



## Efficacy of amoxicillin and azithromycin for the empirical treatment of shelter cats with suspected bacterial upper respiratory infections

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Thirty-one cats showing clinical signs of upper respiratory tract disease with a presumed bacterial component based on clinical signs were administered either amoxicillin or azithromycin to determine which drug protocol was optimal for empirical use. A clinical score was determined and nasal and pharyngeal swabs were collected for bacterial culture, virus isolation and polymerase chain reaction prior to the start of therapy. Cats failing to respond to the initial antibiotic were then administered the other drug. There were no differences in clinical scores between the two groups at the start of therapy. Eleven of 31 cats improved after administration of the first antibiotic, 16 cats were switched to the alternate antibiotic, and four cats were removed from the study for additional supportive treatments. Eight of 27 cats failed to respond to either antibiotic. The  $\chi^2$  test for outcomes revealed no differences in response to therapy for either antimicrobial.

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Upper respiratory tract disease (URTD) characterized by sneezing with or without nasal discharge is extremely common in both traditional shelters (Foley and Bannasch 2004) and no-kill shelters (Pedersen et al 2004). There is on-going debate in animal shelters about the most efficacious and cost effective methods for treating feline URTD. Limited resources rarely allow for determining the definitive causative agent(s); however, the most common organisms detected in recent studies of cats in shelter or cattery environments included feline herpesvirus-1 (FHV-1), feline calicivirus (FCV), *Pasteurella* species, *Chlamydophila felis*, *Mycoplasma* species, *Bordetella bronchiseptica*, and coagulase-negative *Staphylococcus* species (Cape 1992, Stein and Lappin 2001, Johnson et al 2005, Helps et al 2005, Bannasch and Foley 2005, Schultz et al 2006, Veir et al in press). While the majority of bacterial infections are thought to be secondary to other primary diseases, most veterinarians believe antimicrobial therapy is

indicated for cats exhibiting mucopurulent discharge.

$\beta$ -lactams, potentiated  $\beta$ -lactams, fluoroquinolones and tetracyclines are often selected as antimicrobial treatment for cats with suspected bacterial URTD. Results of antimicrobial susceptibility testing were recently reported for bacteria grown from the nasal discharges or airways of cats housed in Germany or north-central Colorado (Stein and Lappin 2001, Schultz et al 2006). All of the drug classes previously mentioned killed > 67% of the isolates in vitro. However, the efficacy of these drugs in treating URTD is variable in the field, likely in part because it is difficult to differentiate cats with primary viral cause of disease with secondary bacterial overgrowth from those with primary bacterial pathogens like *B bronchiseptica*, *Mycoplasma* species, or *C felis*.

Amoxicillin is commonly used for the treatment of cats with suspected bacterial URTD because it is inexpensive and has a good spectrum against bacterial flora like *Pasteurella* species that may overgrow secondary to primary

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viral infections. In addition, amoxicillin is effective for the treatment of many anaerobic bacterial species; this group of organisms has been suggested to be associated with disease in chronic rhinitis (Johnson et al 2005). However, many *B bronchiseptica* isolates have been resistant to amoxicillin (Hoskins et al 1998) and because the drug is cell-wall inhibitor, amoxicillin should not be effective for the treatment of *Mycoplasma* species. Amoxicillin-clavulanate has effect against *C felis* infections (Sturgess et al 2001) but it is unknown whether amoxicillin is also effective against this organism. Lastly, there is also Gram-negative flora in the respiratory passageways that may overgrow secondary to other primary diseases like FHV-1 and FCV that may also be resistant to amoxicillin (Stein and Lappin 2001).

Azithromycin is a macrolide antibiotic with a broad spectrum against bacteria associated with respiratory tract disease in people (Jordan 2001). In cats, it has bacteriostatic effects against many Gram-positive organisms, Gram-negative organisms, and *Mycoplasma* species. In one feline study, azithromycin was equivalent to doxycycline for eliminating clinical signs of *C felis* infection (Owen et al 2003). Because azithromycin has a long tissue half-life in cats, infrequent dosing is adequate to maintain plasma levels which has led to frequent use of the drug in feline practice (Hunter et al 1995, Jordan 2001). This could be of potential benefit in shelter situations where multiple cats may need to be treated at one time and it may be difficult to administer drugs because of the demeanor of the cat. Most of the other drugs used to treat respiratory tract disease in cats need to be administered at least daily. However, there is currently no published information on the efficacy of azithromycin for the empirical treatment of suspected bacterial causes of URTD in cats. Further information is needed to help shelter veterinarians determine the optimal empirical antibiotic choice for cats with URTD with a suspected bacterial component. The purpose of this study was to assess the comparative efficacy of amoxicillin and azithromycin in cats with clinical URTD from a humane society in north-central Colorado.

## Materials and methods

### Experimental design

This study was conducted in combination with another larger study that was designed to

determine the prevalence rates of infectious causes of URTD cats, to determine optimal sample collection sites (nasal or oropharyngeal), and to compare microbiological culture and nucleic acid amplification techniques for select infectious agents (Veir et al in press). The studies were completed in a private humane society with an animal control contract that serves a combined rural and urban area in north-central Colorado. The shelter has an open admission policy and the full-time veterinary staff attempts to manage animals entering with treatable diseases or conditions. However, euthanasia is performed if the animals are non-rehabilitable or non-treatable. Cats admitted to the shelter usually receive a parenteral, modified live feline viral rhinotracheitis-calici-panleukopenia vaccine and one dose of pyrantel pamoate (5 mg/kg PO). Cats entered into this part of the study were sampled between 24 January and 4 December 2003 and had been in the shelter for variable lengths of time. Thirty-one cats with clinical signs of URTD with a suspected bacterial component (oculonasal purulent discharge, sneezing, and stertorous breathing) and no obvious facial deformity were identified by the shelter veterinarian (MS). Cats identified for the study had a temperament consistent with single handler management. Within 24 h of admission, each cat was clinically scored (Table 1) and three swabs from both the nasal cavity and oropharynx were collected by a single investigator (RR) prior to treatment. Nasal swabs were obtained by gently rolling a sterile transurethral culture swab (Ca alginate swabs, Ultrafine Al, product #14-959-78, Fischer Scientific) in the anterior aspect of the right nares after removing any excess mucous. Oropharyngeal swabs were obtained using a sterile cotton tipped applicator gently rotated in the oropharynx of each cat. One swab from each sampling site was placed into a commercial transport medium (BBL CultureSwab Plus Amies Medium with Charcoal, Becton, Dickinson and Company; Sparks, MD) and submitted for culture of *Mycoplasma* species and aerobic bacteria species within 4 h. A second swab was placed in viral transport medium (viral transport media: modified Eagle's medium with 1% HEPES, 4% bovine growth serum, 0.0025% amphotericin B + antibiotics) and submitted for virus isolation within 4 h. The final swab was placed in 1 ml sterile phosphate buffered saline (PBS) solution, allowed to equilibrate for 2–3 h at room temperature according to the DNA/RNA extraction kit (Qiagen, Valencia,

**Table 1.** Clinical scoring sheet used to evaluate URTD in shelter cats

| Study cat # _____                       | Entry date _____                        |       |                         |       |                         |        |                         |
|---|---|-------|-------------------------|-------|-------------------------|--------|-------------------------|
| 1 <sup>st</sup> Antibiotic (code) _____ | 2 <sup>nd</sup> Antibiotic (code) _____ |       |                         |       |                         |        |                         |
| Outcome: Resolved _____                 | Outcome: Resolved _____                 |       | Outcome: Resolved _____ |       | Outcome: Resolved _____ |        | Outcome: Resolved _____ |
| Antibiotic 2 _____                      | Antibiotic 2 _____                      |       | Antibiotic 2 _____      |       | Antibiotic 2 _____      |        | Antibiotic 2 _____      |
| Removed _____                           | Removed _____                           |       | Removed _____           |       | Removed _____           |        | Removed _____           |
| Clinical scores                         |   |       |                         |       |                         |        |                         |
|   | Day 0                                   | Day 3 | Day 6                   | Day 9 | Day 12                  | Day 15 | Day 18                  |
| <i>Rectal temperature (°F)</i>          |   |       |                         |       |                         |        |                         |
| 102.5–103.5                             | 1                                       | 1     | 1                       | 1     | 1                       | 1      | 1                       |
| 103.6–104.5                             | 2                                       | 2     | 2                       | 2     | 2                       | 2      | 2                       |
| >104.5                                  | 3                                       | 3     | 3                       | 3     | 3                       | 3      | 3                       |
| <i>Conjunctivitis</i>                   |   |       |                         |       |                         |        |                         |
| Serous                                  | 1                                       | 1     | 1                       | 1     | 1                       | 1      | 1                       |
| Mucopurulent                            | 2                                       | 2     | 2                       | 2     | 2                       | 2      | 2                       |
| Bloody                                  | 3                                       | 3     | 3                       | 3     | 3                       | 3      | 3                       |
| <i>Keratitis (visible)</i>              | 4                                       | 4     | 4                       | 4     | 4                       | 4      | 4                       |
| <i>Sneezing and nasal discharge</i>     |   |       |                         |       |                         |        |                         |
| Sneezing                                | 1                                       | 1     | 1                       | 1     | 1                       | 1      | 1                       |
| Mucopurulent                            | 2                                       | 2     | 2                       | 2     | 2                       | 2      | 2                       |
| Mucopurulent with blood                 | 3                                       | 3     | 3                       | 3     | 3                       | 3      | 3                       |
| <i>Lower respiratory signs</i>          |   |       |                         |       |                         |        |                         |
| Coughing                                | 1                                       | 1     | 1                       | 1     | 1                       | 1      | 1                       |
| Crackles on auscultation                | 2                                       | 2     | 2                       | 2     | 2                       | 2      | 2                       |
| Dyspnea                                 | 3                                       | 3     | 3                       | 3     | 3                       | 3      | 3                       |
| <i>Systemic signs</i>                   |   |       |                         |       |                         |        |                         |
| Anorexia                                | 1                                       | 1     | 1                       | 1     | 1                       | 1      | 1                       |
| Dehydration                             | 1                                       | 1     | 1                       | 1     | 1                       | 1      | 1                       |
| Depression                              | 1                                       | 1     | 1                       | 1     | 1                       | 1      | 1                       |
| <i>Oral cavity</i>                      |   |       |                         |       |                         |        |                         |
| Salivating                              | 1                                       | 1     | 1                       | 1     | 1                       | 1      | 1                       |
| 1 ulcer, <4 mm                          | 1                                       | 1     | 1                       | 1     | 1                       | 1      | 1                       |
| >1 ulcer, <4 mm                         | 2                                       | 2     | 2                       | 2     | 2                       | 2      | 2                       |
| >1 ulcer, >4 mm                         | 3                                       | 3     | 3                       | 3     | 3                       | 3      | 3                       |
| Bleeding ulcers                         | 4                                       | 4     | 4                       | 4     | 4                       | 4      | 4                       |
| <i>Death</i>                            | 5                                       | 5     | 5                       | 5     | 5                       | 5      | 5                       |
| <i>Total score</i>                      |   |       |                         |       |                         |        |                         |

CA) manufacturer's instructions and then stored at  $-70^{\circ}\text{C}$  until assayed for the presence of FHV-1 DNA, *Chlamydomphila* species DNA, *Mycoplasma* species DNA, and calicivirus RNA. Culture, virus isolation, and nucleic acid amplification methods are described elsewhere (Veir et al in press). Antimicrobial susceptibility testing was performed using the Kirby-Bauer method.

After samples were obtained, cats were randomly grouped into those administered amoxicillin (22 mg/kg PO q12 h) or azithromycin (15 mg/kg PO q 72 h) (Zithromax, Pfizer Labs, New York, NY) by the shelter veterinarian. The

amoxicillin protocol was that currently used by the shelter and the azithromycin protocol was selected based on extrapolation from previous literature (Hunter et al 1995, Westfall et al 2001, Owen et al 2003). Cats were given a clinical score prior to treatment and then every 3 days by an investigator blinded to the treatment group (RR). Trained shelter personnel administered the medications. Amoxicillin tablets were prescribed for each cat and new dosing syringes were used for each azithromycin liquid dose. Following the primary treatment period of days 0–9; those cats with persistent clinical signs

were administered the other antibiotic for an additional 9 days. The shelter veterinarian retained the right to remove cats from the study for any reason. Cats enrolled in the study remained housed individually in the isolation ward of the humane society. The study was completed with the approval of the Humane Society Board of Directors and a campus-wide Animal Care and Use Committee at Colorado State University.

### Statistical analyses

Data was entered into Microsoft Excel. Difference between clinical scores for each group prior to treatment and at cross-over was determined by Student's *t*-test. Difference between clinical outcomes of antimicrobial therapy was determined by the  $\chi^2$  test for outcome between groups. Significance was defined at  $P < 0.05$ .

### Results

Of 31 cats entered into the study, 30 had descriptive data (age, sex, reproductive status and breed) recorded. Six were intact male, five intact female, 15 altered male and four altered female. Ages ranged from 3.5 months to 6 years (mean 2.5 years, median 2 years). Twenty-three cats were classified as domestic shorthairs, three as domestic longhairs and four as purebred (three Siamese, one Manx). Over half the cats had positive virus isolation from either the nasal or oropharyngeal swab (67.7% or 51.6%, respectively). Each of the cats that were positive on virus isolation was also positive for FHV-1 DNA by polymerase chain reaction (PCR) assay but negative for calicivirus RNA by real-time PCR assay and so we assume that these cats were infected with FHV-1 only (Veir et al in press). All cats were PCR negative for *Chlamydomphila felis*. Eighteen bacterial species were cultured; *Mycoplasma*, *Pasteurella* and *Moraxella* species were the most common isolates (Table 2). *Pasteurella*, *Moraxella*, *Streptococcus*, *Staphylococcus*, *Simonsiella* and *Flavobacterium* species isolates were determined to be sensitive to ampicillin except for *Staphylococcus aureus* (resistant) and *Streptococcus* B (intermediate). *Pasteurella* and *Moraxella* species had intermediate sensitivities to erythromycin, the only macrolide antimicrobial tested.

Twenty-one cats were initially administered amoxicillin and 10 were administered azithromycin. Pre-treatment clinical scores (Table 3) ranged from 1 to 11 (mean 5.7, median 5) and did not differ between antibiotic groups (Student's *t*-test;  $P = 0.33$ ). There were no differences in age (Student's *t*-test;  $P = 0.08$ ) or sex ( $\chi^2$  test;  $P = 0.21$ )

**Table 2.** Aerobic organisms isolated from nasal or pharyngeal swabs of cats with URTD with suspected bacterial involvement

| Bacterial isolate                                  | Nasal (%) | Pharyngeal (%) |
|--|-----------|----------------|
| <i>Mycoplasma</i> species                          | 58.1      | 61.3           |
| <i>Pasteurella multocida</i>                       | 35.5      | 67.7           |
| <i>Moraxella</i> species                           | 12.9      | 29.0           |
| <i>Staphylococcus</i> species (coagulase-negative) | 12.9      | 16.1           |
| <i>Streptococcus</i> species (non-hemolytic)       | 9.7       | 16.1           |
| <i>Simonsiella</i> species                         | 0.0       | 9.7            |
| <i>Flavobacterium</i> species                      | 0.0       | 22.6           |
| <i>Pasteurella dogmatis</i>                        | 0.0       | 9.7            |
| <i>Staphylococcus aureus</i>                       | 0.0       | 3.2            |
| <i>Staphylococcus intermedius</i>                  | 3.2       | 0.0            |
| <i>Enterobacter</i> species                        | 0.0       | 3.2            |
| <i>Clostridium</i> species                         | 3.2       | 0.0            |
| <i>Escherichia coli</i>                            | 0.0       | 3.2            |
| <i>Streptococcus</i> (group B)                     | 22.6      | 19.4           |
| <i>Corynebacterium</i> species                     | 3.2       | 3.2            |
| <i>Haemophilus</i> species                         | 0.0       | 3.2            |
| <i>Bacillus</i> species                            | 3.2       | 0.0            |
| <i>Bordetella bronchiseptica</i>                   | 3.2       | 0.0            |

Within 24 h of admission, samples were collected from admissions to a combined rural and urban humane society shelter with clinical signs of URTD. Routine aerobic culture was performed on samples within 4 h of collection.

between the two groups. Of the 21 cats initially administered amoxicillin, eight had resolution of clinical signs, 10 were switched to azithromycin, and three were removed from the study. Of the 10 cats initially administered azithromycin, three had resolution of clinical signs, six were switched to amoxicillin and one was removed from the study. The four cats removed from the study had persistent anorexia or severe dehydration requiring intravenous fluid administration. There were no differences in outcome between groups of cats after the primary antibiotic treatment ( $\chi^2$  test of outcomes between groups;  $P = 0.8$ ). Clinical scores of the 16 cats administered the second antibiotic ranged from 0 to 9 (mean 4.0, median 4) at the time of cross-over and there were no differences in clinical scores between groups (Student's *t*-test;  $P = 0.16$ ). One of these cats had a resolution of clinical signs on day 9 (clinical score = 0), but recrudescence of signs on day 10 (clinical score = 3) and was maintained in the study. Clinical signs resolved in five of the 10 cats switched from amoxicillin to azithromycin and three of the six cats switched from

**Table 3.** Aerobic bacterial culture, antimicrobial susceptibility testing, FHV-1 PCR results and response to antibiotic administration in 31 shelter cats with suspected bacterial upper respiratory infections

| Cat | FHV-1 PCR | Culture   | Amp sensitivity                       | Azithro sensitivity                   | Drug 1  | Response   | Drug 2  | Response |
|-----|-----------|---|---------------------------------------|---------------------------------------|---------|------------|---------|----------|
| 614 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i><br><i>Moraxella</i> species<br><i>Staph</i> (coag neg)<br><i>Strep</i> (non-hemolytic)  | ND                                    | ND                                    | Amox    | Yes        | NA      | NA       |
| 604 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i><br><i>Moraxella</i> species<br><i>Staph intermedius</i><br><i>Enterobacter</i> species  | ND<br>S<br>S<br>S<br>R                | ND<br>I<br>S<br>S<br>R                | Amox    | Yes        | NA      | NA       |
| 514 | Pos       | <i>Staph</i> (coag neg)<br><i>Clostridium</i> species<br><i>E coli</i>  | ND<br>ND<br>ND                        | ND<br>ND<br>ND                        | Amox    | Yes        | NA      | NA       |
| 782 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i><br><i>Strep B</i>   | ND<br>ND<br>ND                        | ND<br>ND<br>ND                        | Amox    | Yes        | NA      | NA       |
| 135 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i><br><i>Flavobacterium</i> species<br><i>Strep B</i>  | ND<br>ND<br>ND<br>ND                  | ND<br>ND<br>ND<br>ND                  | Amox    | Yes        | NA      | NA       |
| 789 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i><br><i>Flavobacterium</i> species<br><i>Strep B</i>  | ND<br>S<br>S<br>S                     | ND<br>I<br>S<br>S                     | Azithro | Yes        | NA      | NA       |
| 799 | Pos       | <i>P dogmatis</i><br><i>Strep B</i>   | S<br>I                                | I<br>S                                | Amox    | Yes        | NA      | NA       |
| 000 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i><br><i>Haemophilus</i> species   | ND<br>S<br>ND                         | ND<br>I<br>ND                         | Azithro | Yes        | NA      | NA       |
| 036 | Pos       | <i>Mycoplasma</i> species<br><i>Flavobacterium</i> species<br><i>P dogmatis</i><br><i>Bacillus</i> species  | ND<br>ND<br>S<br>ND                   | ND<br>ND<br>S<br>ND                   | Amox    | Yes        | NA      | NA       |
| 638 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i><br><i>Moraxella</i> species<br><i>Staph</i> (coag neg)<br><i>Strep B</i><br><i>Corynebacterium</i> species<br><i>B bronchiseptica</i> | ND<br>S<br>ND<br>ND<br>ND<br>ND<br>ND | ND<br>S<br>ND<br>ND<br>ND<br>ND<br>ND | Amox    | Yes        | NA      | NA       |
| 099 | Pos       | NG  |                                       |                                       | Azithro | Yes        | NA      | NA       |
| 165 | Pos       | <i>P multocida</i><br><i>Moraxella</i> species  | S<br>S                                | I<br>I                                | Amox    | No-crossed | Azithro | No       |
| 890 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i>   | ND<br>S                               | ND<br>I                               | Amox    | No-crossed | Azithro | Yes      |

Table 3. (continued)

| Cat | FHV-1 PCR | Culture  | Amp sensitivity         | Azithro sensitivity     | Drug 1  | Response   | Drug 2  | Response |
|-----|-----------|--|-------------------------|-------------------------|---------|------------|---------|----------|
| 747 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i>  | ND<br>S                 | ND<br>I                 | Azithro | No-crossed | Amox    | Yes      |
| 409 | Pos       | <i>P multocida</i><br><i>Moraxella</i> species<br><i>Flavobacterium</i> species  | S<br>ND<br>ND           | I<br>ND<br>ND           | Azithro | No-crossed | Amox    | Yes      |
| 416 | Pos       | <i>P multocida</i><br><i>Moraxella</i> species<br><i>Strep</i> (non-hemolytic)<br><i>Simonsiella</i> species<br><i>P dogmatis</i>              | S<br>S<br>ND<br>S<br>S  | I<br>S<br>ND<br>S<br>I  | Amox    | No-crossed | Azithro | No       |
| 722 | Pos       | <i>Mycoplasma</i> species<br><i>Staph aureus</i>   | ND<br>R                 | ND<br>S                 | Amox    | No-crossed | Azithro | Yes      |
| 504 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i><br><i>Staph</i> (coag neg)<br><i>Strep</i> B   | ND<br>S<br>ND<br>S      | ND<br>I<br>ND<br>S      | Amox    | No-crossed | Azithro | No       |
| 937 | Neg       | <i>Mycoplasma</i> species<br><i>P multocida</i><br><i>Moraxella</i> species  | ND<br>S<br>S            | ND<br>I<br>S            | Amox    | No-crossed | Azithro | Yes      |
| 774 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i><br><i>Staph</i> (coag neg)<br><i>Corynebacterium</i> species                                   | ND<br>S<br>ND<br>ND     | ND<br>I<br>ND<br>ND     | Amox    | No-crossed | Azithro | Yes      |
| 104 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i><br><i>Strep</i> B  | ND<br>S<br>S            | ND<br>I<br>S            | Azithro | No-crossed | Amox    | No       |
| 004 | Neg       | <i>Mycoplasma</i> species<br><i>P multocida</i><br><i>Strep</i> (non-hemolytic)<br><i>Flavobacterium</i> species<br><i>Haemophilus</i> species | ND<br>S<br>ND<br>S<br>S | ND<br>S<br>ND<br>I<br>S | Azithro | No-crossed | Amox    | Yes      |
| 467 | Pos       | <i>P multocida</i><br><i>Strep</i> (non-hemolytic)<br><i>Flavobacterium</i> species  | S<br>ND<br>S            | S<br>ND<br>I            | Amox    | No-crossed | Azithro | No       |
| 041 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i>  | ND<br>S                 | ND<br>I                 | Amox    | No-crossed | Azithro | Yes      |
| 628 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i><br><i>Strep</i> B  | ND<br>S<br>S            | ND<br>S<br>S            | Amox    | No-crossed | Azithro | No       |
| 359 | Pos       | NG   |                         |                         | Azithro | No-crossed | Amox    | No       |
| 058 | Pos       | NG   |                         |                         | Azithro | No-crossed | Amox    | No       |
| 635 | Pos       | <i>Mycoplasma</i> species<br><i>P multocida</i><br><i>Moraxella</i> species<br><i>Staph</i> (coag neg)<br><i>Strep</i> (non-hemolytic)         | ND                      | ND                      | Amox    | No-removed | NA      | NA       |

(continued on next page)

Table 3. (continued)

| Cat | FHV-1 PCR | Culture                       | Amp sensitivity | Azithro sensitivity | Drug 1  | Response   | Drug 2 | Response |
|-----|-----------|-------------------------------|-----------------|---------------------|---------|------------|--------|----------|
| 166 | Pos       | <i>Mycoplasma</i> species     | ND              | ND                  | Amox    | No-removed | NA     | NA       |
|     |           | <i>P. multocida</i>           | S               | I                   |         |            |        |          |
|     |           | <i>Moraxella</i> species      | S               | S                   |         |            |        |          |
|     |           | <i>Simonsiella</i> species    | ND              | ND                  |         |            |        |          |
| 860 | Pos       | <i>Mycoplasma</i> species     | ND              | ND                  | Amox    | No-removed | NA     | NA       |
|     |           | <i>P. multocida</i>           | S               | I                   |         |            |        |          |
|     |           | <i>Moraxella</i> species      | S               | S                   |         |            |        |          |
|     |           | <i>Simonsiella</i> species    | ND              | ND                  |         |            |        |          |
| 071 | Pos       | <i>P. multocida</i>           | ND              | ND                  | Azithro | No-removed | NA     | NA       |
|     |           | <i>Flavobacterium</i> species | ND              | ND                  |         |            |        |          |

Cats were randomly placed on amoxicillin 22 mg/kg PO bid or azithromycin 15 mg/kg PO q 72 h. Cats that failed to respond to treatment were then placed on the other antibiotic. Culture and sensitivity results are pre-treatment results. Pos = positive; Neg = negative; NA = not applicable; amp = ampicillin; amox = amoxicillin; azithro = azithromycin; ND = not determined; S = susceptible; I = intermediate; R = resistant.

azithromycin to amoxicillin. There were no differences in the cross-over outcome between groups ( $\chi^2$  test of outcomes between groups;  $P = 0.71$ ).

Aerobic bacteria or *Mycoplasma* species were grown from 24 of the 31 cats that completed the drug trial (Table 3). All 11 cats that resolved during the first antibiotic treatment period were documented with FHV-1 infection. Based on pre-treatment susceptibility results and assuming azithromycin has anti-*Mycoplasma* species activity and amoxicillin does not, six of the eight amoxicillin-only treated cats and one of the three azithromycin-only treated cats would have been predicted to fail treatment because of the presence of bacteria resistant to the first antibiotic used. Of the 16 cats that required the cross-over, 14 were concurrently infected by FHV-1. After cross-over to the second antibiotic, clinical signs resolved in eight of 16 cats of which only two (cat 409 and cat 722) would have been predicted to resolve based on the bacteria isolated. Of the eight cats still clinically ill after both antibiotic treatment periods, two had no bacteria cultured and the other six would have been predicted to respond to the combination of the drugs. All of these cats had known FHV-1 infections and were transferred to an anti-viral treatment study (Veir et al 2006).

## Discussion

With the exception of FCV and *C. felis*, each of the known or suspected primary pathogens thought to be associated with UR TD in cats were detected

in this study; *Pasteurella* and *Mycoplasma* species were the most commonly isolated bacteria. The results of the study document the difficulty in using bacterial culture and susceptibility from nasal samples or the pharynx to predict antibiotic responses. This likely relates to the fact that these areas are home to a rich normal flora and so not all bacteria that are cultured are causing clinical disease. The results suggest that culture and sensitivity of nasal discharges or pharyngeal swabs is a low yield procedure when assessing cats with acute disease UR TD.

One of the primary limitations of this study is that it is currently impossible to prove bacterial or viral causation of clinical signs. The UR TD syndrome in cats is multi-factorial and most of the organisms isolated here can be detected in both healthy and clinically ill cats. The eight cats in this study that failed both antibiotics were likely to have primary FHV-1 infection or other undiagnosed nasal diseases, including undiagnosed, antimicrobial drug resistant bacteria. The data from these cats also suggest that the presence of mucopurulent discharge does not definitely prove that a bacterial component to the disease process exists. Overall, FHV-1 infection was documented in 17 of 19 cats that ultimately had their clinical signs resolve, eight of eight cats with persistent disease, and four of four cats removed from the study.

In the 31 shelter cats described here, there were no outcome differences detected between groups of cats treated with amoxicillin or azithromycin. Thus, there was no clear advantage to selecting one drug over the other as the initial empirical

therapy. This finding may merely reflect the fact that the cats did not have a bacterial component to their URTD or the number of cats included in the study was too few to detect a difference. Clinical signs of bacterial or FHV-1 associated disease often wane over time. Thus, even the cats in this study with clinical resolution while on antibiotics may have been spontaneously resolving. Twenty-one of 31 cats cultured were positive for *Mycoplasma* species; 75% (6/8) of cats positive for *Mycoplasma* species had clinical resolution of disease when treated with amoxicillin alone. Two of three cats that were administered azithromycin alone were positive for *Pasteurella* and *Mycoplasma* species. One cat did culture positive for *Bordetella bronchiseptica* but clinical signs resolved with amoxicillin alone.

Although azithromycin is readily bio-available in cats and has a long tissue half-life (Hunter et al 1995), dose recommendations vary and are not well defined. Plumb's Veterinary Drug Handbook (5th edition, 2005) lists three dosages for cats including 5–10 mg/kg PO daily for 3–5 days for susceptible infections. Azithromycin was unsuccessful at eliminating *Chlamydomphila felis* at 10–15 mg/kg daily for 3 days, then twice weekly (Owen et al 2003) and *Haemobartonella felis* at 15 mg/kg twice daily for 7 days (Westfall et al 2001). Cats in these studies reportedly tolerated the drug well. An increased dose interval is the primary benefit of using azithromycin in animal shelters and 15 mg/kg every 3 days was selected based on extrapolation from the previous studies. A greater response may have been detected if a daily loading dose had been used.

Carry-over effects can bias cross-over study data. Including a long wash out between cross-over can alleviate this bias. However, the fact that there were no differences between the treatment groups and 8/31 (25.8%) cats were clinically ill at the end of both antimicrobial trials suggests carry-over was not a factor. Cats were not randomly enrolled in the study but selected for convenience. Cats likely to be easily managed by a single person were preferentially selected by the shelter veterinarian. It is unlikely that these cats had different clinical signs or pathogens than other cats entering the shelter as total clinical scores ranged widely as did pathogens identified.

Shelters will continue to look for ways to decrease the morbidity and mortality related to URTD. This study showed in a limited number of cats, azithromycin and amoxicillin have a similar efficacy. Amoxicillin is relatively

inexpensive (US\$2.44 for the 9-day treatment for an average size cat) with rare side effects (none in this study). However, the twice daily protocol selected may be a hardship for shelter personnel, leading to treatment failure and increasing the risk of disease transmission through multiple handlings of sick cats. Azithromycin is comparatively expensive (US\$6.60 for the 9-day treatment for an average size cat) but has the advantage of longer dosing intervals. No adverse reactions were recorded with azithromycin treatment in this study. Given the stress and crowding inherent in most sheltering situations, upper respiratory infections will continue to effect animals in that environment. Veterinarians will need to select antimicrobial treatments based on each shelter's need following the AVMA judicious antimicrobial use guidelines including implementation of biosecurity and sanitation protocols, as well as managed housing and vaccination. While empirical antimicrobial therapy may not always be warranted in a shelter environment, azithromycin may be a valid choice. Further investigation into the efficacy of azithromycin in shelter situations is warranted before recommending the drug for routine use.

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