**Antibiotic duration in uncomplicated cystitis and outpatient pyelonephritis**

****There is growing evidence supporting shorter durations of antibiotic therapy in uncomplicated cystitis and pyelonephritis to minimize, antibiotic resistance, adverse events and infection reoccurrence.

Data from the early 2000’s were incorporated in the 2011 Infectious Disease Society of America (IDSA) guidelines that highlighted >90% cure rates with nitrofurantoin x 5 days, fluoroquinolones x 3 days, and beta-lactams x 3-5 days in females with uncomplicated cystitis. In pyelonephritis, these guidelines also identified fluoroquinolones x 5-7 days being effective compared traditional 14 day antibiotic courses that were associated with greater rates of resistance, *Clostridioides difficile* (*C diff*) infections, and increased risk for serious adverse events.1 Newer data has since confirmed these recommendations in pyelonephritis and provided further insight into appropriate antibiotic durations in unique situations not previously addressed, including women with diabetes and men with uncomplicated cystitis.

Regarding pyelonephritis, two major studies, published since the 2011 guidelines, have identified shorter durations (5-7 days) of fluoroquinolones as non-inferior to longer durations (10-14 days) in non-elderly women. One prospective, multi-site randomized, double blind, non-inferiority trial compared oral ciprofloxacin 500 mg twice daily for 7 versus 14 days in women with community acquired, acute pyelonephritis. The majority of urinary isolates revealed *Escherichia coli (E. coli)* and 27% of participants with positive blood cultures and 17% initially receiving intravenous doses of ciprofloxacin. Results from this study found clinical cure in 97% of patients treated for 7 days versus 96% treated for 14 days (-0.9% difference, 90% CI -6.5 to 4.8, p=0.004) and long term cure rates were equal for both study groups (-0.3% difference, 90% CI -7.4 to 7.2, p= 0.015).2 The other study tested non-inferiority of fluoroquinolones in acute, community acquired pyelonephritis with 5 days versus 10 days of oral levofloxacin 500 mg daily or ofloxacin 200 mg twice daily. This study was prospective, multi-site, randomized, open-label and included 68 female patients with confirmed pyelonephritis, 97.7% with urinary isolates of *E coli* and 3.4% with positive blood cultures. This study found similar cure rates at day 10 and day 30 between both groups (93% versus 97.7% at day 10, p=1.00; and 100% for both groups at day 30, p=1.00).3 Results from these two trials are consistent with past literature, including key trials, that also enrolled male participants, finding shorter antibiotic courses non-inferior to longer courses in complicated urinary tract infections and pyelonephritis.4, 5

Furthermore, unique populations have been studied and found to benefit from shorter antibiotic durations in uncomplicated cystitis. One large, retrospective study conducted at Baylor Medical School in 2017, identified a trend for longer antibiotic durations in women with cystitis and comorbid diabetes that ironically correlated to an increased risk for early cystitis reoccurrence when treatment durations were greater than 5 days compared to 5 days or less (OR 2.17, 95% CI 1.07-4.41).6 Similarly, a recent study found 7 day antibiotic courses sufficient in men with uncomplicated cystitis and found more than double infection reoccurrence rates with longer antibiotic durations (> 7days) in a subgroup of patients with fewer complications (i.e. no anatomical abnormalities, catheterization, or immunosuppression; OR 2.62, 95% CI 1.04-6.61).7 This observational study has prompted a randomized, controlled trial comparing 7 versus 14 day antibiotic therapy for urinary tract infections in men that is currently underway8 and is consistent with other previous trials finding antibiotic durations longer than 7 days do not provide a protective benefit in infection reoccurrence rates7 and fluoroquinolone durations of 5 days being as effective as 10 days.10 It has been suggested that the longer durations may alter normal urogenital flora thus predisposing patients to unnecessary treatment failure as observed in these trials.

Shorter antibiotic durations have been incorporated into the A2SC’s Alaska specific Urinary Tract Infection Treatment Guidelines published in November of 2018. These recommended durations reflect the latest literature that supports shorter durations of therapy to prevent collateral damage and treatment failure (Table 1) in conjunction with antibiotic susceptibility specific to Alaska.

Table 1: Antibiotic durations for urinary tract infections

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| --- | --- |
| **Cystitis** |  |
| Nitrofurantoin | 5 days |
| or Cephalexin | 7 days |
| or Ciprofloxacin (second line) | 3 days |
| **Pyelonephritis** |  |
| Ceftriaxone and | 1 dose |
| Cephalexin | 10-14 days |
| or Ciprofloxacin (second line) | 7 days |

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