



EXPLORING NEW THERAPIES FOR A COMMON CAUSE OF FELINE INFECTIOUS DIARRHEA

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INTRODUCTION

Feline trichomonosis is an intestinal disease caused by the protozoal pathogen, *Tritrichomonas foetus*. *T. foetus* was definitively identified as a cause of waxing and waning large bowel diarrhea in cats in 2003 and since then its prevalence has been recognized worldwide. The prevalence of *T. foetus* can be quite high (>30%) especially in young purebred cats that are maintained in high-density housing environments (e.g. shelters, catteries). However, older, mixed breed cats have also been identified with the infection. No breed of cat is known to be resistant to infection. The pathophysiology of feline trichomonosis is largely unknown. The route of infection is presumed to be fecal-oral (e.g. sharing of litter boxes and mutual grooming). Following transmission, the pathogen can be cleared by the cat or can establish infection in the cat's intestine. Infected cats can be carriers of the infection and show no clinical signs or can develop chronic diarrhea.

HISTORY AND CLINICAL PRESENTATION

The most characteristic clinical sign of feline trichomonosis is chronic waxing and waning diarrhea that is frequently malodorous with the consistency of cow patty feces. Occasionally, frank blood and/or mucus may be observed in the diarrheic feces. Young, severely affected cats may also have signs of rectal inflammation, fecal incontinence, and/or rectal prolapse. *T. foetus*-induced diarrhea may resolve with antibiotic administration but returns following discontinuation of antimicrobial therapy. This phenomenon suggests that *T. foetus* may have a symbiotic relationship with resident bacteria and triggered our Winn-funded exploration of probiotics as an adjunctive treatment for feline trichomonosis (see below in novel therapies). Untreated cats may

develop new onset signs (or demonstrate relapse) following stressful events (diet change, new cat introduced into household, etc). Infected cats generally present in good body condition unless they are immunocompromised (young, FELV/FIV, FIP, etc) or have a comorbidity.

TREATING FELINE TF INFECTION CAN BE FRUSTRATING

Infected cats can often be treated with ronidazole (30mg/kg PO q24hr for 14 days). Drug compounding issues and expense are common concerns with the use of ronidazole.

Additionally, neurologic toxicity can be a side effect of treatment although most reported cases of ronidazole toxicity occurred when cats were given higher than recommended daily doses of drug. Nevertheless, cats should be carefully monitored during treatment for signs of neurotoxicity. More concerning is that ronidazole-resistant strains of *T. foetus* infection are increasingly recognized. The lack of safe AND effective therapies for *T. foetus* infection dictates the need to understand more about how feline *T. foetus* causes disease and to identify novel targets to decrease clinical signs of disease (see more in novel targets).

If diarrhea continues well-beyond ronidazole treatment, cats should be retested for *T. foetus* infection. A positive result may be attributed to resistant infection, poor owner compliance, re-infection, and/or improper drug compounding or ineffective dose. Untreated cats may experience resolution of clinical signs however they often remain infected and can spread the organism to previously uninfected cats. Therefore, if concern for transmission to uninfected cats exists, the author recommends that infected cats be treated or be isolated from uninfected cats until shedding ceases (based on multiple negative PCR results).

NOVEL THERAPIES IN DEVELOPMENT FOR FELINE TF INFECTION

Through support of the Winn Feline Foundation, our lab has been dedicated to understanding how feline *T. foetus* causes disease and identifying novel targets to prevent infection or reduce clinical signs of disease. In this seminar, we will discuss two of the three targets that Winn has

helped us to identify. These targets include anti-cysteine protease 30 drugs, probiotics, and drugs that specifically target a binding site on feline *T. foetus*. The latter treatment will not be discussed in the interest of time. Using a laboratory (in vitro) model of infection, we have demonstrated that all of these targets help to decrease adhesion of feline *T. foetus* to the intestinal lining and result in reduced damage of the intestinal lining. Specifically in regards to the use of probiotics, timing and species of bacteria used appear to be critical to the success of these therapies in decreasing *T. foetus* infection. Our work also demonstrates that a multi-modal approach to *T. foetus* will likely be needed to completely eliminate the parasite and signs of disease. We are hopeful that these targets will serve as building blocks towards the development of novel therapies for feline trichomonosis.

Winn-funded Related References:

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3. Gould E, Corbeil L, Kania S, Tolbert MK. Evaluation of surface antigen TF1.17 in feline *Tritrichomonas foetus* isolates. *Vet Parasit.* 2017;244:144-153.
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6. Gould E, Brand M, Tolbert K. "Qualitative and quantitative identification of feline *Tritrichomonas foetus* surface antigens: Putative targets for diagnosis and treatment." *J Vet Intern Med* 2015;29(4). 33rd Annual Forum of the ACVIM. Indianapolis, Indiana.