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Diagnosing Feline GI Disease: Setting Yourself Up For Success

Learning Objectives

1. Give clinicians an appreciation of their critical role as clinicians-first in feline practice.

2. Understand the role of key features and important incongruities in working up feline cases.

3. Demonstrate the impact of clinical effort and expertise on diagnostic testing.

Introduction

This presentation addresses the importance of signalment, presenting complaint, history, and physical examination with case examples. Positive predictive value will be use to illustrate the central role of clinical expertise in both the choice and interpretation of diagnostic testing.

Clinicians First and Foremost

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.

Definitions

Sensitivity – the proportion of true positives that are correctly identified by the test.
Specificity – the proportion of true negatives that are correctly identified by the test.

- True positive: Sick pets correctly diagnosed as sick
- False positive: Healthy pets wrongly identified as sick
- True negative: Healthy pets correctly identified as healthy
- False negative: Sick pets wrongly identified as healthy

Positive Predictive Value (PPV) - The ratio of true positives to combined true & false positives; the proportion of pets with positive test results who are correctly diagnosed. It is the most important measure of a diagnostic method as it is a measure of the probability that a positive test result reflects the underlying condition being tested for. Its value depends on the prevalence of the disease.

Diagnostic Technology Example: Feline Infectious Diarrhea

- ELISA – Enzyme-linked immunosorbent assay: uses specific antibodies directed at particular antigens, these antibodies are linked to an enzyme that catalyzes a substrate reaction that results in a quantifiable color change
- IFA – Immunofluorescence antibody assay: uses specific antibodies directed at particular antigens, these antibodies are linked to a fluorophore (primary) whose emission can be visualized with a fluorescence microscope or plate reader.
- IHC – Immunohistochemistry: antibodies directed at specific antigens within tissues (ex. cell surface markers), these antibodies can be conjugated to an enzyme that catalyses a color producing reaction or they can be attached to a fluorophore.
- Flow Cytometry: flurophores attached to antibodies directed at specific cell surface markers are used to label cells, which are then passed by lasers single-file, the resulting emission is captured and quantified
- PCR - Polymerase chain reaction: the amplification (using specific primers, a DNA polymerase, and thermal cycling) of a specific DNA sequence within a sample, allows detection, identification and quantification of target sequences.

Ironically, the advent of these incredible advances in diagnostic technology (and list is the condensed version) have significantly magnified, not diminished, the importance of the basic clinical skills of the veterinarian. With these diagnostic tools and the client's money we have reached the point where we can find almost anything, almost anywhere, in almost every patient – if we are willing to spend the time, effort, and money. But a positive test result is only as meaningful as the quality of the question it addressed – once again highlighting the importance of our ability to ask the right questions.

EXAMPLE: Fecal Technology. *Giardia and Tritrichomonas*

Both *Giardia* and *Tritrichomonas* can cause diarrhea in cats. Young cats, and those from crowded environments such as kennels, catteries, and cat shows are at higher risk. Although *Tritrichomonas* is thought to cause predominantly large bowel diarrhea and *Giardia* appears more likely to cause small bowel diarrhea, there is certainly overlap in the target patient population and the presenting clinical signs. In addition, a number of studies have identified both organisms in a significant percentage of young cats with diarrhea from cat shows and kennels around the world. Because both organisms can be therapeutically challenging, and Giardia is potentially zoonotic, it is important to attempt to confirm a clinical diagnosis prior to trial treating with a best-guess dewormer. This is also an important step on the off-chance the initial trial treatment should fail or similar clinical signs reappear down the road.

Having arrived at a clinical diagnosis of *Giardia* in a cat with diarrhea, the subsequent diagnostic algorithm starts with feces and a microscope. Identification of *Giardia* cysts is challenging because the organism is shed intermittently (sample fresh diarrhea), are very fragile, and are mimicked by pollens, brewer's yeast and other artifacts from the diet or environment. *Giardia* trophozoites must also be differentiated from numerous artifacts as well as *Tritrichomonas* trophozoites on a fecal wet mount (again, the fresher the better).

The next technological step in the attempt to diagnose *Giardia* involves the use of an ELISA assay. The following table was developed by Dr. Stan Marks (used with permission), comparing the performance of different ELISA assays and fecal flotation for diagnosing *Giardia* in 344 cats. Not only does this technology remove the microscopy and the eye sight necessary for cyst identification, it also removes the need for fresh fecal samples.

	Sensitivity (%)	Specificity (%)	False negatives	False positives

Flotation	85.3	99.7	5	1
Immunocard STAT!	72.7	99	9	3
XpectT Giardia/Crypto	79.4	99	7	3
SNAP Giardia ELISA	85.3	100	5	0
ProSpecT Giardia Microplate ELISA	91.2	99.4	3	2

The SNAP® *Giardia* Test Kit (IDEXX Laboratories, Inc.) featured in this table is an in-house assay that can be performed on fresh, previously frozen, or refrigerated fecal samples stored for up to one week. The assay is easily performed, takes a matter of minutes, and is both sensitive and specific. Dr. Marks emphasizes that parallel testing, using both floatation with centrifugation and the SNAP ELISA increases the sensitivity (97.8%) of the diagnostic effort. At the Colorado State Diagnostic laboratory we frequently employ the Merifluor® IFA combination *Cryptosporidium*/*Giardia* assay as a gold standard, but the requirement for a fluorescent microscope precludes the use of this assay in-house in private practice.

The diagnosis of *Tritrichomonas foetus* can be equally challenging. As with *Giardia*, the effort starts with attempted microscopic identification of trophozoites from a fecal wet mount preparation. A reminder that *T. foetus* are spindle-shaped with an undulating membrane and move in a jerky manner while *Giardia* trophozoites have a concave ventral disc and move as if imitating a “falling leaf”. Unlike *Giardia, Tritrichomonas foetus* does not have a cyst stage. This diagnostic effort successfully identifies the offending organism approximately 14% of the time it is used in cats with diarrhea due to *T. foetus*.

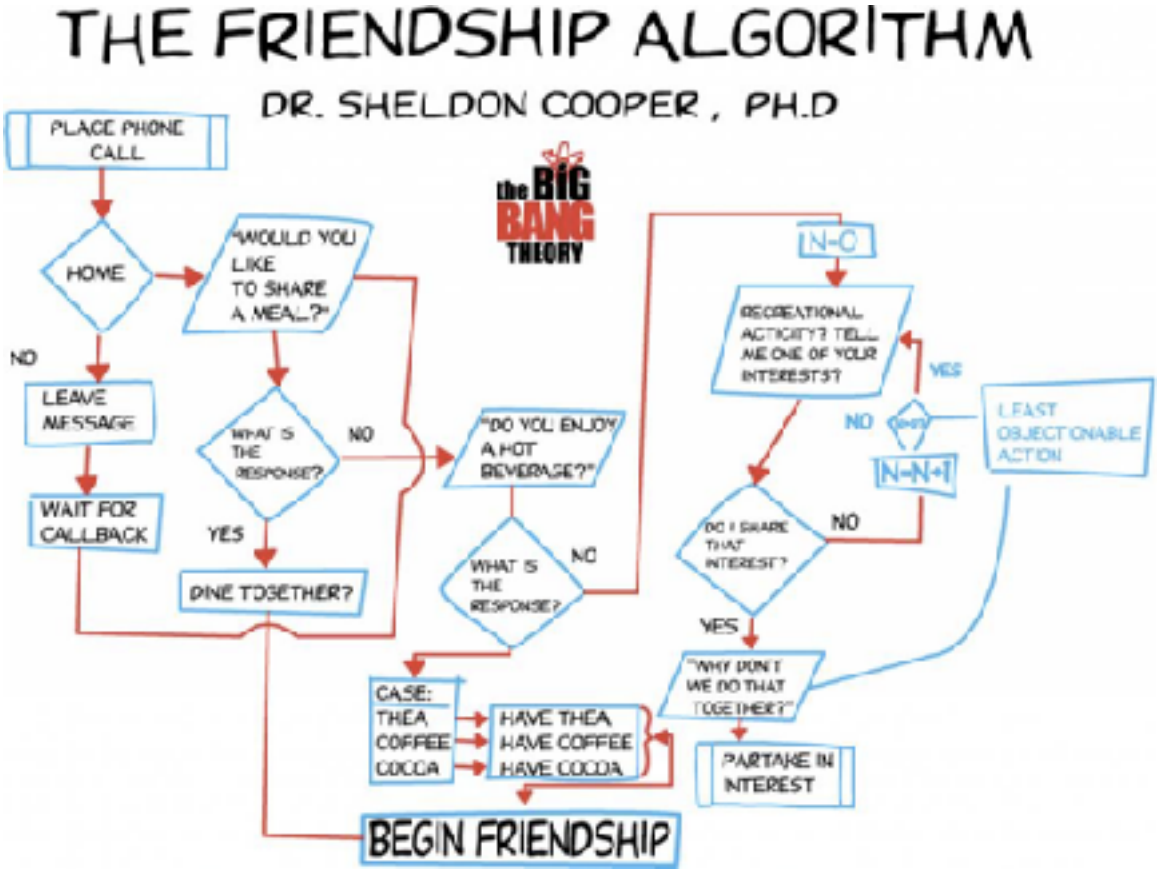
The InPouch TF (Biomed Diagnostics) is a fecal culture system that is significantly more sensitive for the detection of *T. foetus* in cats with diarrhea. This assay requires a very small amount of fresh feces (0.05 grams), acquired either through the cooperation of the patient or with a moist cotton swab up the bum. The InPouch is incubated at 37^{o} for 24 hours, then stored at room temperature in the dark during which time the culture media is examined daily (40X) for 10 days for evidence of the organism. At CSU we frequently employ PCR technology to look for evidence of *T. foetus* in a fecal sample, the detection limit for this technique is only 10 organisms per 50 mg of feces, compared to the greater than 1000 organisms per 0.05 grams of feces reported for the InPouch assay.

Prevalence

Remember that the Positive Predictive Value of a diagnostic test is dependent upon the prevalence of the disease in the population being tested. The prevalence of various “common” causes of feline diarrhea are published for many locations throughout the United States, and even the world. If you find yourself diagnosing *Giardia* in 50% of the cats that present to your clinic in Northern Colorado with diarrhea, something is amiss, EVEN if 90% of those cats seem to respond to your prescription for metronidazole!

Summary

- Diagnostic tests are only as good (Positive Predictive Value) as you are
- Clinical decisions impact the Prevalence of the Disease in the population being tested
- Cats do not read veterinary textbooks


THE FRIENDSHIP ALGORITHM
DR. SHELDON COOPER, PH.D
the BIG BANG THEORY
PLACE PHONE CALL
HOME
NO
LEAVE MESSAGE
WAIT FOR CALLBACK
"WOULD YOU LIKE TO SHARE A MEAL?"
WHAT IS THE RESPONSE?
NO
YES
DINE TOGETHER?
"DO YOU ENJOY A HOT BEVERAGE?"
WHAT IS THE RESPONSE?
NO
CASE:
THEA
COFFEE
COCOA
HAVE THEA
HAVE COFFEE
HAVE COCOA
BEGIN FRIENDSHIP
N=0
RECREATIONAL ACTIVITY? TELL ME ONE OF YOUR INTERESTS?
YES
NO
ONLY
N=N+1
LEAST OBJECTIONABLE ACTION
DO I SHARE THAT INTEREST?
NO
YES
"WHY DON'T WE DO THAT TOGETHER?"
PARTAKE IN INTEREST

Suggested Reading

Margolis C, Jotkowitz A, Sitter H. A problem solving and decision making toolbox for approaching clinical problems and decisions. Inflamm Res Suppl 2:S179-183, 2004.

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