



Antimicrobial Stewardship Program

June 2018

Frequently Asked Question 1: Why Antimicrobial Stewardship?

Background:

Treatment and prevention of infections depends upon the availability of effective antimicrobial agents. In an era when antimicrobial resistance is increasing, and development of new antimicrobials has decreased, the appropriate use of antimicrobial agents is ever more important. The Centers for Disease Control and Prevention (CDC) reports that an estimated 20-50% of antibiotic prescriptions in US acute care hospitals are either unnecessary or inappropriate.¹ Unnecessary or inappropriate antimicrobial use can contribute to antimicrobial resistance, treatment failure, increased incidence of adverse effects, and increased cost of therapy. Improving the use of antimicrobials is an important patient safety and public health issue.¹ Antimicrobial Stewardship Programs (ASPs) have been shown to be an effective way to reduce the unnecessary or inappropriate use of antimicrobials resulting in improved patient outcomes, reduced adverse events, improvement of antibiotic susceptibilities to targeted antibiotics, and optimization of resource utilization.^{1,2} As a result the CDC¹, along with the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA)^{3,4} have developed guidelines for the development of ASPs. In addition as of January 1, 2017 The Joint Commission has implemented a new medication management standard for hospitals, critical access hospitals, and nursing care centers that addresses antimicrobial stewardship practices.⁵

Definition:

Antimicrobial stewardship, as defined in a consensus statement from the IDSA, SHEA, and the Pediatric Infectious Diseases Society (PIDS), is described as “coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy, and route of administration.”²

Summary of Key Guidelines & Requirements:

CDC Core Elements

The CDC has developed a checklist for core elements of hospital antibiotic stewardship programs.¹ This checklist addresses seven key elements including: leadership support, physician leader accountability, pharmacist leader involvement, specific actions to support optimal antimicrobial use, monitoring antimicrobial prescribing, use, and resistance, reporting information to staff, and education. In addition to physician and pharmacist leader responsibilities, support staff involvement is highlighted. Specifically clinicians, infection prevention and healthcare epidemiology, quality improvement, microbiology, information technology, and nursing support are noted.

IDSA/SHEA ASP Guidelines

The IDSA/SHEA guidelines published in 2007 emphasize that “the primary goal of antimicrobial stewardship is to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use.”⁴ This document describes in detail guidelines for the development of an ASP. Core members, stewardship strategies, and outcomes monitoring are reviewed.



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A second IDSA/SHEA guideline was published in 2016 which provides updated and expanded evaluation of ASP interventions and approaches to measure the success of ASP interventions.

The Joint Commission Medication Management Standards

Medication Management Standard, MM.09.01.01 became effective on January 1, 2017. This standard requires hospital leaders to establish antimicrobial stewardship as a priority. Hospitals must have a multidisciplinary antimicrobial stewardship team. Hospitals must have a provide education to staff and prescribers as well as patients regarding the appropriate use of antimicrobial agents. The Joint Commission MM standard requires the ASP to include the seven core elements noted by the CDC and discussed earlier in this document. The ASP must use organization-approved multidisciplinary protocols, these may be diagnosis or population specific. Finally the ASP must collect, analyze, and report data on it ASP activities and take action on opportunities for improvement.⁵

Who Should Be Involved?

The CDC, IDSA, & SHEA all recommend that ASPs should be multidisciplinary teams. It is recommended that ASPs are led by an infectious diseases physician, often supported by a pharmacist, preferably also with advanced infectious diseases training or certification. Other key ASP members include clinicians and nurses as well as microbiology, infection prevention and epidemiology, information technology, quality improvement staff. These multidisciplinary ASP teams will most likely oversee and monitor the ASP activities. The day to day functioning of an ASP program will vary between institutions but will often include daily pharmacist involvement, and the commitment and support of prescribers and nurses.

References:

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Frequently Asked Question 2: Antimicrobial Double Coverage

Background:

Antimicrobial double coverage is defined as prescribing two antimicrobials to treat the same microorganism. The use of double coverage is often justified by a desire to ensure adequate empiric therapy, achieve synergy, or prevent the development of resistance. However, double coverage for pathogens is rarely indicated, and double coverage can be associated with adverse events. The following organizations endorse pharmacy review of double coverage to improve patient care: Infectious Diseases Society of America (IDSA), Society for Healthcare Epidemiology of America (SHEA), and the Centers for Disease Control and Prevention (CDC).^{1,2} The purpose of this FAQ is to review the literature for antimicrobial double coverage, outline the benefits and harms associated with double coverage, and describe when double coverage should be considered.

Summary of Evidence:

Antimicrobial double coverage can be classified into two separate categories: empiric and definitive therapy. Empiric therapy is use when culture results are not yet known. Definitive therapy is when culture results have already resulted.

Empiric Therapy: Improved outcomes are associated with appropriate initial therapy, especially in critically ill patients. Use of local antibiogram data, along with knowledge of patient specific risk factors for antimicrobial resistance should guide empiric therapy choices. Double-coverage of suspected Gram-negative pathogens is rarely indicated.³⁻⁸ For example, Gram-negative monotherapy is appropriate if the antibiotic is expected to be active against $\geq 90\%$ of Gram-negative bacilli. For example, if your antibiogram shows that most Gram-negative pathogens remain susceptible to cefepime, then empiric gram-negative double coverage is not necessary under most circumstances. Furthermore, it is unlikely that a pathogen resistant to a broad-spectrum beta-lactam, like cefepime, will remain susceptible to a fluoroquinolone.³ Similarly, most anaerobic bacteria remain susceptible to beta-lactam/beta-lactamase combinations and metronidazole. Combining two anaerobic agents for empiric therapy is not recommended.

Definitive Therapy: In circumstances where empiric double coverage is employed, de-escalation to a single agent is recommended once susceptibility data are available.¹ For most conditions, there is no evidence to support routine use of combination therapy once susceptibility data are known. Clinicians will occasionally prescribe two antibiotics for synergy. The data behind synergy is limited, and there are few settings where synergy is recommended (e.g. certain types of streptococcal endocarditis, cryptococcal meningitis, treatment of some mycobacterial infections, treatment of HIV, management of necrotizing fasciitis, and treatment of some prosthetic joint infections). Synergy between drug classes is not well documented, and some combinations of antibiotics may be antagonistic, rather than synergistic.^{3,5} An infectious diseases consult is strongly recommended if double coverage for the purpose of synergy is considered for definitive therapy.



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Overview of the Risks and Benefits of Double Coverage:

Benefits: There are limited benefits for double coverage. Situations where double coverage should be considered include:

- Known or suspected multidrug-resistant bacterial infections
- Treatment of prosthetic joints infections with retained hardware
- Treatment of infections where resistance is known to develop on therapy

Risks: There are several risks associated with unnecessary double coverage. These risks include:

- Increased complexity of treatment regimen
 - Particularly significant in patients receiving multiple intravenous medications
- Increased risk of toxicity (including seizures)
- Potential antagonism
- Increased cost of therapy
- Increased risk of superinfections

Summary and Recommendations:

Antimicrobial double coverage for empiric and definitive treatment of patients is rarely warranted and can be associated with adverse events. Pharmacy evaluation of patients receiving double antimicrobial coverage is the standard of care and endorsed by several professional societies.^{1,2} Providers who are interested in prescribing two or more antimicrobials should discuss the case with an antimicrobial stewardship pharmacist and/or an infectious disease physician. These providers can help optimize antimicrobial coverage while minimizing patient harm.

CONSIDER GRAM NEGATIVE DOUBLE COVERAGE:

1. Empiric treatment of serious, suspected multidrug resistant Gram-negative, infections (presenting with hypotension, pressor requirement, or mechanical ventilation) *until microbiology data are available*.
2. Documented infection with a resistant Gram-negative organism with very limited treatment options.
3. Documented infection with a resistant Gram-negative organism after synergy testing has shown benefit.

NOTE: The two agents should be from different antimicrobial classes (i.e. beta-lactam + aminoglycoside or beta-lactam + quinolone) and chosen based on local, or pathogen specific, susceptibility data.

CONSIDER ANAEROBIC DOUBLE COVERAGE:

1. Metronidazole or vancomycin may be added to another agent with anaerobic coverage to treat a *clostridium difficile* infection.
2. Clindamycin may be added to therapy when treating necrotizing fasciitis.



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References:

1. Dellit TH, Owens RC, McGowan JE, Jr., et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis*. 2007;44(2):159-177.
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