer-slip syringe and frosted edge glass slides. Smaller gauge needles (25 G) may be associated with less blood contamination but increased cellular trauma and are not associated with improved FNA sample quality. Larger syringes can be utilized but may make technical control with a single hand more difficult, especially if aspiration is necessary. Additional supplies that are useful to have readily available include extension tubing (for draining cavitary effusions), 3-way stopcocks and butterfly catheters.

Preparation

Choosing a quiet place with minimal interruptions to perform FNAs is strongly recommended – loud noises or interruptions may make the animal startle during the procedure with undesirable consequences. In addition, a room with directed task lighting is best – having light directed on the area being aspirated helps hand coordination, while a dark ultrasound screen improves needle visualization.

Many patients do not require sedation for FNA procedures, especially for aspirating superficial structures (such as the spleen), large masses or lymph nodes. Sedation is recommended for anxious patients and when aspirating vascular structures such as kidneys or deeper, smaller structures in abdomen to prevent unexpected patient movement during the procedure. The patient is placed in dorsal recumbency in a padded positioning trough. The patient's fur should be clipped, and the area being aspirated should be prepared aseptically with careful removal of ultrasound gel, as residual gel mimics necrotic tissue and mast cell granules. The ultrasound probe should also be cleaned with alcohol. The sonographer should wet the abdomen with alcohol (ultrasound gel is never used for FNA), identify the lesion and choose the ideal needle trajectory (shortest distance, safest path). The depth setting on the ultrasound machine should be set to make the target reasonably large, and the focal point should be set to the level of the aspiration target.

The probe should then be changed to be held in the non-dominant hand, while the needle/syringe combination is held in the dominant hand. The syringe should be pre-loaded with 1 ½ to 2 mL of air to make application of syringe contents onto a slide a simple one-step procedure. The needle is held at a 45-degree angle to the probe, with the hub of the needle pointed upward toward the probe, which enhances visualization of the needle. The sonographer's eyes should be on the ultrasound image, *not* on the hands, which requires practice. The needle is slowly guided into the organ to the desired depth, and an in/out pecking motion ("pincushion") is used to collect cells. Negative pressure should not be used initially due to the high probability of hemodilution. Negative pressure can be introduced in minimally vascular structures if the initial sample is minimally cellular. The needle is withdrawn, and the sample is blown out onto a clean slide. The cells should be gently spread using either a squash prep (semi-solid material) or blood smear technique (bloody or serous samples) and allowed to air dry (never heat fix samples, which will damage cell morphology).

Generally collecting two to four samples per organ is recommended to maximize the probability of a good diagnostic yield. The needle should be changed between every sample. A sample slide should be stained in-house using clean Diff-Quik to confirm

cellularity (never utilize the stain used for skin/ear slides). The frosted end of the slides should be labeled with a pencil (e.g. Fluffy Smith, SPLEEN). A complete patient history should be completed for the clinical pathologist, including a summary of the patient history, major lab abnormalities and ultrasound findings.

Fluid samples should be submitted in both EDTA tubes (to prevent clot formation and to allow cell counting) as well as in plain sterile tubes for culture and sensitivity. Sample slides of fluid should also be prepared and included to preserve cell morphology.

FNA is a very safe procedure when ultrasound guided – if the sonographer cannot see the needle, it is not ultrasound guided! If you cannot see your needle trajectory on the ultrasound screen, the probe can be gently, minimally fanned to find the needle while holding the needle still. If you are still unable to observe the needle, withdraw and restart the procedure. Using firm pressure on the transducer will move the transducer closer to the target organ – having an assistant apply lateral pressure to the skin on either side of the probe during to aspiration is also helpful. In addition, do not hesitate to change the patient position to find a better needle trajectory.

To develop skills, I recommend collecting urine with ultrasound guidance as frequently as possible – the needle is easy to visualize in anechoic urine and allows sonographers to develop hand-eye coordination. An ultrasound phantom can also be used for practice and is easy to prepare using Knox gelatin, a freezer bag and pimento stuffed green olives. Food dye can be added to the gel to obscure the olives.

Recommendations for Individual Organs

The liver readily lends itself to FNA, as it is a large organ that is not highly vascular. For diffuse hepatic disease, the liver is typically aspirated from the left side, away from the diaphragm, hilar vessels and gallbladder. Case selection is important in choosing to perform hepatic FNA. Diseases for which FNA is likely to be diagnostic include hepatic lipidosis, lymphoma, mast cell tumor and abscesses. Hepatic or biliary adenocarcinoma can be ruled-in with FNA, but a negative sample cannot rule it out (carcinoma may not exfoliate well). Cholangiohepatitis and biliary cyst adenoma cannot be reliably diagnosed with FNA. Histopathology remains the gold standard for the diagnosis of most hepatobiliary disease in the cat.

Gallbladder bile is safe to sample when cholecystitis is suspected. Indications for bile sampling include thickened gallbladder wall (> 1 mm) or the presence of sludge. Cats with normal gallbladders on ultrasound are unlikely to have a positive bacterial culture. Fluid should be collected for cytology and aerobic and anaerobic culture. Most texts recommend passing the needle through the liver, if possible, to seal the gallbladder and to minimize risk of bile leakage into the abdomen. If the gallbladder is large, as much bile as possible should be removed, also to minimize the risk of leakage.

Due to its size and superficial location, the spleen is the easiest organ in the feline abdomen to sample. Small spleens may be difficult to visualize well, and patients may need repositioning and wider shaving. If platelets are adequate, the risk of hemorrhage is minimal. Conditions that are readily diagnosed via splenic FNA include infiltrative round cell neoplasia (lymphosarcoma, mast cell tumor, plasma cell tumor) and lymphoid hyperplasia. Enlarged spleens (>10 mm thick), spleens with honeycomb pattern, spleens with solid nodules or masses and spleens in which round cell neoplasia is a differential should always be sampled. A pincushion aspiration technique should be used on the spleen, as hemodilution is very common in splenic aspirates. Cavitated or fluid-filled splenic lesions should not be aspirated due to hemodilution and the risk of hemorrhage.

Kidneys, while vascular, are safe to aspirate as long as the needle does not enter the medulla, which is highly vascular. Bleeding from a cortical FNA is usually self-limiting if platelets are adequate. A caudal approach to the left kidney is the simplest. The cranial pole of the right kidney may be difficult to aspirate due to its location near the rib cage. Conditions that can be diagnosed via FNA of the kidney include lymphoma, renal carcinoma and renal abscesses. FNA should not be utilized to diagnose interstitial nephritis, glomerulonephritis or feline infectious peritonitis.

As mentioned previously, the urinary bladder is an ideal organ on which to practice FNA technique, and ultrasound can improve urine collection yield on fat cats and cats with small or thick bladder walls. Care should be taken to visualize the needle so as not to pass through the bladder to the aorta and caudal vena cava dorsal to the bladder. Large bladder masses can be sampled via FNA – the pincushion method is recommended to avoid dilution of the sample with urine. Using FNA to sample bladder tumors is controversial due to the reported risk of seeding neoplastic cells into the abdomen along the needle tract, and the risk should be weighed against the value to make to a rapid, minimally invasive cytologic diagnosis.

Gastrointestinal masses can readily be sampled using ultrasound guidance. Care should be taken to avoid entering the lumen, which can potentially cause leakage of ingesta and peritoneal contamination. Gastric and intestinal lymphoma exfoliate well and are readily diagnosed via FNA, although a negative result must be interpreted cautiously. Blast lymphoma cells are very fragile and can be destroyed if not handled very gently, so obtaining multiple samples and staining one (or more) slides in house to confirm an adequate sample is recommended. Masses arising from lymphoma are very soft and easy to enter with a needle, while masses arising from adenocarcinoma, mesenchymal tumors and feline eosinophilic sclerosing fibroplasia are very firm and more challenging to aspirate and to obtain a diagnostic sample. If both an intestinal mass and enlarged lymph nodes are present, both structures should be sampled to increase the likelihood of a diagnostic sample.

FNA of bowel with mild wall thickening and retention of mural detail is not recommended due to the risk of entering the bowel lumen combined with a low diagnostic yield (biopsies are preferred).

Unless moderately to significantly enlarged, lymph nodes can be challenging to aspirate with ultrasound guidance, as they may move away from the needle tip during FNA and are frequently surrounded by blood vessels. Color flow Doppler should be used to identify the location of vessels prior to aspiration. Lymph node aspirates should be handled very gently when making the slide as lymphoid cells are delicate and prone to rupture.

The left pancreatic limb in the cat is relatively easy and safe to aspirate with few complications. The right pancreatic limb is more challenging due to its proximity to the duodenum and bile duct. Conditions that are may be diagnosed with FNA include pancreatic adenocarcinoma and pancreatic abscesses. Pancreatic pseudocysts can be percutaneously drained if surgical management is not an option – drainage can improve patient comfort.

Ultrasound guided FNA is very useful for sampling pocketed peritoneal effusions and can therefore help differentiate hemoabdomen, bacterial vs. inflammatory peritonitis, uroabdomen, chylous effusions and neoplastic effusions. In addition, nodular or abnormal areas of the mesentery can be directly sampled with ultrasound guidance to diagnose carcinomatosis and lymphomatosis. If there is a large volume of effusion, therapeutic abdominocentesis prior to FNA is recommended to reduce sample dilution.

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NOTES:

The Cat is Losing Weight: Is it GI or FHT, or Both?

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Unexplained weight loss can be a challenge in the ageing feline species. A minimum database, including total T4 can be enlightening, but what if the results are equivocal? If the results seem clear, how do we rule out other contributing comorbidities? In this seminar we will review the ins and outs of diagnosis, management and monitoring these two common feline health issues.

With an overabundance of obese cats,[1,2] weight loss is often a desired goal for our feline patients. Weight loss can be challenging, but the conundrum of unexplained weight loss is an even greater challenge. Unexplained weight loss is a decrease in body weight or body condition score (BCS) that is not accounted for by dieting or for which the cause is yet unknown. Changes in muscle condition score (MCS) due to sarcopenia or cachexia may also contribute to weight loss.[3] The patient may be losing weight in spite of a previous normal body weight or following months to years of unsuccessful weight loss attempts.

Trending body weight can provide valuable *predictive* information about a cat's health. A study of 258 cats in a Nestle Purina colony that died of cancer, renal failure, and hyperthyroidism determined weight loss started about 2.5 years before death.[4] Weight loss can precede CKD 1-3 years prior to diagnosis.[5]

During annual preventive care or senior biannual wellness visits, downward trends in body weight or changes in BCS or MCS may be noted. While we recommend annual preventive care for adult and mature cats, ageing cats require more frequent care. From the age of 7 years, the feline body can change and age rapidly with specific health changes potentially appearing and progressing in a 12-month period. [6] As a result, biannual or more frequent visits are recommended for ageing cats. Maintaining regular care routines are beneficial to being able to identify weight, BCS and MCS changes early, allowing for additional investigation and early intervention.

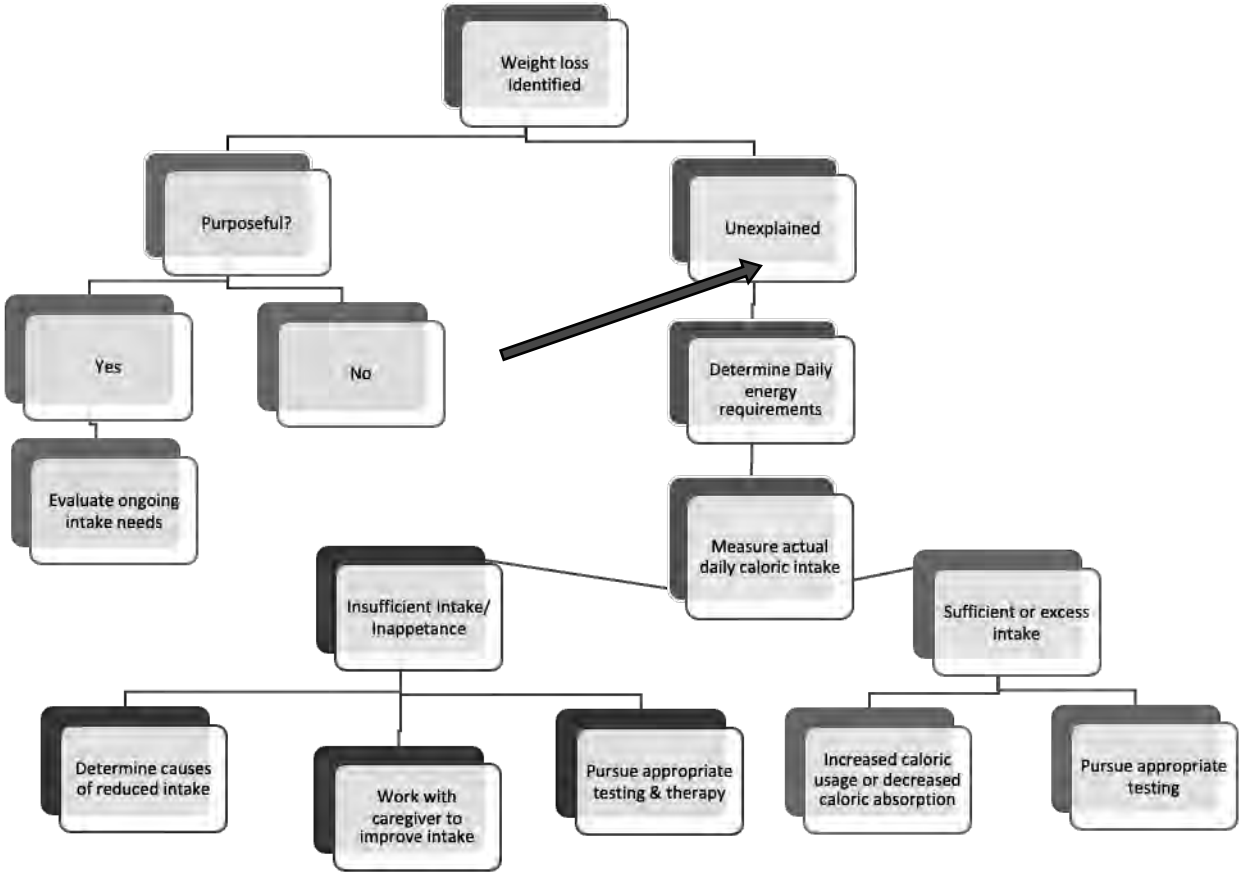
Identified weight loss will need to be classified as purposeful or unexplained. Purposeful weight loss results from specific reductions in caloric and/or carbohydrate intake. **Beware of sudden weight loss in the cat that has been unsuccessfully dieting for a prolonged period.** Caregivers might be gratified with the sudden success ('The diet is finally working!!!'), but this sudden loss is unlikely to be related to the diet. Evaluation of unexplained weight loss is outlined in the attached algorithm. While appropriate diagnostic testing is recommended, determining actual caloric intake compared to caloric needs can clarify whether the cat is not eating enough (inappetence) or losing weight in spite of eating sufficient to excess calories.

Determine Energy Requirements:

Energy requirements can be calculated as an approximation using the following formulas. It is important to note that all cats are different, and the calculated numbers may not represent what is ideal for an individual cat. It is an optimal starting point that can be adjusted with ongoing monitoring.

1. **Determine Caloric Needs**
   Resting Energy Requirements to maintain weight (RER):
   $$\mathbf{RER\ (kcal/d)=[70*BW_{kg}]^{0.75}}$$
   Daily Energy Requirements (DER):
   - Underweight & Illness: 1.2-1.4X RER
   - Geriatric & Frail: 1.1-1.2X RER
   - Weight loss 0.8-1.0 X RER
2. **MEASURE intake to ensure adequate intake.**
   - Guide the caregiver in measuring and recording daily intake
3. **COMPARE RER to intake amounts.**

Algorithm for weight loss in the feline species



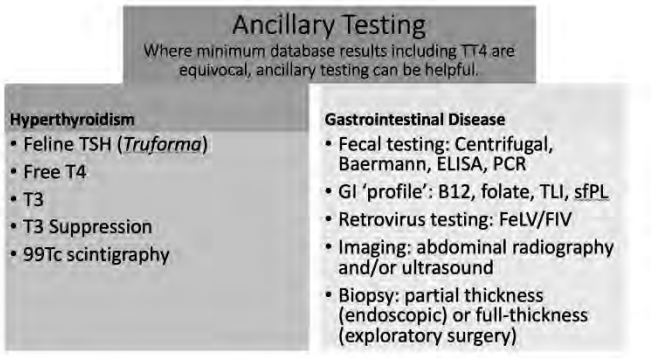
While there can be overlap in the conditions relating to insufficient intake versus those related to sufficient or excess intake, there are enough differences to warrant clarifying this for the patient. Reduced intake may be related to inappetence secondary to nausea, dental disease, gastrointestinal disease, cancer, azotemia secondary to CKD, to name a few.[7] Pursue age and symptom appropriate testing and initiate a treatment plan. It is also important to evaluate potential causes of reduced intake in the home setting:

- Ensure food is accessible: close by, easy to get to, no heroics needed.
- Raised feeding vessel where appropriate.
- Ensure food is in a perceived SAFE location.
- Ensure no other pets have access or are blocking access.

Where sufficient or excess intake is identified, testing will need to target those conditions that cause either increased caloric usage or decrease absorption. Hyperthyroidism is a common age-related disease that increases metabolism and subsequent caloric usage. Other causes of increased caloric usage or decreased absorption include cancer, gastrointestinal disease, diabetes mellitus, and internal parasitism.

Is it hyperthyroidism or gastrointestinal disease or both?

Our suspicions of hyperthyroidism will be increased in patients with appropriate signalment (>7 years of age) and clinical signs. Clinical signs may include unexplained weight loss in the face of normal or increased food intake, vomiting, muscle wasting, increased activity (caregivers may perceive the cat to be having a youthful rejuvenation), PU/PD, tachycardia etc.[8] Measuring total thyroid (TT4) will often provide diagnostic information, however occasionally the value is within normal range in spite of a high index of suspicion. Measuring the feline Thyroid Stimulating Hormone (fTSH) using the Truforma assay can provide clarification. While we may choose to measure other values such as T3, free T4 or cTSH, or perform a T3 suppression test, ambiguities and challenges with these tests and their results also exist.[9] If available, 99Tc scintigraphy for iodine uptake is valuable to confirm the diagnosis.[9] If fTSH is unavailable, another option is to retest the TT4 in 1-3 months (depending on patient status), to evaluate trends. A cat with an upward increasing value and persistent (possibly worsening) clinical signs should be treated as hyperthyroid in the absence of any other diagnoses. Due to the likelihood of comorbidities in the ageing feline species, other concurrent conditions should be considered based on the weight loss algorithm. This includes gastrointestinal disease.



Gastrointestinal (GI) disease includes a wide variety of conditions impacting the stomach, small and large intestine. Common causes in cats include infectious disease (parasitism, viral, bacterial), intestinal wall disease (inflammatory bowel disease, lymphoma), discrete neoplasia, systemic lymphoma, etc. Weight loss from GI disease can be related to decreased intake/inappetence, (ex. due to nausea) or sufficient to excess intake. GI disease and hyperthyroidism have sufficient overlapping clinical signs to cause diagnostic challenges if initial TT4 values fall within the reference range. In cases where a diagnosis of hyperthyroidism is clear, treatment of disease is warranted. Following stabilization of thyroid values, if clinical signs including unexplained weight loss persist, further testing for GI disease is recommended. Where fTSH is normal or a diagnosis of hyperthyroidism is inconclusive, further testing to differentiate potential causes of GI disease is recommended. Abnormalities in biochemical and CBC values may be nonspecific (example, mild anemia). Further testing including fecal ELISA, imaging (abdominal radiographs and ultrasound), GI profile testing (B12, folate, TLI), retrovirus testing and potentially biopsy will be indicated if the caregiver is able to pursue. Subnormal concentrations of B12 can be identified in cats with intestinal wall disease, however a subset of hyperthyroid cats may also exhibit low B12.[10]

Conclusion

1. Weight loss is best detected through regular monitoring of body weight, BCS and MCS
2. Purposeful weight loss is often confused with unexplained weight loss.
3. Unexplained weight loss can be due to inappetence but can also occur in spite of sufficient to excess caloric intake.
4. Hyperthyroidism and GI disease are two common causes of weight loss with similar presentations.
5. Ancillary testing can clarify the cause(s) of unexplained weight loss.

Additional Resources

About Truforma
GI Profile: B12, folate, TLI, sfPL
Companion Animal Parasite Council
AAFP Caregiver Brochures: How to Feed a Cat, Hyperthyroidism,
2016 AAFP Guidelines for the Management of Feline Hyperthyroidism

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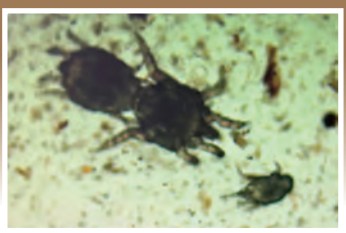
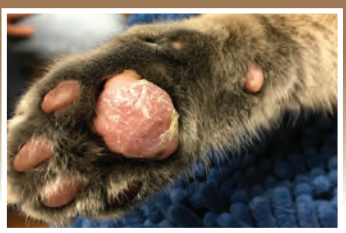
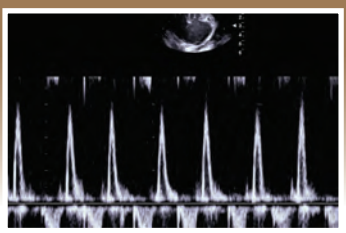

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