Dear Healthcare Practitioner,

People infected with drug-resistant organisms are more likely to have longer and more expensive hospital stays, and may be more likely to die as a result of the infection. When the drug of choice for treating their infection doesn't work, they require treatment with second- or third-choice drugs that may be less effective, more toxic, and more expensive. This means that patients with an antimicrobial-resistant infection may suffer more and pay more for treatment.

Attached is a two-page instructional document entitled "IMPROVING THE QUALITY OF ANTIBIOTIC PRESCRIBING: EMPIRIC AND PATHOGEN-DIRECTED ANTIMICROBIAL THERAPIES". This document can be used in your institution and by your peers to improve antibiotic prescribing in various clinical scenarios.

Part of Arizona Department of Health Services mission is to track the emergence of antimicrobial-resistant microorganisms and to limit their spread. We have implemented several efforts to help prevent the development and transmission of infections that are caused by these organisms through educational programs, campaigns to promote the proper use of antimicrobial agents, and advocacy for vaccine use. Each one of us has a role to play in limiting the development and spread of antimicrobial-resistant microorganisms. We hope that this document will give you and your healthcare practitioners some ideas on how you can help. Please let us know how we can work with you and others to use antibiotics wisely.

Respectfully Submitted,
Arizona HAI Advisory Committee

If you'd like to learn more about the Arizona HAI Advisory Committee, please visit www.preventHAIaz.gov.

IMPROVING THE QUALITY OF ANTIBIOTIC PRESCRIBING: EMPIRIC AND PATHOGEN-DIRECTED ANTIMICROBIAL THERAPIES

Since the 1940s, antimicrobial agents have greatly reduced illness and death from infectious diseases. However, these drugs have been used widely and often inappropriately causing the infectious organisms the antibiotics are designed to kill to adapt to them, making the drugs less effective. In some cases, the microorganisms have become so resistant that no available antibiotics are effective against them. Resistant bacteria are more commonly found in hospitals and other healthcare settings, but have also been seen in the community.

Empiric Antibiotic Prescribing

Empiric antibiotic prescribing refers to the selection of one or more antibiotics prescribed prior to the availability of culture and antibiotic susceptibility test (AST) results, often referred to as "C&S". Choices for selection of antibiotics prior to C&S results involve two sequential processes. The first is based on the microorganisms commonly involved in specific infections. For example, community-acquired pneumonia often involves infection by *Streptococcus pneumoniae*, *Haemophilus influenzae*, and atypical bacteria; while urinary tract infections usually involve *Escherichia coli* and a few additional members of *Enterobacteriaceae*. The second process involves referral to the institution's annual cumulative antibiogram. This tool is developed by the microbiologist in consultation with infectious disease physicians, pharmacy, and infection prevention and control specialists. The antibiogram provides percent susceptibility (%S) of specific "bacteria-antibiotic" combinations and forms the basis of evaluating optimal drug choices when combined with recent antibiotic exposure, drug allergies, and other precautions. For example, many *E. coli* are resistant to ampicillin, and so ampicillin should not be used for the empiric treatment of a urinary tract infection. Cumulative antibiograms provide a better "educated guess" when selecting antibiotics.

Culture and Susceptibility (C&S)

C&S may be valuable when considering certain patient groups in a healthcare setting. Most antibiotic regimens prescribed in the community setting do not involve culturing the infected source, and therefore validation of the treatment selection is dependent on the resolution of signs and symptoms of infection. For mild infections the failure of empiric antibiotic prescribing is considered low. A C&S result may be important following clinical failure. The assortment of suspected bacterial culprits is greater, thereby making some empiric antimicrobial regimens broader in spectrum. Infections due to resistant pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa* and *Acinetobacter* spp, or fluoroquinolone-resistant *E. coli* may be a concern in patients who have recent antibiotic exposures and/or have experienced hospitalization within the past 30 to 60 days. In such patients, ordering a C&S play an important role in selecting appropriate antimicrobial therapy. C&S results also assist in choosing subsequent antimicrobial therapy tailored to the causative organisms.

Pathogen-Directed Therapy

"Empiric" antibiotic prescribing is contrasted with "pathogen-directed" therapy–optimizing the antibiotic regimen once C&S results are available. As empiric therapy transitions to a pathogen-directed treatment the antimicrobial spectrum may be changed to fewer agents or narrower spectrum agents. Each of the following strategies should be considered once final C&S results are available (see Table 2). These are general recommendations and must be considered in the context of the individual patient. However, the recommendations may be applied to both community and healthcare settings. Also, it remains important to assess the validity of specimens submitted to the laboratory (e.g. skin swabs to assess the microbiology of infected wounds should be considered invalid). The risk that bacterial isolates may actually represent contaminants should be assessed.

Prudent antibiotic prescribing considers both clinical and public health implications – providing optimal patient care while at the same time seeking to minimize selective pressure that may result in the emergence and spread of antibiotic resistance. Optimal management of infections improves the quality of the initial decision to prescribe an antibiotic, including making an informed choice of empiric drug and dose, and ensuring rapid prescribing and administration in presumed sepsis or other severe infections. Another focus involves the critical importance of carefully reviewing antibiotic therapy at 48 hours and the availability of microbiology test results. Such actions lead to a clear decision to stop or change antibiotic, if possible to a narrower spectrum. The above strategies are encompassed within antimicrobial stewardship which, via a multidisciplinary approach, promotes optimal patient care while at the same time seeking to minimize selective pressure that may result in the emergence and spread of antibiotic resistance as well as other undesirable side effects such as *Clostridium difficile* infection or drug toxicity. Collateral damage is unique to antimicrobials since resistance can affect other patients. These strategies are listed in Table 1 – starting smart and focusing at 48 hours.

Table 1. Actions to Optimize Antimicrobial Prescribing During the First 48 hours

Start Smart When Initiating Empiric Selection of Antimicrobials

- Send appropriate specimens to the microbiology laboratory for culture, identification and susceptibility testing prior to starting antimicrobial treatment in seriously ill or hospitalized patients, and in those with risk of infection due to resistant bacteria.
- Prescribe in accordance with local and national policies and guidelines, avoiding broad-spectrum agents when feasible
- Document indication(s) for antibiotic prescription in clinical notes, along with the route of administration, the dose and the planned duration
- Prescribe the shortest antibiotic course likely to be effective
- Select agents with a view to minimizing collateral damage (e.g. potentially severe side effects, selection of multi-resistant bacteria or *Clostridium difficile*)
- Use single dose antibiotic surgical prophylaxis wherever possible and in accordance with hospital pathways
- Consult infectious diseases experts when managing patients with difficult infections

Then Focus

- At 48 hours review the need for on-going antibiotic therapy based on the patient's clinical condition and available microbiology results
- Use individual, local and national antimicrobial susceptibility data to substitute or change agents, moving to a narrow-spectrum antibiotic if possible
- Stop antibiotics if no evidence of infection
- Wherever possible switch from intravenous to oral therapy

Table 2. Potential Strategies Applied at 48-72 Hours

- Infection is ruled out → Discontinue antibiotics
- Infection is unlikely and C&S results are negative → Discontinue antibiotics
- Infection is likely, C&S results are negative → Consider consulting an infectious diseases specialist, particularly if the patient is not improving or is worsening. If the patient is improving, treat the suspected infection for the shortest effective duration, based on pathways and/or guidelines.
- Infection is very likely and C&S results are available → Change to an agent with the narrowest spectrum to which the bacteria is sensitive and is appropriate for the type of infection.