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Antimicrobial Stewardship

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Antimicrobial stewardship originated out of the need to systematically provide guidance to providers on appropriate antibiotic use. In 2013 there were more than 260 million antibiotic prescriptions dispensed in the outpatient setting, with 30% or more of these deemed unnecessary.[1] Reducing the overuse of antibiotics and optimizing selection of correct antibiotics plays a large role in reducing antibiotic resistance. Antibiotic resistance is a major health concern, leading to 35,000 deaths a year in the United States (US).[2] Additionally, inappropriate antibiotic use has been shown to cause millions of dollars of excess healthcare expenditures.[3] Antibiotic stewardship programs are an important component of providing valuable direction on antibiotic use. This newsletter will discuss common areas of inappropriate prescribing and programs designed to facilitate best practices of antimicrobial use, with a focus on the outpatient setting.

Inappropriate Antimicrobial Prescribing

Inappropriate prescribing of antimicrobials is directly linked to antibiotic resistance. More than 2.8 million people annually in the US get infected with bacteria that are resistant to antibiotics.[2] Antibiotic selection, dosing, and duration all contribute to rising resistance rates. A study evaluating inappropriate antibiotic use in the outpatient setting found antibiotics were most commonly prescribed for sinusitis, suppurative otitis media, and pharyngitis.[4] The use of antibiotics for sinusitis and suppurative otitis media is not always warranted. An analysis of the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS) data estimated half of the prescriptions written for these conditions were appropriate.[4] The Centers for Disease Control (CDC) recommends treatment of pharyngitis only for patients testing positive with a Rapid Antigen Detection Test (RADT) for streptococcal pharyngitis.[5,6] First-line treatment recommendations are amoxicillin or penicillin V for adults and children.[6,5] Penicillin-allergic adult antibiotic recommendations are cephalexin, cefadroxil, clindamycin, or macrolides and for children the recommendations are cephalexin, cefadroxil, clindamycin, clarithromycin, or azithromycin.[5,6] Children with acute otitis media should be treated if they have middle ear effusion. First line recommendations are for the use of amoxicillin or amoxicillin/clavulanate if recent amoxicillin use.[6] For children with a non-type I hypersensitivity to penicillin, the use of cefdinir, cefuroxime, cefpodoxime, or ceftriaxone is recommended.[6]

Adverse drug reactions are also a common consequence of antibiotic overuse. One out of every 5 emergency department (ED) visits is due to an adverse drug event related to antibiotics.[7] This is especially true in children, as adverse drug events due to antibiotics are the most common cause of ED visits in children under the age of 18 years.[7] A study of pediatric patients found that 31% to 36% of bacterial infections and 4% to 70% of viral infections were prescribed antibiotics inappropriately. An adverse event of these inappropriately prescribed antibiotics was an increase in *Clostridioides difficile* infection rates in children treated for otitis media (hazard ratio [HR] 6.23; 95% confidence interval [CI] 2.24 to 17.32).[8] There was also an increased rate of severe allergic reactions.

Antimicrobial Use During the COVID-19 Pandemic

Coronavirus disease (COVID-19) brought about additional concerns because antibiotics were frequently prescribed early in the pandemic. There were more resistant infections, increased antibiotic use, and less data and prevention actions compared to pre-pandemic years.[9(p19)] There were 15% more deaths and infections due to antimicrobial-resistance in 2020.[9(p19)] Increased resistance among specific pathogens are presented in **Table 1**. A meta-analysis found bacteria co-infection in patients with COVID-19 was generally low, with an incidence of 6.9%, but antibiotics were prescribed in 71.9% of cases.[10] The use of azithromycin was higher than expected across all healthcare settings during the COVID-19 pandemic (outpatient numbers based on retail prescriptions and Medicare carrier claims), partly due to initial thoughts that it could be used as a treatment for COVID .[11] In contrast, other outpatient antibiotic prescriptions decreased in 2020 which was thought to be due to COVID-19 pandemic mitigation measures.[11]

Table 1. Specific Pathogens with an 15% Increase in Resistance from 2019 to 2020[9]

Pathogen	Infection Rate Increase
Carbapenem-resistant *Acinetobacter*	78%
Multidrug-resistant *Pseudomonas aeruginosa*	32%
Vancomycin-resistant *Enterococcus* (VRE)	14%
Methicillin-resistant *Staphylococcus*	13%

Following national treatment guidelines for the management of COVID-19 is recommended.[12] If antibiotics are used in patients with COVID, utilization should be guided by laboratory diagnostics once available and de-escalating therapy if no bacterial infection is present.[9] The watchful waiting and symptom relief approach should be used when there is no clear diagnosis related to a bacterial etiology. Providing patients with guidance and education on managing symptoms related to viral illness can improve safe and appropriate antibiotic use.[12]

Fundamentals of Antimicrobial Stewardship

Identifying high-priority conditions and barriers to appropriate antibiotic prescribing are an important initial step in an antibiotic stewardship program. The Centers for Disease Control published guidance on the core elements of an antimicrobial stewardship program in the outpatient setting. The focus of the program is to measure and improve how antibiotics are prescribed by providers and used. The core elements of antimicrobial stewardship are[1]:

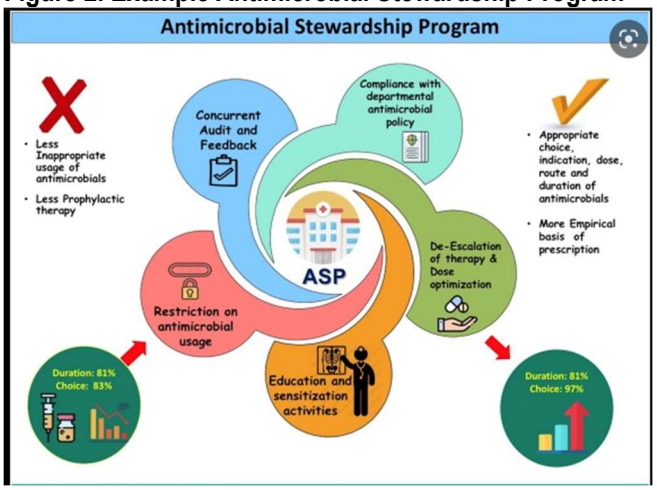
1) Commitment
2) Action for policy and practice
3) Tracking and reporting
4) Education and expertise

Goals of antimicrobial stewardship programs and an example of an antibiotic stewardship program are presented in **Figure 1 and Figure 2**.[1,13]

Figure 1. Goals of Antimicrobial Stewardship Programs

1. Measure antibiotic prescribing
2. Improve antibiotic prescribing by clinicians and use by patients so that antibiotics are only prescribed and used when needed
3. Minimize misdiagnoses or delayed diagnosis leading to underuse of antibiotics
4. Ensure the correct drug, dose, and duration are selected when an antibiotic is needed

Figure 2. Example Antimicrobial Stewardship Program[13]



- Duration percents represent inappropriate duration and choice percents represent wrong antibiotic selection

Circumstances that lend themselves to being targets for antimicrobial stewardship interventions include:

- Conditions in which antibiotics are commonly overprescribed or not indicated (e.g., acute bronchitis, nonspecific upper respiratory tract infection, viral pharyngitis or asymptomatic bactereiura)[1,14]
- Conditions in which antibiotics are indicated but the wrong agent, dose, or duration is often selected[1]
- Conditions for which watchful waiting or delayed prescribing is appropriate but often not utilized (e.g., acute otitis media or acute uncomplicated sinusitis)[1]
- Conditions in which antibiotics are underused or the need for timely antibiotics is not recognized (e.g., missed diagnoses of sexually transmitted infections or severe bacterial infection such as sepsis)[1]

Promotion of appropriate antibiotic prescribing practices can be accomplished through use of evidence-based diagnostic criteria and treatment recommendations. Important resources include clinical practice guidelines and knowledge of local pathogen susceptibilities. Health System antibiograms, which detail antibiotic resistance patterns, are a helpful resource to guide empiric antibiotic selection. Antibiograms need to be continually updated and applied to the health care setting in which they originated, as they vary by institution and region. In some cases, pathogens may be initially susceptible but become resistant such as with the ampC beta-lactamase producing organisms, in particular *Enterobacter cloacae, Klebsiella aerogenes,* and *Citrobacter freundii*. Therefore, patient clinical response should be

monitored and repeat testing may be needed. Pathogen susceptibility varies between health systems, patient treatment settings and demographic locations.[15]

Oregon Metrics on Antibiotic Prescribing

The state of Oregon tracks several areas to evaluate antibiotic stewardship. For example, the number of outpatient antibiotic prescriptions per 1000 people is less in Oregon compared to the nation as a whole (475 vs. 625, respectively - 2020 data).[1] In addition, antibiotic prescriptions in Oregon, compared to the national average, are consistently lower across all major antibiotic classes including: cephalosporins, fluoroquinolones, macrolides and penicillins.[1]

The CDC also publishes state-specific information on antibiotic prescribing and resistance patterns. Certain pathogens of particular interest are specifically tracked and reported.

- The rates hospital-associated carbapenem-resistant *Enterobacteriaceae* was 1.7% in 2019 in Oregon, compared to 2.4% for the US.
- The standardized infection ratio (SIR) was 0.51 for *C.difficile* in Oregon.[1] The SIR is a statistic used to track healthcare associated infections (HAIs) over time, at a national, state, or facility level. The SIR compares the actual number of HAIs at each hospital, to the predicted number of infections. *C.difficile* is the single most common pathogen responsible for healthcare-associated infections.[1]

Conclusion

Antibiotics are life-saving treatment options for susceptible organisms. Appropriate antibiotic use will ensure effective therapies are available and resistance rates are kept low. Inpatient and outpatient antimicrobial stewardship programs should be utilized to encourage appropriate antibiotic use. There are many resources available to assist providers in developing antibiotic stewardship programs and to inform best antibiotic prescribing practices (**Figure 3**).

Figure 3. Resources for Appropriate Antibiotic Use

- Antibiotic Resistance and Patient Safety Portal: https://arpsp.cdc.gov/
- Core Elements of Antibiotic Stewardship Programs: https://www.cdc.gov/antibiotic-use/core-elements/index.html
- CDC National Healthcare Safety Network (national infection tracking system): https://www.cdc.gov/nhsn/index.html
- Oregon Health Authority Treatment Algorithms: https://www.oregon.gov/oha/PH/DISEASESCONDITIONS/COMMUNICABLEDISEASE/ANTIBIOTICRESISTANCE//provider.aspx
- Society of Infectious Disease Pharmacists: https://sidp.org/Clinician-Education

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