



### Rusty – UTI

In August 2015 I noticed that Rusty (10 years old, not spayed) wasn't as interested in eating meals and I knew that one of the three dogs was occasionally throwing up undigested meals (kibble; FROMM which they have been on for several years and tolerated well). The home environment was somewhat unsettled (Bill started chemo and radiation in June after major neck resection in April to remove recurrent squamous cell cancer) and I thought that may have upset her.

When she continued to eat poorly and seemed grouchier than usual, I went directly to our second vet (out of town) who we use for surgical procedures or are referred to by the local vet for consultation. A sterile urine sample was obtained by ultrasound guided bladder tap. It showed many white blood cells, red cells, and many bacteria. The culture identified *Staph epidermidis*; clavamox was prescribed for 10 days as *Staph epid* was sensitive to most antibiotics. Her appetite improved quickly.

Among other lab work done at the time, her T4 was low. Having expended considerable resources on the initial workup and after discussion with the vet, we decided to give 6 weeks of thyroid replacement based only on the T4 and understanding that it may have been depressed because of the UTI. Soloxine was not available so a generic thyroid supplement was prescribed. Rusty's disposition continued to improve (less grouchy). Another urine sample and a follow-up thyroid evaluation were planned. However, given Bill's survival of multiple procedures for a dire diagnosis, we opted to take a week's vacation in celebration.

The Sunday of Thanksgiving weekend, Rusty developed fever (106) and chills. Off we went to the closest reliable vet emergency clinic (an hour away) in the late afternoon. After extensive evaluation including an ultrasound guided bladder tap, we knew she had at least another UTI; ampicillin was given IV and Rusty stayed overnight. There was no clinical or ultrasound evidence for pyometra, nor any organ enlargement. The next am her temperature was normal. I picked her and the sterile chilled urine sample up and went to the vet we had been to in August – the urine culture and sensitivity this time was a moderately resistant *Klebsiella pneumoniae*. She had been started on Clavamox and that was changed to Cipro when the sensitivity results were back. A follow-up sterile urinalysis that was done 3 weeks after completion of antibiotics was normal.

The UTI recurred in early March 2016 with a less resistant *Klebsiella*. Her only symptom was less appetite for breakfast. After 10 days of Cipro there were still 15-20 WBC in a first morning clean catch urine so Cipro was resumed for 10 more days. Rusty is generally a happy girl, really happy when she is able to work ducks or see cattle. Her weight has remained 39-42 lbs; coat density and quality is unchanged; vets don't find anything abnormal on exam other than mild teeth tartar, an umbilical hernia always present, lack of muscle mass in L rear leg (has had a hip pop that side on exam) which I thought she injured years ago when running in the yard. Like the other dogs, she is on monthly Nexgard and Heartgard.



The questions are why the recurring UTI? Is she getting an ascending infection from a mild vaginitis (she has an occasional nonodorous vaginal discharge after very light seasons about every 10 mos)? Is there an underlying disease? Dr. Aronson sheds some light for on the topic of recurrent UTI's below. Elsa Sell

### **The Recurrent Urinary Tract Infection**

A urinary tract infection (UTI) occurs when a bacterium overcomes the body's natural defenses and manages to set up shop, multiply, and persist. Infection usually affects the bladder and there is no accompanying illness or compromise of the immune system. UTIs may also accompany infections of the kidney or prostate, and are more common in dogs with compromised immune systems (diabetes, Cushing's disease or dogs on corticosteroid therapy, etc), cancer (as well as those receiving chemotherapy) or bladder stones. Dogs that are catheterized, and bitches with immature or inverted vulvas also have a higher risk, as do bitches in general as the urethra is shorter and closer to the coat fur and outside world. (Any UTI in a male dog is usually considered complicated.)

Uncomplicated urinary tract infection is estimated to occur in 14% of all dogs during their lifetime, although that number seems low in my experience. Most UTIs occur as single episodes, however recurrent UTI (defined as 3 or more infections within 12 months, 2 or more within 6 months) is not uncommon. Often recurrent UTI involves one or more bacterial organisms that are resistant to commonly used antibiotics, but in Rusty's case her first UTI was a different organism entirely suggesting they were separate events and at

a higher risk for infection. This could have been the result of either stress and/or hypothyroid function both of which can impair the function of the immune system.

Spayed bitches are also at increased risk for recurrent UTIs. These can develop at any age. Typical presenting complaints include pollakiuria (frequent, small urinations), stranguria (slow, painful urination often with spasming), dysuria (painful urination), hematuria (blood in the urine), urine dribbling, and inappropriate urination indoors. The urine often smells bad - and some male dogs may mistake it for a bitch in season. (If a dog shows signs of systemic illness - lethargy, vomiting, anorexia as well as increased thirst and urination you are more likely to have a dog with kidney or prostate infection rather than just a bladder one.) However, some dogs may be asymptomatic. A healthy immune system, normal urogenital anatomy, being given the opportunity to urinate at appropriate intervals, normal urine composition, being well hydrated and having appropriate bladder mucosal barriers all help the dog avoid UTIs. Often an abnormality in one or more of these defenses can be found in patients with recurrent UTIs, and obviously needs to be addressed; however, in about a third of cases no underlying cause is identified.

E.coli is the bacterium most commonly associated with UTIs (it is isolated in almost half of all infections). It is a normal part of the flora of the gut and outer end of the urethra - the close proximity of the anus to the vaginal opening of the urethra, and the tendency of the hair coat to retain fecal matter increase the likelihood of fecal bacteria entering the urinary tract. Other bacteria associated with UTI include *Staphylococcus*, *Streptococcus*, *Enterococcus*, *Proteus*, and *Klebsiella* species.

Pathogenic bacteria have a variety of adhesive and binding molecules that help them attach to the urethral wall and make their way to the bladder despite opposing forces such as the flow of urine – which quite amazingly E.coli appears to sense and cause it to cling even tighter to the urethral wall. Cells of the immune system engulf and destroy most of the bacteria. Virulence factors however enable pathogenic E.coli to enter cells in the bladder wall where they combine to form little biofilm-like clusters surrounded by a sticky mess of proteins and sugars. This grows using the host's nutrients and takes over the cell causing it to swell until its wall starts to leak out bacterial filaments that invade other cells and start to colonize the bladder wall, releasing toxins as they go. The bacteria also suppress cytokine production effectively shutting off the immune system. Because the superficial cells of the bladder wall are constantly sloughing off, the bacteria start to burrow deeper into the walls of the bladder. In the basal epithelium they surround themselves in a network of actin filaments protected from antibiotics, and can remain dormant for several months before something triggers a recurrent infection.

Each bout of infection leaves the bladder lining inflamed and more open to infection from not only the initial bacteria but any other pathogenic bacteria that have reached the bladder. On top of that, many bacteria have developed genetic resistance to antibiotics rendering them invisible to the drugs.

Optimally whenever a UTI is suspected urine should be collected from the bladder by cystocentesis and any bacteria found should be cultured and the colonies tested for susceptibility to a variety of bacteria. In practice, when a dog presents with a simple UTI a presumptive diagnosis is made, the dog is prescribed antibiotics that are generally effective against bacteria causing UTIs and money and time saved. If urine is collected by free catch it is contaminated with bacteria in the lower urethra, vagina and fur and must be evaluated to determine the likelihood that there are enough bacteria present to account for infection.

Unless prostatitis, kidney infection or other diseases are suspected as causing a complicated UTI blood work is not necessary. Radiographs may be performed if bladder stones are suspected, as well as an ultrasound to look for contributing pathology. Normally, these are not necessary in cases of recurrent UTIs. Obviously any contributory condition(s) would need to be addressed, but antibiotics are necessary to treat UTIs.

In the case of a simple UTI suitable antibiotics are usually prescribed for 10-14 days, and it is important that the complete course of antibiotics is given even if the symptoms of the UTI have resolved. Not doing so will set the dog up for recurrent infection. As most UTIs are caused by E.coli and most E. coli are susceptible to amoxicillin, Clavamox or cephalexin, those will usually be scripted. (Some vets will prescribe Baytril (enrofloxacin) but we have been advised to reserve this and other drugs in the class fluoroquinolones for resistant strains.)

Antibiotics for recurrent or complicated UTIs must be based on culture and susceptibility testing (although an antibiotic may be prescribed while waiting for these results.) The course of antibiotics will usually last for 4-6 weeks. In conjunction with appropriate antibiotics there are other supportive treatments that may help resolve recurrent infections. Proanthocyanidins (found in cranberries) can prevent E. coli adhering to the bladder lining and displace those that have already adhered. D-mannose is the active sugar in cranberry extract that competes with and unglues E.coli. The Chinese herb coleus forskohlii may help remove E.coli from bladder cells and is especially useful in cases where antibiotics can't reach the bacteria.

I'm not a fan of the urinary antiseptic methanamine which is given with a urinary acidifier like Vitamin C. If the urinary pH is below 5.5 methanamine is converted to formaldehyde - which kills bacteria but is carcinogenic, and ammonia which prevents bacterial colonization. It also seems to increase the risk of bladder stone formation. Lactic acid-producing bacteria (e.g., Enterococcus canintestini, Lactobacillus spp) are found in the urogenital tract of healthy female dogs. They have been shown to inhibit growth of common pathogens by making an acidic environment within the urogenital tract and competing for nutrients. Daily oral administration of Lactobacillus and/or Enterococcus spp containing probiotics might also help prevent UTIs.

Patients with recurrent or complicated UTIs should be carefully monitored. The urine culture should be repeated 3 to 5 days after starting antibiotics. If there is no growth then the antibiotic is effective and should be continued, if there is growth however, the patient must be switched to another antibiotic. (Antibiotics may be effective on culture plates but not in the animal.) Cultures should be repeated and no growth seen prior to discontinuing the antibiotic and also 5 to 7 days after the antibiotic has been stopped.

If a UTI recurs with the same organism it may be that the antibiotic chosen slowed the infection (bacteriostatic) rather than killing the bacteria (bacteriocidal). It may also be that there is a cause for the infection that was missed – neoplasia, bladder stones etc. If a UTI occurs with a different organism there should be further investigation for a cause of immunosuppression. Preventive low-dose antimicrobial treatment may be indicated for recurrent E coli UTI with an identifiable underlying cause. Low-dose treatment should be initiated only after the most recent infection is properly controlled (following 4–6 weeks of antimicrobial treatment at the therapeutic dose and a negative urine culture).

To investigate possible risk factors for development of recurrent UTI a complete physical examination, complete blood count, serum chemistry profile, urinalysis, quantitative urine culture, and urinary tract imaging are necessary. Imaging might include abdominal radiography and/or ultrasonography, contrast studies, and cystoscopy depending upon preliminary findings. In some patients, biopsy specimens of the bladder wall for histopathologic evaluation and culture would also be taken. In order to successfully address recurrent UTIs not only must there be a complete resolution of any current infection with appropriate antimicrobial therapy, but any underlying factors that may increase the patient's risk for recurrence must be identified and treated. However, as noted above, no such risk factors will be identified in a third of the cases of recurrent UTI.

UTIs are painful and left untreated or undertreated infection can spread through the pelvis. They are also common and something we need to be aware of. If your dog has recurrent UTIs don't just accept the

antibiotics, insist that they are worked up properly, treated appropriately and adequately and any underlying causes addressed.

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