Raw Feeding for IBD Cats

Healing Can Happen!

Flagyl (Metronadizole) is Gentoxic, Potentially Carcinogenic, and Neurotoxic

This is not intended to scare people. But it is important information that needs to be carefully considered. Flagyl (generic: Metronadizole) is potentially carcinogenic both to humans and cats. It is to mice. From a 2009 study in cats:

> Metronidazole kills target organisms by inducing formation of reactive intermediates within these organisms, resulting in disruption of DNA. This disruptive effect is not restricted to microorganisms, and both carcinogenic and mutagenic effects have been documented in experimental animals and metronidazole disrupts DNA in human blood lymphocytes. The importance of these disruptions is unclear in humans - damage was not evident within 6 days of discontinuation of the drug. No information about genotoxicity in cats is available.

The study, *Single-dose pharmacokinetics and genotoxicity of metronidazole in cats* (Sekis et al. 2009. Journal of Feline Medicine and Surgery (2009) 11, 60-68) found (Abstract only, here).

> Genotoxicity, as measured by DNA disruption in PBMC obtained from cats administered metronidazole for 7 days and a feline lymphocyte cell line incubated with metronidazole, was observed in all cats and all lymphocyte experiments. This is similar to observations in people treated with metronidazole. The DNA damage resolved within 6 days of discontinuing metronidazole, also similar to findings in humans, suggesting that DNA repair mechanisms correct the disruption induced by metronidazole. **However, experimental studies in rodents have demonstrated both carcinogenic and mutagenic effects of metronidazole. Lymphoma is the most common hematological neoplasia in cats and cats have a propensity to develop intestinal T-cell lymphoma. It is interesting to speculate that chronic metronidazole therapy may damage lymphoid DNA, which, if unable to be effectively repaired by a defective repair system, could result in development of lymphoma. This may be particularly relevant to cats receiving chronic metronidazole to treat inflammatory bowel disease. Currently, no evidence exists that chronic metronidazole therapy results in lymphoma formation in cats, and additional associative studies are needed to show a correlation between chronic metronidazole exposure and subsequent development of lymphoma.**

Bold, my emphasis.

Importantly, when used for 7 days, the DNA damage resolved in 6 days. So if *needed* for short term use, it is likely fine. But so many vets throw metro at just about any diarrhea, and many IBD kitties are put on it for long lengths of time. It is something that should be discussed with the vet in terms of risks vs. rewards, and hopefully members of the Raw for IBD Cats group are becoming familiar with alternatives.

Also of note is a 2002 study, *Is metronadizole carcinogenic?* Bendesky et al., Mutation Research 511 (2002) 133–144 http://www.ncbi.nlm.nih.gov/pubmed/12052431

Neurotoxicity

Metronidazole Toxicity: Prevention and Treatment:
http://www.vetneuro.com/Resources/Reference/NeuroNews/eNewsletterApril2010/tabid/9024/Default.aspx

OF NOTE:

> Metronidazole has long been used in veterinary medicine as an antibiotic to treat many infectious diseases in dogs and cats. Neurotoxicity can occur from acute overdoses or even from "recommended" doses in animals on chronic therapy. Cats and small dogs may be more susceptible to acute overdoses. Common strengths for metronidazole are 500 mg and 250 mg tablets. **Even a quarter of a 250 mg tablet given twice daily to a 10 pound dog has the potential to cause neurological signs.**

Bold my emphasis. This article also has links to video clips of dogs with metro toxicosis.

Putative Metronidazole Neurotoxicosis in a Cat - Veterinary Pathology September 2005 vol. 42 no. 5 665-669

> Metronidazole (Flagyl, G. D. Searle & Co., Chicago, IL) is a nitroimidazole antibiotic that is commonly used in veterinary medicine to treat a wide variety of conditions, including anaerobic bacterial infections, protozoal infections (e.g., giardiasis), Helicobacter-associated gastritis, and hepatoencephalopathy. In addition to its anti-protozoal and bactericidal properties, metronidazole is thought to have some immunomodulatory effects and is commonly used to treat inflammatory bowel disease (IBD) in both dogs and cats. The drug is lipophilic and has a wide tissue distribution with oral bioavailability ranges from 50 to 100%. Metronidazole is

primarily metabolized in the liver and has been shown to rapidly cross the blood-brain barrier. Another study using 14C-labeled metronidazole detected accumulation of the unchanged drug in the cerebellum and hippocampal areas of mice after intravenous (IV) administration. **Central nervous system (CNS) side effects associated with metronidazole toxicosis have been reported in humans and in veterinary species, including rats, dogs, and cats. Peripheral neuropathies are frequently reported in human cases of metronidazole toxicosis; however, nausea, dizziness, tremors, ataxia, and seizures have also been reported. In dogs and cats, central vestibular and cerebellar dysfunctions resulting in ataxia, nystagmus, head tilt, tremors, and seizures are commonly reported in cases of metronidazole toxicosis.** To our knowledge, this is the first report to document histologic lesions in the CNS associated with metronidazole administration in a cat.

Bold, my emphasis

Also see:

Diazepam as a Treatment for Metronidazole Toxicosis in Dogs: A Retrospective Study of 21 Cases – Evans et al Journal of Veterinary Internal Medicine Volume 17, Issue 3, pages 304–310, May 2003.

Metronidazole: beware of neurotoxic side effects
http://www.vetcontact.com/en/art.php?a=572

Metronidazole: Uses, toxicity and management of neurologic sequellae
http://veterinarynews.dvm360.com/dvm/article/articleDetail.jsp?id=113198