Actionable Patient Safety Solution (APSS) #3B: ANTIMICROBIAL STEWARDSHIP
THE ROLE OF PHARMACY AND THE MICROBIOLOGY LAB IN PATIENT SAFETY

Executive Summary Checklist

Inappropriate use of antimicrobial drugs (antibiotics, etc.) is a significant cause of patient morbidity and mortality.

- Commitment from institutional leadership (administration, medicine, pharmacy, nursing, microbiology, and technology) to develop and support an Antimicrobial Stewardship Program.
- Create a multidisciplinary Antimicrobial Stewardship Committee that includes infection prevention, infectious disease professionals from Medicine, Surgery, Pharmacy, Microbiology Laboratory, Nursing, and Information Technology. This group will ensure the:
  - accountability of ASP chair or co-chairs.
  - development of protocols to support ASP initiatives and interventions.
  - personnel training and support.
  - necessary infrastructure for measuring antimicrobial use and outcomes.
  - monitoring of microbial resistance and its effect on disease patterns.
  - development of clear goals for the ASP, including timelines and metrics.
  - delivery of regular updates to the institutional antibiogram and compliance with Clinical Laboratory Standards Institute (CLSI) guidelines.
- Implement Computerized Physician Order Entry (CPOE) with Clinical Decision Support (CDS) and computer-based surveillance software to provide real-time data at the point of care for ASP initiatives.
- Develop mechanisms to educate clinicians regarding ASP initiatives and progress. Identify and educate clinicians who exhibit outlying prescribing patterns. Monitor progress and include the results in staff educational sessions.
- All antimicrobial orders are reviewed by a hospital pharmacist, including a review of allergy profiles.
The Performance Gap

In 2014 the CDC recommended that all acute care hospitals implement Antibiotic Stewardship Programs and in September 2014 California Governor Jerry Brown approved SB 1311 that will require all general acute care hospitals in California to establish a physician supervised multidisciplinary Antimicrobial Stewardship committee by July 1, 2015 (CLI, 2014). As of January 2017, the Joint Commissions’ new Medication Management Standard on Antimicrobial Stewardship went into effect, requiring hospitals and critical access hospitals to have an antimicrobial stewardship program in place. Additionally, the Centers for Medicare and Medicaid Services will require facilities participating in Medicare and Medicaid to have formal Antimicrobial Stewardship Programs in place.

The overall objectives of the Antimicrobial Stewardship Program (ASP) committee are to identify and reduce risks of developing, acquiring, and transmitting infections; reduce healthcare costs and toxicities associated with antimicrobials and inappropriate therapy; and, most importantly, improve patient outcomes (e.g., reduced antimicrobial/antifungal/antiviral resistance rates, reduced C. difficile rates, and reduced hospital LOS). More importantly, an effective ASP committee or team is comprised of an ID-trained physician, pharmacist (preferably ID-trained), infection control personnel, information technology personnel, quality improvement personnel, nursing, and microbiology. With leadership commitment and accountability being key requirements of a successful ASP.

Inappropriate use of antimicrobials can have unintended consequences on both the pathogen and patient. From the perspective of the pathogen, resistance may be acquired and spread within the healthcare system and into the community. From the patient perspective, adverse reactions, super-infections, selection of resistant pathogens, and poor clinical outcomes may occur. Hence, optimized and judicial use of antimicrobials is a critical component of patient safety. Any institution implementing an ASP must be able to measure two key variables: 1) antimicrobial use to assess whether interventions lead to changes in use, 2) resistance patterns among microorganisms, and 3) outcomes associated with changes in antibiotic use. For instance, metrics that are used to determine the impact of the ASP is by calculating the defined daily doses (DDDs) or days of therapy (DOT) of antibiotics per 1000 patient days (see under “Pharmacy Driven Interventions for ASPs” section). The cost per quality adjusted life-year (QALY) could also be used as another metric to measure the cost-effectiveness of the program in preventing specific infections (e.g., bloodstream infections).

While typically not thought of as a component of patient safety, it should be apparent that one of the key components of the ASP is the prevention of adverse drug events by decreasing the indiscriminate use of antibiotics. It should be realized that antimicrobial therapeutics are the only medications where use in one patient can affect the efficacy of that therapeutic in another patient. Additionally, the common notion that antimicrobials are benign medications is false. According to a number of studies, approximately 25% of adverse drug events arise from antimicrobial use (Lesar, 1997). Antimicrobials in one study were responsible for 19% of emergency department visits (2004-2006), in which the majority were allergic reactions. Based on this data, the study found that risks for adverse events from antimicrobial therapy were three times higher than those reported for aspirin, phenytoin, and clopidogrel (Shehab, Patel, Srinivasan and Budnitz, 2008). Another critical adverse outcomes associated with the use of antibiotics is Clostridium difficile colitis, often a complication associated with broad spectrum antibiotic use, but has also been reported to occur with almost any type of antibiotic. This type of infection carries an increased risk of readmission, as well as an increased risk for mortality. Hence, judicial and prudent use of antimicrobial therapy may prevent resistance, adverse drug events, and improve patient safety.

Pharmacy Driven Interventions for ASPs

- Protocols for changes from intravenous to oral antibiotic therapy in appropriate situations.
  - **Rationale:** Decrease cost, decrease hospital stay, and reduce line infections.
  - **Clinical Stability Criteria for IV to PO:**
    - Afebrile
    - Stable heart rate
    - Stable respiratory rate
    - Systolic blood pressure >90mm Hg
    - O2 saturation >90% (O2 partial pressure >60 mm Hg)
    - Functional GI
    - Normal mental status
Dosage adjustments in cases of organ dysfunction.
  ○ Rationale: Avoid toxicities.
Dose optimization (pharmacokinetics/pharmacodynamics) to optimize the treatment of organisms with reduced susceptibility.
  ○ Rationale: Avoid toxicities, optimize PK/PD, improve patient outcomes.
Automatic alerts in situations where therapy might be unnecessarily duplicative.
  ○ Rationale: Avoid toxicities and decrease costs.
Time-sensitive automatic stop orders for specific antibiotic prescriptions.
  ○ Rationale: Decrease cost and unnecessary antimicrobial therapy, and decrease development of resistance.
Initiation of necessary treatment for patients who should be receiving antibiotics.
  ○ Rationale: With no empiric or directed therapy against infecting or suspected organisms, the delay in time to an active antibiotic against the pathogen increases mortality.
Antimicrobial use and efficacy analysis
  ○ Rationale: Need to determine the patient days for the hospital ward being analyzed for the time period of the data. The calculation is: (DDDs / patient days) * 1000. Recent guidelines from the Infectious Disease Society of America, recommend the use of days of therapy (DOT) per 1000 patient days over DDD, with DDD being an alternative at institutions that cannot collect DOT data.
Development of Institution Specific Antimicrobial Stewardship Guidelines
  ○ Rationale: Source specific treatment pathways for infections should be developed based on antimicrobial resistance patterns at the institution and should align with ASP initiatives. Institutional treatment pathways will provide physicians a resource that is based on institutional data and provide guideline-concordant best practices. Utilization of clinical decision support can streamline this process.

Microbiology Laboratory Contribution

● Providing at least yearly antibiograms (if possible twice a year). Antibiogram reporting should be location specific (e.g., ICU, general wards, or pediatric areas).
● Incorporate rapid diagnostics such as multiplex PCR and Matrix Assisted Laser desorption/ionization – time of flight (MALDI-TOF).
  ○ Rapid diagnostics have been demonstrated to decrease the time to appropriate antibiotics and decrease the time on unnecessary antimicrobial therapy.
● Incorporate Pro-calcitonin level measurement in the laboratory to aid in antibiotic initiation and discontinuation.
  ○ During bacterial infection, Pro-calcitonin is produced in large quantities by body tissues. Strong evidence supports its use in antibiotic management of infections, particularly, pneumonia or other lower respiratory tract infections, and has been demonstrated to significantly decrease unnecessary antibiotic use and shorten duration of therapy.
● Automatic testing and reporting of tigecycline and colistin or newer agents if formulary (ceftazidime/avibactam, meropenem/vaborbactam) for Carbapenem Resistant Enterobacteriaceae (CRE) isolates.
  ○ As carbapenem resistance is increasingly reported, it is critical that alternative agent susceptibilities be made available. These alternative agents include tigecycline and colistin. While breakpoints for susceptibility are not available by CLSI, FDA breakpoints are available and should be used for interpretation.
● Reporting of minocycline susceptibility for Acinetobacter isolates.
  ○ Minocycline susceptibility remains high in most institutions against multi-drug resistant Acinetobacter spp, hence this should be taken advantage of as its resistance patterns allow.
● Selective reporting of susceptibilities of antimicrobials.
  ○ Selective reporting is a process of withholding susceptibility results from selected categories of antibiotics that may have deleterious effects on the hospital antibiogram/resistance rates, or financial cost that do not have a therapeutic advantage over other commonly used antimicrobial agents. For example, if an E. coli strain is isolated from a bloodstream infection and is not
susceptible to a 1st generation cephalosporin but is susceptible to cefotaxime, other broader agents such as ceftape, meropenem, or ceftaroline can be withheld and available upon the request of the physician.

Leadership Plan

Commitment from the hospital leadership is required for the successful implementation and progress of any clinical program, including the ASPs. Commitment and support of ASPs should not only come from the ASP committee or infectious diseases physicians, but also from the senior administration. Formal statements made at the administrative level in support of the program implementation and progression should be clear, in this way practitioners at the hospital will know and understand the importance of the ASP’s presence and goals. Some approaches that hospital/facility leadership should include in support of the ASP are (Dellit, 2007):

- Financial support
- Formal statements supporting the ASP and optimal use of antimicrobials within the hospital
- Protected/acknowledged time for personnel from various departments to participate in the ASP.
- Provide training and support to personnel
- Provision of necessary infrastructure for tracking and measuring antimicrobial use and outcomes.

Practice Plan

Each hospital should create a multidisciplinary team that includes an ID physician, ID-trained or clinical pharmacist, microbiologist, infection control, and information technologists (CDC, 2015). Depending on the size, type, and resources available to the hospital different strategies can be employed. In a large academic hospital it may be possible to form an antimicrobial stewardship committee and implement either a restrictive ASP or prospective audit with feedback.

In a restrictive program, select antimicrobials are placed on formulary restriction for use in only select indications. Dispensing of a restricted agent would require approval by designated personnel, usually an ID physician, ID fellow, or clinical pharmacist. The advantages of this program are:
(a) the direct oversight in the use of targeted antimicrobials,
(b) reduction of pathogen resistance within the hospital and communities,
(c) reduced hospital LOS, and
(d) reduced risks of antimicrobial-related side effects and drug-drug interactions.

The disadvantages may include:
(a) the requirement of personnel availability around-the-clock,
(b) physicians may perceive this as a loss of autonomy, and
(c) review of appropriateness only occurs with targeted/restricted agent, but not for non-restricted agents which can also lead to problems (Dellit, 2007; Goff et al., 2012).

An alternative to the restrictive program is a prospective audit with feedback program. In this program, a retrospective (hours to days) review of antimicrobial orders takes place for targeted and in some institutions non-targeted antimicrobials for appropriateness. It is also common to find programs that use a hybrid approach in which audit and feedback are employed along with a restricted formulary. Advantages of the prospective audit with feedback are the avoidance of loss of autonomy and the opportunity to educate individuals rather than only restrict utilization. A disadvantage is compliance is often voluntary (Dellit, 2007).

Implementation of the above two strategies require personnel dedicated to the ASP. In most academic and medium-to-large community hospitals, formation of an ASP with either of these strategies would be possible. On the other hand, in smaller hospitals where dedicated personnel may not be available, some of the pharmacy driven interventions mentioned previously can be implemented, as they require less resources and effort. These have been referred to as “low hanging fruit” interventions as they are the simplest to implement and yet have been shown to have a positive impact (Goff et al., 2012). Such interventions include intravenous-to-oral conversions, therapeutic
substitutions, batching of intravenous antimicrobials, monitoring and discontinuing preoperative antibiotic prophylaxis.

The Centers for Disease Control and Prevention has provided recommendations on core elements that should be implemented for hospital ASPs. These include:

- Commitment from institutional leadership (technology, personnel, finance)
- Accountability of ASP chair or co-chairs
- A clinician with drug expertise in antimicrobials [e.g., clinical pharmacist (Infectious Disease trained)]
- Actionable program components (e.g., prospective audit, automatic discontinuation orders)
- Monitoring of microbial resistance and infection patterns
- Reporting of and education about ASP findings to hospital staff (physicians, nurses, pharmacists, etc.)

**Technology Plan**

To be successful in implementing this Actionable Patient Safety Solution will rely on implanting a technology plan using the following systems. Other specific strategies will be developed or become apparent as the above are implemented. This action plan will include careful observation of the consequences of each new strategy, which will in turn lead to additional novel ideas for further improvement in medication administration safety.

*Suggested practices and technologies are limited to those proven to show benefit or are the only known technologies with a particular capability. As other options may exist, please send information on any additional technologies, along with appropriate evidence, to info@patientsafetymovement.org.*

<table>
<thead>
<tr>
<th>System or Practice</th>
<th>Available Technology</th>
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| **ONC Meaningful Use Certified EHR system** Electronic Health Record (EHR) System with the following capabilities:  
- Computerized Physician Order Entry (CPOE)  
- Drug-drug interaction check  
- Drug-allergy interaction check  
- Clinical Decision Support tools (CDS) | *The following EHR vendors have signed the Patient Safety Movement Open Data Pledge:*¹  
- Cerner  
- Epic  
- Allscripts  
- Athena Health |
| **CPOE simulation tool to quantify the risk of serious ADEs with your current system CPOE**²³ | * Leapfrog CPOE Evaluation Tool*⁴ |
| **Drug Libraries** | *  
- Alaris®  
- Baxter®  
- Hospira®  
- Fresenius® |

Technology has significantly advanced in the last decade within the hospital setting with the development of Electronic Health Records (EHR) and computer physician order entry (CPOE) systems. The CPOE, in particular, has been identified as a potential key action in improving patient safety (Kuperman and Gibson, 2003). Computer clinical decision support programs exist that complement the EHR and CPOE, which can provide epidemiologic data (e.g., antibiogram), warnings (drug interactions, excess dosages), allergies, or therapy guidelines (drug-bug mismatches) in real-time during order entry or chart review. Such performance capabilities have demonstrated increases in patient safety, cost savings, and decreased time allotted to ASP activities (Kullar and Goff, 2014; Evans et al, 1998).

As a complement to EHRs, CPOE systems, and decision support software, computer-based surveillance programs have also been developed and implemented in the hospital settings and used specifically in ASPs. These programs have been used to collect data on hospital-acquired infections and adverse drug reactions (Dellit et al, 2007; Evans, 1986). Thus, incorporating surveillance programs and CPOE with decision support programs can likely benefit patient safety and the ASP by providing real-time data at the point of care, leading to improved clinical decisions and facilitating data collection for antimicrobial targeting or interventions (Dellit et al., 2007).

**Conclusion**

The ASP plays a critical role in patient safety. Hospitals that undergo Joint Commission accreditation or participate in Medicare and Medicaid are now required by law to have a formal antimicrobial stewardship program in place comprised of at least an ID physician and clinical pharmacist, but should ideally also include nursing, a microbiologist, infection control and IT personnel. A number of interventions and different program types can make up the ASP, which includes actions from the pharmacy, microbiology, and IT departments. The resources required for implementing the ASP can range from minimal resources to dedicated resources (Table 1); however, once implemented, ASP initiatives can increase patient safety, reduce resistance rates, decrease hospital costs, and improve patient clinical outcomes.

**Table 1: Interventions and required resources**

<table>
<thead>
<tr>
<th>Intervention/Program</th>
<th>Minimal resources required</th>
<th>Dedicated resources required</th>
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<tbody>
<tr>
<td>IV to PO conversion</td>
<td>Pharmacist</td>
<td></td>
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<tr>
<td>Antimicrobial dosage adj.</td>
<td>Pharmacist</td>
<td></td>
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<tr>
<td>Automatic alerts</td>
<td>IT</td>
<td></td>
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<tr>
<td>Automatic stop orders</td>
<td>IT</td>
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<tr>
<td>Restrictive/Formulary ASP</td>
<td>ID physician, clinical pharmacist</td>
<td></td>
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<tr>
<td>Prospective audit with feedback</td>
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<td>ASP committee</td>
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Hybrid: Prospective audit with feedback & Restrictive ASP

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<tr>
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<th>ASP committee</th>
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<tbody>
<tr>
<td>Antibiogram (hospital-specific)</td>
<td>Micro lab</td>
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<tr>
<td>Selective susceptibility reporting/SDD</td>
<td>Micro Lab</td>
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<tr>
<td>EHR/CPOE</td>
<td>IT, funding</td>
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<tr>
<td>Decision support programs</td>
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**Conflicts of Interest Disclosure**
The Patient Safety Movement Foundation partners with as many stakeholders as possible to focus on how to address patient safety challenges. The recommendations in the APSS are developed by workgroups that may include patient safety experts, healthcare technology professionals, hospital leaders, patient advocates, and medical technology industry volunteers. Some of the APSS recommend technologies offered by companies involved in the Patient Safety Movement Foundation that the workgroups have concluded, based on available evidence, are beneficial in addressing the patient safety issues addressed in the APSS. Workgroup members are required to disclose any potential conflicts of interest.
References


