



Antimicrobial Stewardship:

Arizona Partnerships Working to Improve the Use of Antimicrobials in the Hospital and Community

Part 6

“Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.”

- Glenn Tillotson; Clin Infect Dis. 2010;51:752

“...we hold closely the principles that antibiotics are a gift to us from prior generations and that we have a moral obligation to ensure that this global treasure is available for our children and future generations.”

**- David Gilbert, et al (and the Infectious
Diseases Society of America). Clin Infect Dis.
2010;51:754-5**

A Note To Our Readers and Slide Presenters

The objectives of the Subcommittee on Antimicrobial Stewardship Programs are directed at education, presentation, and identification of resources for clinicians to create toolkits of strategies that will assist clinicians with understanding, implementing, measuring, and maintaining antimicrobial stewardship programs.

The slide compendium was developed by the Subcommittee on Antimicrobial Stewardship Programs (ASP) of the Arizona Healthcare-Associated Infection (HAI) Advisory Committee in 2012-2013.

ASP is a multidisciplinary committee representing various healthcare disciplines working to define and provide guidance for establishing and maintaining an antimicrobial stewardship programs within acute care and long-term care institutions and in the community.

Their work was guided by the best available evidence at the time although the subject matter encompassed thousands of references. Accordingly, the Subcommittee selectively used examples from the published literature to provide guidance and evidenced-based criteria regarding antimicrobial stewardship. The slide compendium reflects consensus on criteria which the HAI Advisory Committee deems to represent prudent practice.

Disclaimers

All scientific and technical material included in the slide compendium applied rigorous scientific standards and peer review by the Subcommittee on Antimicrobial Stewardship Programs to ensure the accuracy and reliability of the data. The Subcommittee reviewed hundreds of published studies for the purposes of defining antimicrobial stewardship for Arizonan clinicians. The Arizona Department of Health Services (ADHS) and members of its subcommittees assume no responsibility for the opinions and interpretations of the data from published studies selected for inclusion in the slide compendium.

ADHS routinely seeks the input of highly qualified peer reviewers on the propriety, accuracy, completeness, and quality (including objectivity, utility, and integrity) of its materials. Although the specific application of peer review throughout the scientific process may vary, the overall goal is to obtain an objective evaluation of scientific information from its fellow scientists, consultants, and Committees.

Please credit ADHS for development of its slides and other tools. Please provide a link to the ADHS website when these material are used.

Introduction to Slide Section

Reasons to Optimize Antibiotic Use

Pathways to a Successful ASP

Antimicrobial Stewardship: Making the Case

ASPs: Nuts & Bolts

Antimicrobial Stewardship: Measuring Antibiotic Utilization

Antimicrobial Stewardship: Daily Activities

Antimicrobial Stewardship: Computerized & Clinical Decision Support Services

Microbiology: Cumulative Antibigram & Rapid Diagnostics

Antimicrobial Stewardship Projects: Initiation & Advanced

Antimicrobial Stewardship Barriers & Challenges: Structural & Functional

Antibiotic Use in the Community

Opportunities to Justify Continuing the ASP

Antimicrobial Stewardship: Perspectives to Consider

Summary

- **Preface:**

Deciding upon an antimicrobial formulary strategy, such as pre-authorization versus prospective audit-review-feedback will depend upon the ASP's philosophy, desired intensity of antimicrobial order review, and the available workforce and level of education. Various strategies and tactics are discussed as parts of low-hanging fruit (initial) and high-hanging fruit (advanced) programs. Seven potential intervention categories (for documentation) are studied.

- **Content:**

15 slides including 3 back-up slides. This slide section provides a valuable starting point for defining the daily activities of the ASP pharmacist and other members of the team. Please allow one hour for presentation and discussion.

- **Suggestions for Presentation:**

ASP team members and pharmacists are important audiences.

- **Comments:**

A brief history of institutional activities is discussed, but the initial daily activities may be more dependent on defining opportunities, such as patient rounds, high-admission physicians, or specific prescribing issues. However, as the ASP evolves additional activities as well as projects should become obvious.

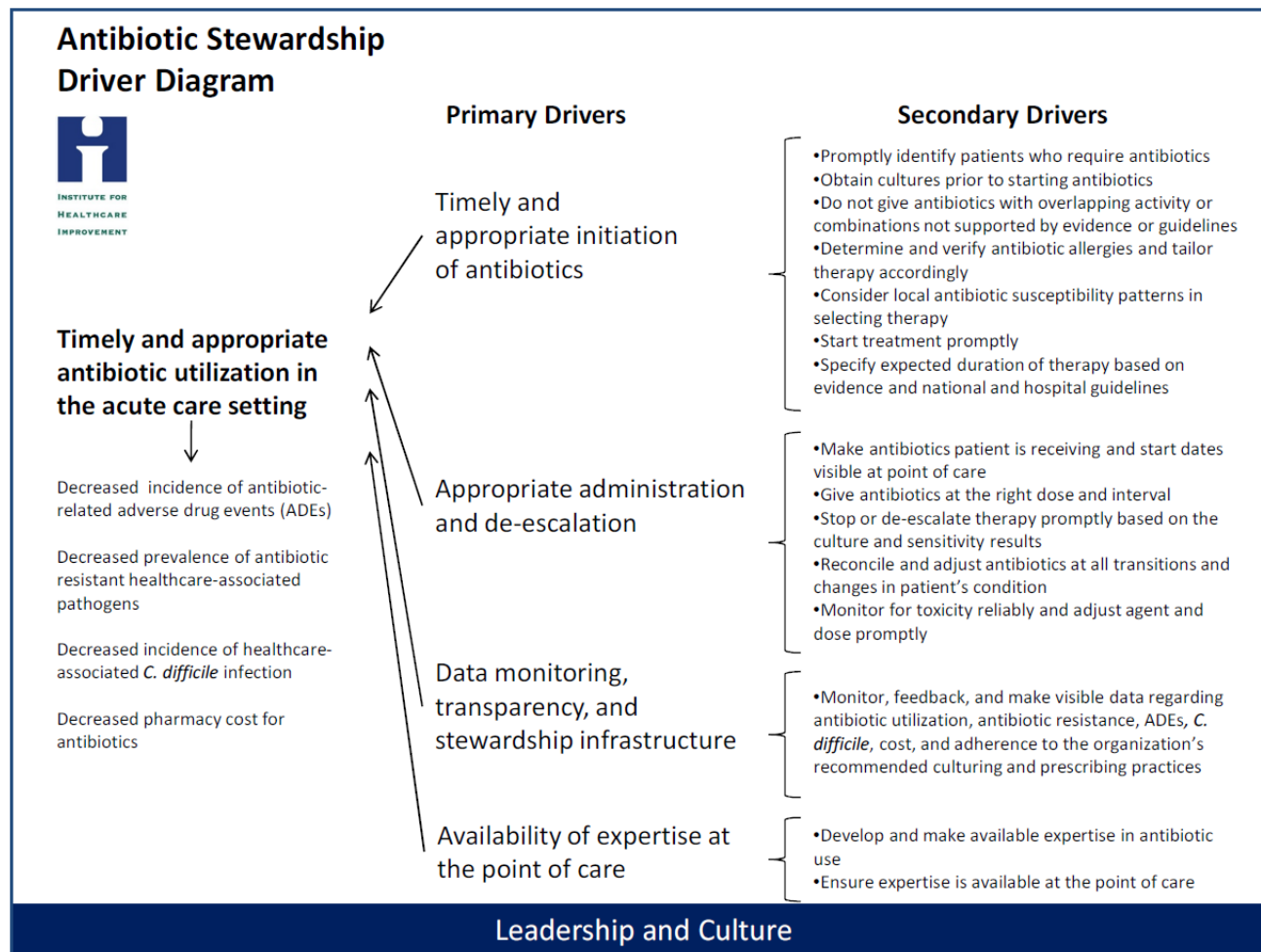
ANTIMICROBIAL STEWARDSHIP: DAILY ACTIVITIES

Applying Antibiotic Stewardship Principles to Everyday Practice

- Antibiotic stewardship includes the following key principles:¹
 - Selection of the most appropriate antimicrobial treatment
 - Optimization of drug selection, dosing and duration of therapy needed to cure infection and reduce emergence of resistance
 - Improvement of patient safety through reducing the risk of toxicity, adverse effects, and hospital-acquired infections
- Core Strategies:
 - Pre-authorization/formulary restriction
 - Prospective review and feedback
- Other Strategies: Education, guidelines, order sets, dose optimization, IV to PO switch, streamlining of therapy, information technology
- Institutional comprehensive programs incorporate multiple strategies and gain cooperation among different professionals in health care

CDC and the Driver Diagram

IHI and CDC partnership to organize theories and ideas needed for improvement



Current Antibiotic Stewardship Programs: Two Month Electronic Survey (2008, n=357)

- Hospitals with established or developing ASPs demonstrated use of two core stewardship strategies:
 - Prospective monitoring of prescribing and appropriateness after the first dose of a targeted antibiotic (66%)
 - Preauthorization/restriction (38%)
 - Other strategies: time-sensitive automatic stop orders with reevaluation (40%); use of local antibiograms (95%); and tracking resistance patterns (76%)
- 52% of respondents stated their hospital did not have an antibiotic stewardship program, although most of these hospitals performed supplemental strategies of stewardship to a similar extent as hospitals with established ASPs:
 - Closed formularies (73% vs 80%), education of prescribers (69% vs 77%), guidelines/clinical pathways (60% vs 69%), automatic substitutions (72% vs 72%), automatic dose adjustments by pharmacy (49% vs 49%), and IV-to-PO conversion protocols for pharmacy (41% vs 46%), respectively
- Hospitals with an established ASP differed from those without an ASP:
 - Proactive pharmacy-driven streamlining and/or de-escalation (42% vs 26%) and dose optimization (56% vs 45%)

Approaches to Core Stewardship Strategy: Formulary Restriction and Preauthorization

Procedure	Personnel	Advantages	Disadvantages
▪ Restrict dispensing of targeted antimicrobials to approved indications ▪ Formulary adherence ▪ Automatic switches within class	▪ Antimicrobial committee to create guidelines ▪ Approval personnel (physicians, ID fellows, clinical pharmacist)	▪ Most direct control over antimicrobial use – immediate and significant reductions in use and cost ▪ Individual educational opportunities ▪ Compliance rates not determined by contacting physician ▪ More guidelines mean more interventions ▪ Most responsive measure to nosocomial outbreak of infection ▪ Can serve as ID hotline for general advice	▪ Perceived loss of autonomy for prescribers; confrontational ▪ Need for all- hours consult; labor-intensive; ▪ Potential delay in therapy ▪ Non-targeted antimicrobials not reviewed ▪ May simply shift use from one agent to another (“squeezing the balloon”) ▪ Intense monitoring of overall trends in use

Approaches to Core Stewardship Strategy: Prospective Audit, Intervention and Feedback

Procedure	Personnel	Advantages	Disadvantages
▪ Prospective and daily review of antimicrobials for appropriateness ▪ Contact prescribers to recommend alternative therapy ▪ Focus on other activities, e.g., IV-to-PO switch, de-escalation, disease state management and outcomes	▪ Antimicrobial committee to create guidelines ▪ Personnel available for regimen review (usually clinical pharmacists)	▪ Post-prescription intervention by clinician given authority (or AST) ▪ Avoids loss of autonomy for prescribers ▪ Direct individual educational opportunities and feedback	▪ Compliance is voluntary and may be as low as 20% ▪ Delayed antimicrobial stewardship ▪ Additional staffing and/or responsibility at each facility

Seven Potential Interventions

INTERVENTION and DOCUMENTATION CLASS	COMMENTS and EXAMPLES
IV-to-PO sequential therapy	• Many agents have oral formulations or similar oral equivalents • It involves a target IV antibiotic list and simple guidelines for assessing patient clinical and GI status <u>EXAMPLES:</u> fluoroquinolones, clindamycin, ampicillin/sulbactam, linezolid, metronidazole, fluconazole, voriconazole, etc.
Dose optimization (PK/PD principles)	• Adjusting doses for renally-eliminated antibiotics • Addresses under-utilized strategies for pharmacodynamic applications (extended infusions, etc) <u>EXAMPLES:</u> Maximum doses of beta-lactams and fluoroquinolones, and extended interval aminoglycosides, in severe disease
Elimination of duplicative therapy	• Consult with ID on frequent combinations observed; prepare guidelines for intervention (e.g., automatic D/C) <u>EXAMPLES:</u> 3rd generation cephalosporin + amikacin for <i>E.coli</i> (both agents demonstrate susceptibility; no ESBL); beta-lactam/beta-lactamase inhibitor + metronidazole for anaerobes; respiratory FQ + clarithromycin for community-acquired pneumonia

Seven Potential Interventions (cont'd)

INTERVENTION and DOCUMENTATION CLASS	COMMENTS and EXAMPLES
Institutional guideline-specific therapy	• Develop and implement once approved by P&T Committee <u>EXAMPLE</u>: Empiric antibiotic treatment of sepsis using hospital antibiogram data; treatment of specific infections where targeted antibiotics are commonly used (e.g. diabetic foot infection)
Discontinuation of therapy based on lack of infectious process	• Evaluate empiric antibiotic regimens on hospital day #2 or #3 for differential diagnosis – determine if infection has been ruled out • Physicians document daily antibiotic plan
De-escalation (based on C&S on HD #2-3; patient improving on current therapy)	• D/C vancomycin if cultures are negative for resistant gram positive bacteria • Follow C&S reports to de-escalate antibiotics to narrower spectrum agents • <u>EXAMPLE</u>: Pneumococcal pneumonia therapy changed to amoxicillin PO if fully susceptible to penicillin
Discontinuation based on clinical resolution of infection	• For CAP, discontinue therapy after ≥ 5 d of treatment if afebrile x 24 hrs and no more than 1 symptom remains indicative of initial infection • Uncomplicated UTI generally resolves with only 3 days of trimethoprim-sulfamethoxazole or fluoroquinolone

Example: Antibiotic Order Form

University of _____

ADULT ANTIMICROBIAL ORDER FORM

USE THIS FORM TO ORDER ALL
ANTINFECTIVE AGENTS FOR TREATMENT

PATIENT IDENTIFICATION

Allergies ☐ Penicillin ☐ Cephalosporins ☐ Sulfonamides ☐ Other _____
Age _____ years Height _____ inches Weight _____ lb/Kg Serum Creatinine _____ mg/ml

All Antibiotic Orders have an Automatic 7 Day Stop Unless Specified. Surgical prophylaxis is initiated in OR.
Continuation of prophylactic antimicrobial therapy, if required at all, MUST be written on the surgical prophylaxis form
(obtained from intranet -go to clinical links/ antimicrobial management) or post operative order sets.

Indication: ☐ Empiric / awaiting culture results ☐ Documented / culture proven

Sites: ☐ Abdominal ☐ Bone and Joint ☐ Genitourinary ☐ Upper Respiratory
☐ Bacteremia ☐ Lower Respiratory ☐ CNS ☐ Skin & Soft Tissue (including surgical wounds) ☐ Other: _____

Pathogen: ☐ Anaerobes ☐ Gram Negative Rods ☐ Streptococcus ☐ Pseudomonas ☐ Viral
☐ Fungal ☐ Staphylococcus ☐ Other: _____

THE FOLLOWING AGENTS REQUIRE APPROVAL OF THE ANTIMICROBIAL TEAM OR THE ID CONSULTANTS:

ANTIMICROBIAL TEAM BEEPER 2847

Amikacin	Cefepime	Fluconazole IV	Imipenem	Moxifloxacin IV
Amphotericin products	Ciprofloxacin IV	Flucytosine	Itraconazole P.O.	Tigecycline
Azithromycin IV	Daptomycin	Foscarnet	Linezolid IV/ P.O.	Vancomycin P.O.
Aztreonam	Ertapenem	Ganciclovir IV	Micafungin	Voriconazole IV/ P.O.
Caspofungin				

RESTRICTED AGENTS APPROVED BY ID ATTENDING OR FELLOW: _____

Select antimicrobial agent and check dose if available. Drugs that are in **BOLD** below require dosage adjustment in renal insufficiency. Consult pharmacy for dosing.

If Initial therapy, please indicate here ☐ STAT

What to Implement and Measure: Low-Hanging vs High-Hanging Fruit

EARLY and SUSTAINED:

(measure basic performances based on initial objectives)

- Decrease antibiotic use (DDD, DOT, or grams utilized adjusted for census)
- Decrease unnecessary combinations (e.g., pip/tazo + metronidazole)
- Decrease vancomycin use
- Increase IV-to-PO conversion (decrease ratio of IV days/PO days)
- Increase compliance with de-escalation when cultures are available
- Improve dose-optimization (not just dose reduction)
- Discuss improvements to antibiogram design

LATER:

(as costs plateau, and initial programs become “auto-pilot”):

- Develop evidence-based guidelines, tailored to institutional data (disease-state)
- Improve appropriateness of empiric therapy
- Discontinue therapy when appropriate
- Institute antibiogram education
- Optimize serum concentration monitoring policies

Approaches to Core Stewardship Strategy: Additional Tactics

Automatic Stop Orders			
Procedures	Personnel	Advantages	Disadvantages
Automatic stop is part of initial antibiotic order	- Approved by Antibiotic Utilization Review (AUR), P&T, and Medical Executive - Strong and experienced ASP	- Decreased antibiotic use and costs - Prescriber needs to justify extended duration - Can be disease-specific when evidenced-based	- Must be closely monitored - All prescribers must be aware of policy - Difficult to implement if CPOE
Development of Clinical Practice Guidelines & Protocols			
Procedures	Personnel	Advantages	Disadvantages
Implementation of best practices	- Approved by AUR, P&T, and probably Medical Executive - Strong and experienced ASP	- Dictates therapy without direct intervention - Educates while enforcing evidenced-based therapies	- Long development phase - Approval by multiple departments - Need to offer alternative regimens

Other Activities: Restricting Target Antibiotics to Reduce Selection of Drug-Resistant Bacteria and *C. difficile*

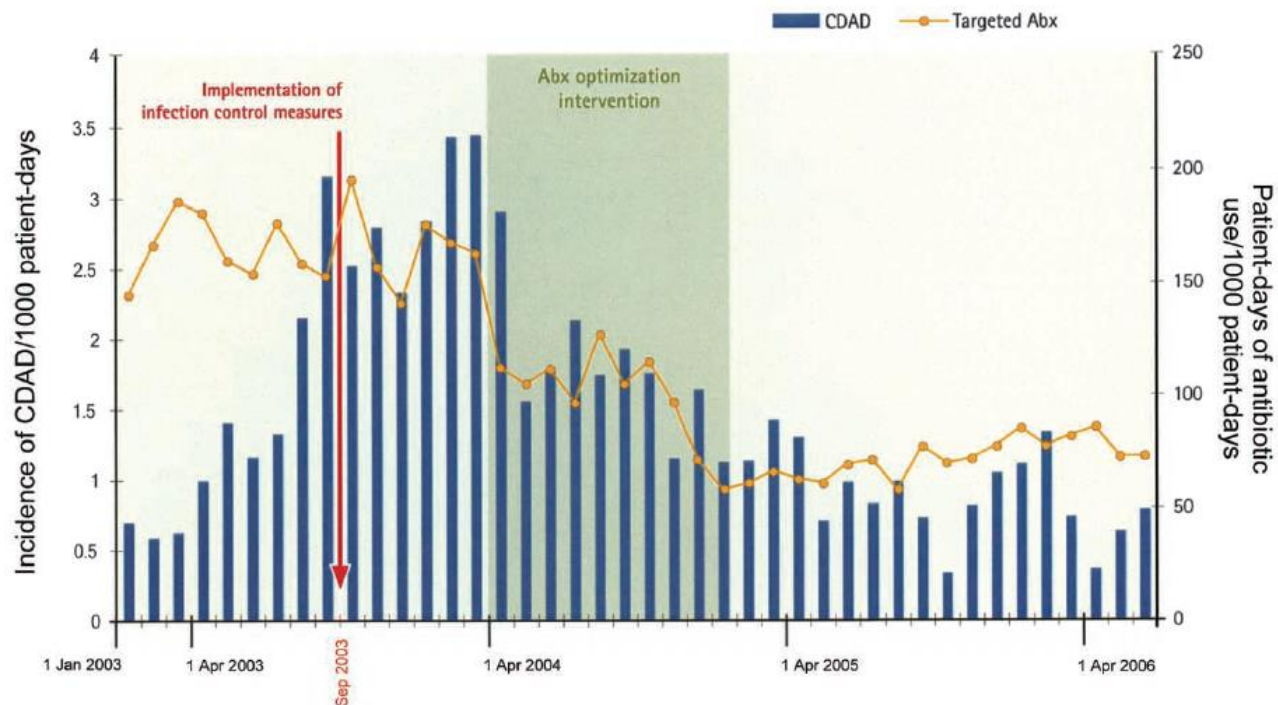
Antimicrobials Associated with Emergence of Resistance in Gram-Negatives	High-Risk Antimicrobials Associated with <i>Clostridium difficile</i> Infection ¹
Fluoroquinolones (example: <i>E. coli</i>)	Fluoroquinolones
Third-generation cephalosporins (example: ESBLs)	2 nd , 3 rd -, or 4 th -generation cephalosporins
Carbapenems (example: KPC)	Carbapenems, clindamycin

Addressing use of selected antimicrobials may decrease selection of some ESBL- and carbapenemase-producing Gram-negative bacilli while also potentially decreasing *C. difficile*

Could be an initial stewardship step in an outbreak situation

Impact of the Use of High-Risk Antibiotics on the Course of an Epidemic of *C. difficile*

- Quebec hospital with epidemic hypervirulent NAP1/027 *C. difficile* strain
- Enhanced infection control procedures did not alter CDI incidence (P=0.63)
- Implementation of an antibiotic stewardship program decreased both total antibiotic consumption (23%) and targeted antibiotic consumption (54%)
- Targeted drugs: cephalosporins, macrolides, clindamycin, ciprofloxacin



Daily Activities: Summary

- Create a reliable and basic daily or weekly on-service plan, allowing time for projects, education, and meetings (e.g., P&T)
 - Example: ICU rounds AM, wound care or transplantation service rounds late morning, lunch with the ASP physician champion/ID physician, educational presentation midday, prospective review of targeted antimicrobials in the afternoon, meeting the ASP ID physician late afternoon (as available), and projects in between
- Ensure that daily activities have high “pay-off potential” determined by the number of intervention opportunities or change of practice
 - ICU rounds are likely to encounter antibiotic use in almost every patient with many consultants for a single patient (“cooks in the kitchen”)
 - Development of CAP guidelines and educational meetings
- Take advantage of complex situations which offer multiple points of intervention
 - Example: Patient A is started on 3 antibiotics, an antiviral, and 2 anti-fungals; de-escalation, consolidation, pathogen-directed therapy, renal dose adjustment, and IV-to-PO conversion may lead to several interventions over 3-5 days
- Every potential intervention or meaningful interaction should be captured through documentation in a well-designed and thorough monthly/quarterly report – “no time to be modest”

ADDITIONAL SLIDES

Adequate Opportunities to Exercise Stewardship: “The 5 D’s” and Interventions

Select Accurate Empiric **D**rug Therapy

- Education using antibiograms
- Consensus Guidelines & clinical pathways; clinical decision support tools
- Antibiotic order forms
- Appropriate consideration of combination therapy

→ Select **D**ose

- Education using PK/PD concepts
- Consensus Guidelines & clinical pathways; clinical decision support tools
- Antibiotic order forms, especially for prolonged infusions
- Use adequate dose/duration to cure infection & reduce toxicity

→ **D**e- Escalate

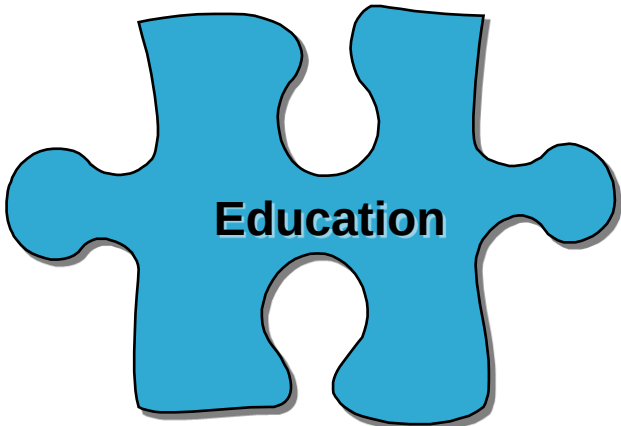
- Education
- Discontinue combinations if not indicated by C&S
- Pathogen-directed therapy based on C&S results
- IV-to-PO therapy

→ Adequate **D**uration

- Education
- Consensus Guidelines & clinical pathways for some infections
- Antibiotic order forms with automatic stop orders
- Clinical decision support tools and computer prompts
- Use adequate dose/duration to cure infection & reduce toxicity

****D**ecreased Potential for Emergence of Resistance**

Selected Activities of Antimicrobial Stewardship



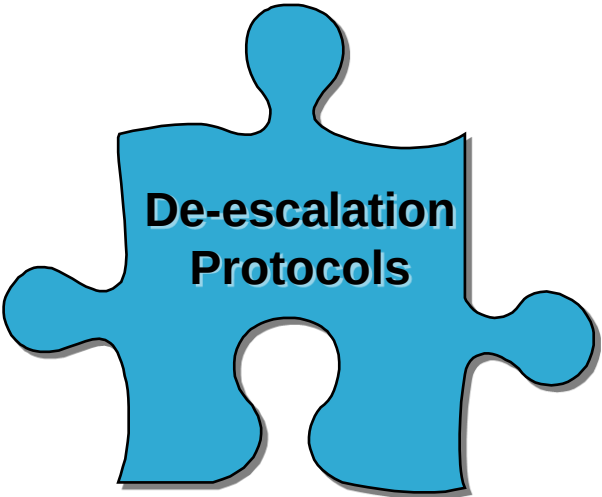
Education



**Appropriate
Duration**



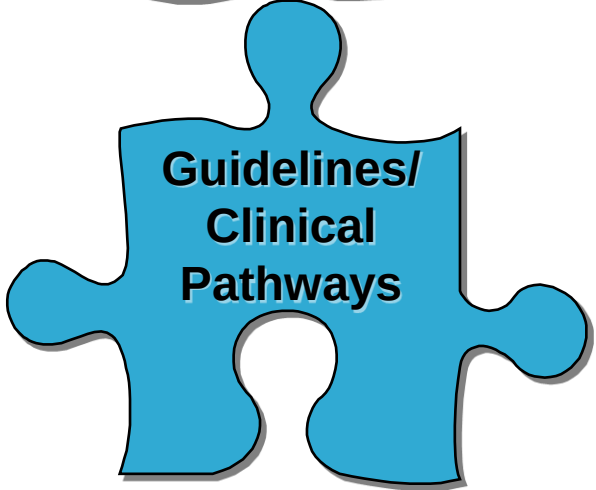
**Parenteral to
Oral Conversion**



**De-escalation
Protocols**



**Drug Selection
and
Dose
Optimization**



**Guidelines/
Clinical
Pathways**

Focus and Intervention:

Another Means of Aligning ASP Objectives and Tactics

