Antimicrobial Stewardship News
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It's That Time of Year: Flu Shots

Actually, it's passed that time of year, but it is not too late. Influenza activity is escalating for the 2018-2019 season. We know this from data collected each week by the CDC.[3] Over 100 national influenza centers around the world prepared for the arrival of this flu season. Countless hours of surveillance and research helped predict which strains will dominate. Millions of doses of flu vaccine were manufactured, distributed, and administered across the United States (US) in hopes of preventing thousands of deaths and much suffering. For the most part, these efforts were successful. The CDC estimates the flu vaccine prevented 5.3 million illnesses and 85,000 hospitalizations in 2017.[2] However, these estimates only take into account flu-related illness and death; secondary effects that include antibiotic over-use and bacterial super-infection are harder to measure.

This newsletter will address influenza's impact on local antimicrobial stewardship efforts regarding the rise in inpatient antibacterial use and antibiotic resistance that is seen with each flu season. We will also offer suggestions on how to mitigate the impact of these effects.

Seasonal Antibiotic Prescriptions, Secondary Bacterial Infections, & Antimicrobial Resistance

The first recognition of an outbreak of influenza in a specific population or geographic location is a surrogate marker and harbinger of a corresponding rise antimicrobial overuse. Data collected in prior years consistently shows that an increase in influenza cases correlates with a corresponding increase in antimicrobial prescribing. For example, Polgreen et al. used a time series model to study fluoroquinolone use over a 7-year period and found a "contemporaneous relationship between seasonal influenza activity and antibiotic use."[4]

Their model, although now outdated with respect to fluoroquinolone use trends, estimated that a 20% reduction in influenza cases would result in an 8% decrease in the number of fluoroquinolone prescriptions.

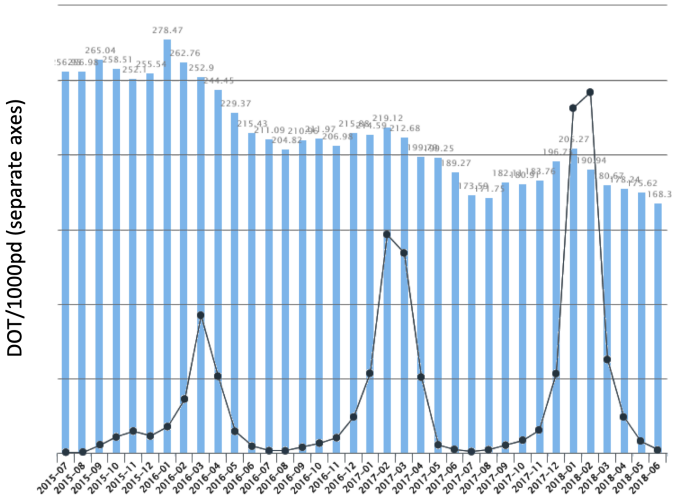

Figure 1. Broad Spectrum (Community Acquired) therapy vs. Oseltamivir (Different y-axes)

This seasonality of antibiotic use is reflected in DASON data. An increase in inpatient antibiotic use occurs each year during the winter season. Figure 1 shows total inpatient antibiotic use for broad-spectrum antimicrobials (in DOT/1000pd) for the entire DASON cohort of hospitals. Oseltamivir (Tamiflu) use is graphed to approximate the "peak" of each flu season.

Pneumonia accounts for a large percentage of the increased antibiotic use during flu season. Influenza-related pneumonia however, is a preventable illness. In a 2015 JAMA paper, Grijalva et. al found that patients hospitalized with influenza-related pneumonia are less likely to have received prior influenza vaccination compared to those with typical community-acquired pneumonia.[7] The authors estimated a vaccine effectiveness of 56.7% during their study period and highlighted the importance of vaccination among community populations. Increasing vaccination rates in the community decreases total antibacterial use.[8]

Secondary bacterial infections related to influenza are an important cause of morbidity and mortality, yet It is often difficult to directly attribute these infections to influenza. For example, Glica et al. showed that *C. difficile* infection rates increase in correlation to increased influenza activity.[6] This effect was independent of variations in antibiotic use. *C. difficile* infections, however, are not typically calculated as influenza-related complications.

Antimicrobial Resistance

Increased antibiotic use has an additional consequence: Antibiotic resistance rates are consistently and predictably linked to rates of antibiotic use both in individual hospitals and in broader geographic areas. An increase in the prevalence of antimicrobial resistance may occur within weeks or months of the onset of increased antimicrobial use in a given population. For example, Sun et al. evaluated antibiotic use in the entire US over an 8-year period and compared it to *E. coli* resistance rates.[5] Multiple antibiotic classes had seasonal variations in use. Antimicrobial resistance lagged the increased antibiotic use by approximately 1 month (Figure 2). *E. coli* resistance was significantly correlated with increased antibiotic use for multiple types of antibiotics.

Reducing Influenza's Burden

There are multiple ways to reduce the costs and consequences of the predictable increases in antibiotic use during every annual influenza season. Universal vaccination policies for healthcare workers is an effective technique was discussed at length in our September 2018 DICON newsletter. This newsletter will address three additional ways to reduce unnecessary antibiotic use and improve patient outcomes during outbreaks of influenza.

Real-Time Rapid Polymerase Chain Reaction (RT-PCR) and other molecular based tests for influenza have a high sensitivity and specificity.[9] Use of RT-PCR to rapidly diagnose influenza is associated with decreased antibacterial use in children and adults.[10,11] IDSA recently updated their guidelines for the diagnosis and treatment of influenza. These guidelines promote the use of molecular based assays such as RT-PCR and discourage the use of rapid-influenza diagnostic tests (immunoassays) because they lack specificity and sensitivity.[12] We now recommend that all of our member community hospitals modify and update their hospital-wide order-sets for treatment of upper and lower respiratory tract infections to include RT-PCR testing when influenza is known or suspected to be present in their community.

Figure 2. Annual fluctuations in drug resistance are linked to seasonal antibiotic use. Image credit: Center for Disease Dynamics and Economic Policy. Data source: Sun et al.

The 2018 updated IDSA guidelines also recommend aggressive empiric antiviral treatment for patients with known or suspected influenza who are judged to be at high risk of hospitalization or death. Categories of patients deemed to be "high risk" include children younger than 2, immunocompromised patients, pregnant women, those with chronic medical conditions, and extremely obese patients (BMI > 40). Treatment with antiviral therapy should be started in high-risk patients prior to molecular influenza test results regardless of the duration between symptom onset and hospitalization when influenza virus is known or suspected to be present in the local community.

Skepticism of the efficacy of influenza vaccines is widespread in the general population. We support and encourage all of our member hospitals and their staff attempt to counter and overcome this skepticism with

educational initiatives. We also strongly endorse and support mandatory vaccination policies for healthcare workers in our member hospitals. We urge the antibiotic stewardship programs in our member hospitals to find ways to educate staff and patients that antibacterial prescriptions are inappropriate for viral infections. Educational materials that address this important fact and recommendation made in this newsletter are available from the CDC's Be Antibiotics Aware program**: www.cdc.gov/features/antibioticuse/.**

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