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Actionable Patient Safety Solution (APSS) #3B: Antimicrobial Stewardship: The Role of A Pharmacy And The Microbiology Lab In Patient Safety

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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. This risk can be greatly reduced by an Antimicrobial Stewardship Program (ASP), which requires an implementation plan that includes the following actionable steps:

☐ 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 and 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

The Performance Gap

On September 29, 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.[1] 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 and microbiologist. 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] and 2) outcomes associated with changes in antibiotic use. For instance, a metric that is used to determine the impact of the ASP is by calculating the defined daily doses (DDDs) 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 an aid in 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. According to a number of studies, approximately 25% of adverse drug events arise from antimicrobial use.[2,3] 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.[4] 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.

As antimicrobials are dispensed by the pharmacy, it is an important clinical responsibility of the pharmacist to ensure the optimal use of antimicrobial agents and educate healthcare professionals and patients within the hospital setting. Functions related to this responsibility of the pharmacist may include and are not limited to the interventions described below.

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

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[1] California Legislative Information. (2014). SB-1311 hospitals: Antimicrobial stewardship. Retrieved from: http://leginfo.legislature.ca.gov/faces/billNavClient.xhtml?bill_id=201320140SB1311

[2] Bates, D. W., Cullen, D. J., Laird, N., Petersen, L. A., Small, S. D., Servi, D., ... & Vander Vliet, M. (1995). Incidence of adverse drug events and potential adverse drug events: Implications for prevention. Jama, 274(1), 29-34.

[3] Lesar, T. S., Briceland, L., & Stein, D. S. (1997). Factors related to errors in medication prescribing. Jama, 277(4), 312-317.

[4] Shehab, N., Patel, P. R., Srinivasan, A., & Budnitz, D. S. (2008). Emergency department visits for antibiotic-associated adverse events. Clinical Infectious Diseases, 47(6), 735-743.

- 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 specified 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.*

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 for Carbapenem Resistant Enterobacteriaceae 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 cefepime, 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:[5,6]

- 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.[5] 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.[7,8]

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

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[5] Centers for Disease Control and Prevention. (2015). Core elements of hospital antibiotic stewardship programs. Retrieved from: https://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html

[6] Dellit, T. H., Owens, R. C., McGowan, J. E., Gerding, D. N., Weinstein, R. A., Burke, J. P., ... & Brennan, P. J. (2007). Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clinical Infectious Diseases, 44(2), 159-177.

[7] Goff, D. A., Bauer, K. A., Reed, E. E., Stevenson, K. B., Taylor, J. J., & West, J. E. (2012). Is the "low-hanging fruit" worth picking for antimicrobial stewardship programs?. Clinical Infectious Diseases, cis494.

[8] Dellit, T. H., Owens, R. C., McGowan, J. E., Gerding, D. N., Weinstein, R. A., Burke, J. P., ... & Brennan, P. J. (2007). Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clinical Infectious Diseases, 44(2), 159-177.

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.[8]

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.[7] 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.[5] 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.

System or Practice	Available Technology
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:*[9] ● Cerner ● GE Healthcare
CPOE simulation tool to quantify the risk of serious ADEs with your current system CPOE[10,11]	● Leapfrog CPOE Evaluation Tool[12]
Drug Libraries	● Alaris® ● Baxter® ● Hospira® ● Fresenius® ● B.Braun® I.V. pumps ● BD Intelliport™ Medication Management System for I.V. injectables, or comparable systems.
Pharmacy Workflow Manager	● DoseEdge® from Baxter Healthcare®

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,

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[9] Patient Safety Movement Foundation. Healthcare Technology Pledges. Retrieved from: http://patientsafetymovement.org/challenges-solutions/commitments-pledges/healthcare-technology-pledges/
[10] Metzger, J., Welebob, E., Bates, D. W., Lipsitz, S., & Classen, D. C. (2010). Mixed results in the safety performance of computerized physician order entry. Health Affairs, 29(4), 655-663.
[11] Leung, A. A., Keohane, C., Lipsitz, S., Zimlichman, E., Amato, M., Simon, S. R., ... & Seger, D. L. (2013). Relationship between medication event rates and the Leapfrog computerized physician order entry evaluation tool. Journal of the American Medical Informatics Association, 20(e1), e85-e90.
[12] The Leapfrog Group. (2016). Prepare for CPOE Tool. Retrieved from: http://www.leapfroggroup.org/survey-materials/prepare-cpoe-tool

has been identified as a potential key action in improving patient safety.[13] 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.[14,15]

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.[8,16] 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.[8]

Conclusion

The ASP plays a critical role in patient safety. Hospitals in California are now required by law to have an antimicrobial stewardship committee comprised of at least an ID physician and clinical pharmacist, but should ideally also include 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.

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[13] Kuperman, G. J., & Gibson, R. F. (2003). Computer physician order entry: Benefits, costs, and issues. Annals of Internal Medicine, 139(1), 31-39.

[14] Evans, R. S., Pestotnik, S. L., Classen, D. C., Clemmer, T. P., Weaver, L. K., Orme Jr, J. F., ... & Burke, J. P. (1998). A computer-assisted management program for antibiotics and other antiinfective agents. New England Journal of Medicine, 338(4), 232-238.

[15] Kullar, R., & Goff, D. A. (2014). Transformation of antimicrobial stewardship programs through technology and informatics. Infectious Disease Clinics of North America, 28(2), 291-300.

[16] Evans, R. S., Larsen, R. A., Burke, J. P., Gardner, R. M., Meier, F. A., Jacobson, J. A., ... & Hulse, R. K. (1986). Computer surveillance of hospital-acquired infections and antibiotic use. Jama, 256(8), 1007-1011.

Table 1: Interventions and required resources

Intervention/Program	Minimal resources required	Dedicated resources required
IV to PO conversion	Pharmacist	
Antimicrobial dosage adjustments	Pharmacist	
Automatic alerts	IT	
Automatic stop orders	IT	
Restrictive/Formulary ASP	ID physician, clinical pharmacist	
Prospective audit with feedback		ASP committee
Hybrid: Prospective audit with feedback & Restrictive ASP		ASP committee
Antibiogram (hospital-specific)	Micro lab	
Selective susceptibility reporting/SDD	Micro Lab	
EHR/CPOE		IT, funding
Decision support programs		IT, funding

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Revision History

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