Antimicrobial resistance in microorganisms is driven by exposure to antimicrobial agents, especially subinhibitory concentrations. This exposure results in natural selection of more resistant variants in the population. Thus, to the extent that antimicrobial agents can be used appropriately and judiciously, and in doses and delivery that reduce the likelihood of resistance emerging, antimicrobial resistance can be prevented or reduced. Likewise, it is exposure to antibiotics that precipitates disease due to Clostridium difficile by suppressing the normal bacterial flora of the bowel and providing a favorable environment for the germination, growth and toxin production that leads to C. difficile-associated diseases (CDAD). The appropriate, judicious and correct use of antimicrobial agents to prevent antimicrobial resistance and reduce the likelihood of resistance is referred to as “antimicrobial stewardship”.

Antimicrobial stewardship is designed to assure the most appropriate, effective treatment of infection while reducing emergence of resistance, C. difficile infection and other adverse events. These programs can also reduce costs by maximizing efficacy and minimizing costly complications. Antimicrobial stewardship is a structural approach to reducing undesirable outcomes that has deep roots, but emerged as a comprehensive approach in recent years driven by increasing resistance and the problem presented by CDAD. Some facilities have robust programs in place and many facilities are further developing antimicrobial stewardship programs. There is a need across the spectrum of healthcare provision for information on antimicrobial stewardship and the components of a comprehensive approach.

For more information, see related article on page 6 and recommended resources pp. 6-9. Also visit APUA’s Web site www.apua.org to read back issues of the APUA Newsletter Vol. 26 No. 2&3 “Infection control: a potent AMR containment strategy,” Vol. 26 No. 1, and Vol. 28 No. 1, “Urinary Tract Infections: Antibiotic Guidelines for a Global Problem”.

Mrs. B was a pleasant 56-year old female with a long history of primary biliary cirrhosis who underwent a liver transplantation. Her post-operative course was complicated by recurrent hospitalizations with abdominal wound dehiscence (splitting open) and failure to heal. She was diagnosed with a post-operative wound infection and was treated with appropriate antibiotics. Her abdominal wound improved, but she was hospitalized three months later with shortness of breath and failure to

Continued on Page 3
California’s Model for Antimicrobial Stewardship: Legislation, Consultation, and Accountability

Kavita Trivedi, M.D., Public Health Medical Officer California Department of Public Health

The Healthcare Associated Infections (HAI) Program of the California Department of Public Health (CDPH) has developed a statewide Antimicrobial Stewardship Program (ASP) Initiative in order to strengthen and promote optimization of antimicrobial utilization in California health care facilities. The purpose of an ASP is to promote the appropriate use of antimicrobials by selecting the appropriate agent, dose, duration and route of administration in order to improve patient outcomes, while minimizing toxicity and the emergence of antimicrobial resistance. Although guidelines exist for developing ASPs, there is limited information on practical implementation of these guidelines, particularly in resource limited settings.

California Senate Bill 739 (Health & Safety Code §§ 1288.5 to 1288.9 [2006]) mandated that, by January 1, 2008, CDPH require general acute care hospitals to monitor and evaluate the utilization of antibiotics and assemble a quality improvement committee to oversee the judicious use of these medications. While hospitals were aware of this mandate, they were left to implement programs on their own. In December 2009, the HAI Program was staffed, and by February 2010, a physician was identified to spearhead this initiative. The Licensing and Certification Program at CDPH now assesses hospitals for compliance with this mandate on routine patient licensing surveys.

Current program activities include assessing ASPs in California facilities. With information on specifics of ASPs throughout the state, CDPH is developing evidence-based recommendations on how to implement and strengthen ASPs, given available resources and facility attributes. As of March 2011, preliminary information from 229 acute care hospitals indicates that 48% have a current ASP in place and 28% are planning one. Furthermore, 10% of the 229 hospitals developed an ASP because of SB 739, underscoring the positive effect of statewide legislation. Of hospitals assessed, 177 self-identified community hospitals indicate that 45% currently have an ASP and 29% have one.
forthcoming. Many community hospitals, previously thought to have limited programs regarding the prudent use of antimicrobials, in fact represent best practices regarding antimicrobial use optimization since ASPs help utilize existing resources efficiently.

Other program activities include providing consultative advice and practical evidence to facilities in order to gain administrative and pharmacy buy-in. CDPH is also developing regional and special setting collaborations among hospitals with similar difficulties, such as long-term acute care hospitals, and/or healthcare systems so that facilities can learn from one another and develop system-wide ASPs. CDPH is developing statewide recommendations regarding internal and external outcome measures for ASPs. CDPH is also committed to educating long-term care facilities on the benefits of antimicrobial use optimization and collaborating on research proposals to better study the efficacy of antimicrobial oversight in the long-term care setting. Finally, CDPH is working to expand current statewide legislation/regulation to specify characteristics of ASPs required in California acute care hospitals.

For additional information:  [http://www.cdph.ca.gov/programs/haipages/AntimicrobialStewardshipProgramInitiative.aspx](http://www.cdph.ca.gov/programs/haipages/AntimicrobialStewardshipProgramInitiative.aspx)

**IDSA Stewardship Continued from Page 1**

thrive. She developed septic shock and required intubation with mechanical ventilation. Blood and respiratory cultures revealed a multidrug resistant *Acinetobacter baumanii*, susceptible only to meropenem and colistin. Despite two weeks of appropriate antimicrobial therapy, she remained bacteremic and no clear focus of infection could be identified. After three weeks with persistent bacteremia, the organism became resistant to all drugs including colistin. The patient never cleared the bacteremia and ultimately died.

If you have any doubt that we are getting closer to the pre-antibiotic area, you are probably wrong. Perhaps you will be the next physician taking care of a patient with a multidrug resistant infection or, worse (depending on one’s perspective), you yourself could contract a multidrug resistant organism for which there is no effective antimicrobial therapy available. Unfortunately, this is not science fiction, or a new unknown infection from an exotic land. Antimicrobial resistance is a serious problem worldwide - there are no new options to treat multidrug resistant gram-negative organisms, with very few drugs in the development pipeline.

This year, The World Health Organization (WHO) selected “combat antimicrobial resistance” as the theme for World Health Day. On April 7, 2011, WHO issued an international call for concerted action to halt the spread of antimicrobial resistance and recommends a 6-point package of policies for governments and stakeholders to prevent and counter the emergence of highly resistant microorganisms. Development of new antimicrobials is one of the issues. We agree that the development of new drugs for multidrug resistant organisms should be a public health priority; nonetheless, “The development of new antibiotics without having mechanisms to insure their appropriate use is much like supplying your alcoholic patients with a finer brandy.” (Dennis Maki, IDSA meeting, 1998).

In an effort to improve the appropriate use of antibiotics and prevent the development of further antimicrobial resistance, the Infectious Diseases Society of America published in 2007 the “Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship”. The purpose of an Antimicrobial Stewardship Program (ASP) is to improve patient care by optimizing selection, dosing, route, and duration of antimicrobial therapy to maximize clinical cure or prevention of infection while limiting the unintended consequences, such as the development of resistance, adverse drug events, and costs. Successful programs have been shown to improve patient care while being financially self-supporting.

As discussed in the IDSA ASP guidelines, there are two core strategies recommended for use by ASPs:

- Prospective audit and feedback
- Formulary restriction and preauthorization

Other important components to effectively impact the appropriate use of antibiotics are:

- Education
- Guidelines and clinical pathways
- Antimicrobial order forms or electronic order sets
- Streamlining or de-escalation of empirical antimicrobial therapy
- Optimization of antimicrobial dosing
- Parenteral to oral conversion
- Health care information technology
- Computer-based surveillance

**Continued on p. 4**
The clinical microbiology laboratory plays a critical role in antimicrobial stewardship by providing patient-specific culture and susceptibility data to optimize individual antimicrobial management and by assisting infection control efforts in the surveillance of resistant organisms. Rapid molecular diagnostics are urgently needed to assist in the selection of appropriate empirical antimicrobial therapy, and to avoid the prolonged unnecessary use of antimicrobial agents while awaiting culture results.

It is extremely important that physicians recognize the need for, and the value of, ASPs and support their existence in hospitals. The optimal structure and components of ASPs will vary according to local circumstances. However, a successful program requires the involvement of well trained and enthusiastic physicians and pharmacists and the strong support of the hospital administration and medical staff. Interested physicians and pharmacists can usually demonstrate to institutions that an ASP can pay for itself in short order by reducing pharmacy costs and reducing length of stays.

In summary, we need to use our resources wisely; “to widen access to appropriate medications to encompass all people – regardless of race, gender, or socio-economic status – while at the same time reserving these precious compounds to treat only those diseases for which they are specifically required”. Our grandparents lived during an age without antimicrobials. The potential of drug resistance to catapult us all back into a world of premature death and chronic illness is all too real. As we age and ponder our inevitable entry into the age demographic in which our risk of hospitalization is not negligible, such as for joint replacement or other such procedure, it is worth thinking about how we might react to acquiring a prosthetic device MRSA infection or a multidrug-resistant Pseudomonas or Acinetobacter pneumonia. We must all recognize the seriousness of this problem and commit ourselves to using these precious resources wisely. Many of us believe that knowingly using antimicrobials in situations where they are not indicated is unethical. ASPs can help us identify such situations and avoid inappropriate antimicrobial use. We have the means to ensure that our antimicrobial armamentarium remains effective, but we are running out of time. Please support (or initiate) your local antimicrobial stewardship program. The time to act is today.

For additional information: [http://www.idsociety.org/STAARAct.htm](http://www.idsociety.org/STAARAct.htm)

For guidelines: [http://cid.oxfordjournals.org/content/44/2/159.full.pdf](http://cid.oxfordjournals.org/content/44/2/159.full.pdf)

For more information on Diagnostics see APUA Newsletter Vol. 25 No. 1

The WHO released “Step-by-step approach for development and implementation of hospital antibiotic policy and standard treatment guidelines” stating that good antimicrobial stewardship involves selecting an appropriate drug and optimizing its dose and duration to cure infection while minimizing toxicity and conditions for selection of resistant bacterial claims. There are many benefits of stewardship including reduced risk for spread of resistance and super infection, development of resistance and suppression of normal flora as well as development of resistance in pathogens infecting the patient.

For full report see [www.searo.who.int/LinkFiles/WHD-11_ha-policy.pdf](http://www.searo.who.int/LinkFiles/WHD-11_ha-policy.pdf)

### The Ideal Antimicrobial Stewardship Program

<table>
<thead>
<tr>
<th>Infectious Diseases</th>
<th>Pharmacy</th>
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<tbody>
<tr>
<td>ASP</td>
<td>Infectious Diseases</td>
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<tr>
<td>Information and Technology (IT)</td>
<td>MD &amp; PharmD</td>
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<tr>
<td>Microbiology</td>
<td>Infection control</td>
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<tr>
<td>Hospital Leadership</td>
<td>Patient Safety</td>
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<tr>
<td>Data analyst</td>
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**References**

When It’s Time for an “Antibiotic Time Out”

Arjun Srinivasan, M.D.
Medical Director, Get Smart for Healthcare Program
Centers for Disease Control

Every few years there are reports of antibiotic resistant microbes that prompt a series of predictions about “the end of antibiotics.” It happened in the 1990s with multi-drug resistant tuberculosis and then again earlier this decade with methicillin-resistant Staphylococcus aureus or MRSA. It’s happening once more with carbapenem-resistant Enterobacteriaceae or CRE.

One of the reasons our current antibiotics are losing their effectiveness is because we don’t use them properly. Studies have shown, repeatedly, that up to 50% of antibiotic prescriptions are either unnecessary or inappropriate. Not only does this overuse reduce the effectiveness of our current antibiotics, it threatens the utility of any new antibiotics that come along in the future. In addition to reducing antibiotic overuse, it is important that we prevent the transmission of resistant organisms through the implementation of effective infection prevention measures, and that we continue to research new vaccines and diagnostics which can aide in their control.

While we work on new antibiotics for the future, there is much that must be done right now to both preserve the lifespan of the antibiotics we currently have and to pave the way to ensure prolonged usefulness of new antibiotics that are developed. The most important immediate need is to reduce the overuse of these drugs. Reducing antibiotic overuse is good for society as a whole, but it is also good for individual patients.

For healthcare providers, there are three simple things that can be done to ensure antibiotics are being prescribed wisely.

First, all antibiotic orders should include three pieces of information – a dose, duration, and indication. Too often, antibiotics in hospitals are continued unnecessarily simply because clinicians caring for the patient do not have the information indicating why the antibiotics were started in the first place, or how long they were to be continued. It is certainly harder to stop therapy if it is unknown why it was started in the first place. This challenge is compounded in today’s healthcare system where the primary responsibility for patient care is transitioned frequently from one clinician to another. Ensuring that all antibiotic orders are accompanied by the dose, duration, and indication will certainly help other clinicians caring for the patient to change – or stop – therapy when appropriate.

Second, when an antibiotic order is placed, it should include microbiology cultures. Knowing the susceptibility of the infecting organism can allow clinicians to narrow a broad-spectrum therapy, change the therapy to better treat resistant pathogens, or stop antibiotics when the culture results suggest an infection is unlikely.

Third, when culture results return in 24-48 hours, it’s time for an antibiotic “time-out”. This is the time to stop and reassess therapy. Antibiotics are generally started before a patient’s full clinical picture is known. After 24 to 48 hours, it is time to re-evaluate why the therapy was started in the first place and gather all of the evidence to determine whether there should be a change in the course of therapy or whether antibiotics should be stopped altogether (if an infection no longer appears likely). If data suggest an antibiotic is needed, this can be a good time to narrow therapy and specify a final duration of therapy.

As we look ahead, we should remember that antibiotics are a shared resource – and for some infections, they are a scarce resource. The solution is not just to identify new antibiotics. Experts agree that it will be years until we have new antibiotics available for use. Even then, if we don’t improve the way antibiotics are used, the new drugs will be lost, too. We must preserve the antibiotics that we have now by implementing effective strategies to use antibiotics wisely. But the benefits are not just societal or long-term. Improving antibiotic use can and will improve outcomes for individual patients right now. We must begin to view antibiotic stewardship as the important patient safety issue that it is.

It is time to take an “antibiotic time out.” It is time to take action and improve our use of antibiotics. These actions – often referred to as antibiotic stewardship – will preserve a precious resource and ultimately save lives.

For additional information:
http://www.cdc.gov/getsmart/
For additional information on Diagnostics see APUA Newsletter Vol. 27 No. 1&2

Expected Benefits of Antibiotic Stewardship Programs (ASP)*

- Savings in the range of 20-35% have been reported
- Mostly realized through reduced acquisition costs
- Indirect savings may also be achieved
- ASP costs mostly driven by salaries and support for ASP leaders and participants
- Consider 0.5 FTE for a physician and a 1.5 FTE for pharmacists

*From the Joint Commission on Accreditation of Healthcare Organizations
APUA and Tufts Medical Center Join Massachusetts Partners in Statewide Stewardship Training

Kenneth Lawrence, BS, PharmD
Lisa Davidson, M.D.
Shira I. Doron, M.D., MS
Tufts Medical Center, Boston, MA.

As names like MRSA, ESBL, KPC, AmpC, NDM-1 and CDI become part of the public’s vocabulary, healthcare providers are witnessing an ever increasing move towards a time when our commercially available antimicrobial agents are no longer able to treat infections caused by the most resistant bacteria—those with so-called “extreme” drug resistance (XDR) or pan-resistance.

Unlike past decades in which the approval of newer antimicrobial agents could keep pace with development of new mechanisms for antimicrobial resistance, FDA approval of new antimicrobials has decreased 56% between 1983 and 2002. The continued overuse and inappropriate use of antimicrobial agents results in a significant negative impact on the healthcare system and society in general. However, this is due not only to the cost of treating patients who may develop infections caused by multidrug resistant organisms, but also to the costs of unintended adverse events associated with overuse of antibiotics.

To combat these issues, many healthcare systems have developed a systematic approach to monitoring prescribing of antimicrobial agents. These interventions seek to ensure that all patients are prescribed antimicrobials for an appropriate indication, while also receiving them at the proper dose and duration based on the available evidence. These programs are collectively referred to as “antimicrobial stewardship”.

Essential participants in an antimicrobial stewardship program include the following: an infectious disease physician and infectious disease pharmacist with support from the microbiology laboratory, an infection preventionist, information technology, and hospital administration.

The literature is replete with single and some multicenter studies that demonstrate the sustained benefit of antimicrobial stewardship programs. Elements of these are varied, but may include: development of institutional based clinical guidelines; the use of computer-based decision support that may assist a clinician in choosing an appropriate antimicrobial agent based on previous antimicrobial use; organ function; and the cumulative susceptibility report for the unit or hospital. Two commonly and often cited means of antimicrobial stewardship include restrictive prescriptive authority and a prospective review with clinician feedback.

Restrictive prescriptive authority limits the availability of antimicrobials through the use of a preapproval process or by use of formulary that limits the availability of specific antibiotics. Restrictive programs may also improve the selection of antimicrobials based on the route of administration, medication allergies, kidney and liver function and concurrent medications.

Prospective review and clinician feedback permits clinicians to make empirical antimicrobial choices based on patient-specific factors. However, once culture and susceptibility data are available, an infectious disease pharmacist or physician provides recommendations about appropriate antimicrobial therapy and its duration based upon the pathogen(s) causing infection.

There is a need across the spectrum of healthcare for information on antibiotic stewardship and the components of a comprehensive approach.

APUA Recommends

When once is not enough – further evidence of procalcitonin-guided antibiotic stewardship
S. Harbarth, W.C. Albrich, and B. Müller in Critical Care: 2009

Emerging trends in antibiotic use in US hospitals: quality, quantification and stewardship
J.T. Jacob; R.P. Gaynes, in the Expert Review of Anti-Infective Therapy, Volume 8, Number 8, August 2010 , pp. 893-902(10)

Antimicrobial stewardship: an evidence-based, antimicrobial self-assessment toolkit (ASAT) for acute hospitals

Improving Antibiotic Stewardship: Order Set Implementation to Improve Prophylactic Antimicrobial Prescribing in the Outpatient Surgical Setting
C.C. Braxton, Carla C. MD, MBA, FACS; Gerstenberger, Patricia A. BSN; Cox, Glendon G. MD, MHSA, MBA in the Journal of Ambulatory Care Management: April/June 2010 - Volume 33
Online Resources for Antibiotic Stewardship

**Comprehensive Web sites from national and international organizations with information on many aspects of antibiotic stewardship**

- Center for Disease Control and Prevention — http://www.cdc.gov/getsmart/healthcare/
- Antibiotic Resistance Alliance Education Wisconsin — http://www.areasinitiatives.org/
- European Project Group "ABS International" — http://www.abs-international.eu/
- Appropriate Antibiotic Prescribing — http://www.dundee.ac.uk/clinskills/projects/apt.htm

**Institutional Web sites with established antimicrobial stewardship programs**

- Nebraska Medical Center — http://www.nebraskamed.com/careers/education-programs/asp
- Wake Forest University Baptist Medical Center — http://www.wakehealth.edu/id/hosp/antimicrobial-stewardship/
- The University of Pennsylvania Health System — http://www.uphs.upenn.edu/bugdrug/
- Johns Hopkins Medical Institutions — http://www.hopkinsmedicine.org/amp
- University of Kentucky Chandler Medical Center — http://www.hosp.uky.edu/pharmacy/

**Other Web sites of interest for persons committed to antimicrobial stewardship**

- Prudent antibiotic User Website — http://pause-online.org.uk/
- Academy for Infection Management — http://infectionacademy.org/
- Premier Inc. — http://www.premierinc.com/quality-safety/tools-services/safety/topics/guidelines/other.jsp
- Bugs and Drugs—Antimicrobial Reference Book — http://www.bugsanddrugs.ca/


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**Antibiogram Template: Sample Tool**

According to accepted standards, data should only be reported for isolates for which 10 or more isolates were recovered during the preceding period.

| ISOLATES FROM ALL ADULTS | A | B | C | D | E | F | G | H | J | K | L | M | N | O | P | Q | T | U | V | W | Z | AA | AB | AC | AD | AE | AF |
| Gram-positive            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Enterococci             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Staphylococci aureus    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Enterococci faecalis    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Staphylococci epidermidis|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Other gram-positive     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Gram-negative           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Enterobacteriaceae      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pseudomonas             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Acinetobacter           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Other gram-negative     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**Antibiogram Template: Sample Tool**

The antibiotics listed can be customized to reflect your hospital's formulary.

*Used with permission from the Joint Commission on Accreditation of Health Care Organizations*
Proactive Strategies for Antibiotic Stewardship Programs

**CORE STRATEGIES**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prospective audits with intervention and feedback to the prescriber</td>
<td>Performed by infectious diseases physician or clinical pharmacist with infectious diseases training. Can assist in reducing inappropriate use of antimicrobials.</td>
</tr>
<tr>
<td>Formulary restrictions</td>
<td>Can lead to immediate and significant reductions in use and cost of antimicrobials. Role of preauthorization requirements has not been established and may shift use to other antimicrobial agents leading to increased resistance. Where preauthorization is used, monitoring is necessary.</td>
</tr>
</tbody>
</table>

**STRATEGIES FOR CONSIDERATION BASED ON LOCAL PRACTICE PATTERNS**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education</td>
<td>Provides foundation to influence prescribing behaviors and accept antimicrobial stewardship. Education alone has marginal effect in changing behavior.</td>
</tr>
<tr>
<td>Guidelines and Clinical Pathways</td>
<td>Develop using multidisciplinary approach and local microbiological information (e.g., resistance patterns to improve utilization); implement through education and provider feedback.</td>
</tr>
<tr>
<td>Antimicrobial Order Forms</td>
<td>Can be an effective component of a stewardship program and assist with practice guidelines.</td>
</tr>
<tr>
<td>Streamlining or De-escalating Therapy</td>
<td>Used on the basis of microbiology culture reports and pharmacokinetic and pharmacodynamic drug characteristics. Can result in decreased antimicrobial exposure and cost savings.</td>
</tr>
<tr>
<td>Optimizing Antibiotic Dose</td>
<td>Based on the individual patient characteristics, causative organism, site of infection, and characteristics of the drug.</td>
</tr>
<tr>
<td>Converting from Parenteral to Oral</td>
<td>Determined by patient condition; can decrease length of stay and costs.</td>
</tr>
</tbody>
</table>

**Antibiotic Audit Report**

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*Used with permission from the Joint Commission on Accreditation of Health Care Organizations*
Sample Antibiotic Order Form for Hospitals*

<table>
<thead>
<tr>
<th>Ventilator-associated/Healthcare-associated/Hospital-acquired pneumonia ORDER SHEET for ADULT PATIENTS</th>
</tr>
</thead>
</table>

**DATE:** (24-hour clock)  
**TIME:**  
**Patient Allergies:**  
**Weight (Kg):**  
**Serum Creatinine:**  
**Creatinine Clearance (mL/min):**

**MEDICATION ORDERS ONLY** (INCLUDES IV MEDICATIONS)

**Order Set A. No Risk factors for Multi-drug Resistant Organisms (see Risk Assessment for Multi-drug Resistant Organisms)**

- **Drug 1:** Cefepime 2g IV Q8h x 72 hours  
- **Drug 2:** Vancomycin  

**Order Set B. Risk factors for Multi-drug Resistant Organisms (see Risk Assessment for Multi-drug Resistant Organisms) AND not intubated:**

- **Drug 1:** Cefepime 2g IV Q8h x 72 hours  
- **Drug 2:** Vancomycin  

**Order Set C. Risk factors for Multi-drug Resistant Organisms (see Risk Assessment for Multi-drug Resistant Organisms) AND intubated:**

- **Drug 1:** Cefepime 2g IV Q8h x 72 hours  
- **Drug 2:** Tobramycin  

**FOOTNOTES**

- Adjust dose for renal dysfunction. See Tufts-MC Antibiotic Guidebook or Tufts-MC Pharmacy website.
- If patient recently received a lactam or quinolone or has history of ESBLs, please call AMT for consideration of therapy targeting ESBLs.
- For patients with acute renal failure and/or CKD, ciprofloxacin may be considered as a second agent; however, gram negative organisms are frequently quinolone resistant. Please call AMT with questions.

**PHYSICIAN'S ORDERS** (EXCLUDES MEDICATION ORDERS)

- **Respiratory Specimen Order (select one):** 
  - Sputum gram stain and culture (if a sputum has been processed by the laboratory in the last 72 hours, use standard micro requisition but write in “new pneumonia”)
  - Mini Bronchoalveolar Lavage (Mini-BAL) for quantitative culture

- **Laboratory Orders:** 
  - Blood cultures x 2
  - Legionella urinary antigen

- **Other Orders:** 
  - Continuous pulse oximetry OR Pulse oximetry Q _______ hours
  - Chest X-ray in A.M. PA/LAT OR Chest X-ray in A.M. portable
  - Check a tobramycin serum concentration 2 hours and 8 hours AFTER the infusion of tobramycin is completed and contact pharmacy for further dosing assistance

**Risk Assessment for Multi-drug Resistant Organisms**

**Step 1:** My patient has a NEW pneumonia that developed in the hospital AND: 
- Is currently hospitalized for 5 days or more OR
- Has received antibiotics for 5 days or more in the last 30 days OR
- Has immunosuppressive disease or therapy

If answer is YES (to 1 or more), then...
- If not intubated – Order Set B
- If intubated – Order Set C

If NO – go to step 2 below

**Step 2:** My patient has pneumonia and one or more of the following risk factors for drug resistant organisms:

**Criteria 1**

- Recent hospitalization 5 or more days in last 30 days OR
- Residence in a nursing home or long-term care facility OR
- Home infusion therapy (i.e. tpm, chemotherapy) OR
- Chronic Dialysis (>30 days) OR
- Recipient of home wound care OR
- Has immunosuppressive disease or therapy

AND

**Criteria 2:** TWO of the following THREE risk factors:

1. Requires ICU admission
2. Three or more days of antibiotics in the past 6 months
3. Inability to perform self care

- Does NOT meet criteria 1 = Order Set A
- Criteria 1 but NOT Criteria 2: Order Set A + Vancomycin
- Criteria 1 and Criteria 2, not intubated = Order Set B
- Criteria 1 and Criteria 2, intubated = Order Set C

*Used with permission from Tufts Medical Center
APUA Report From the Field

Guest Editorial: Discovery & Stewardship of Narrow Spectrum Antibiotics
APUA board member Philip Walson, M.D., Editor-in-Chief of Clinical Therapeutics, provided his comments on the recent article, “Optimer Seeks Quick Green Light From FDA for Antibiotic Against Deadly Bug”

It is too early to be sure what the future holds for this new antibiotic, fidaxomicin (Dificid), especially compared to much cheaper generic drugs like metronidazole. However, the development of any new antibiotic is welcome and development and commercialization of any so called “narrow spectrum” antibiotics is especially encouraging. The company will now have to convince physicians to adopt a totally new strategy to treating infections— one that includes first making a clear, specific diagnosis and then using a drug designed to treat only the one diagnosed infection and not selecting a “shotgun” approach to all possible infectious agents. If they are successful this should both increase the use of this antibiotic and help to combat excessive, non-specific antibiotic use by training physicians to think differently about the use of antibiotics. This includes considering the development of resistance as a major outcome variable in antibiotic selection. Such thinking can only be welcomed given the rapidly developing rates of multidrug antibiotic resistance which is due at least in part to the overuse of broad spectrum antibiotics. Optimer’s new antibiotic received unanimous approval of the FDA Anti-Infective Advisory Committee on April 5, 2011. The FDA officially approved fidaxomicin in May 2011.

To comment please go to APUA’s Blog, http://superbugsanddrugs.blogspot.com

Poverty, Prevention and Antimicrobials: The Impact on Infectious Diseases in Developing Countries
Adebayo Lamikanra, Professor
Obafemi Awolowo University
APUA Nigeria Chapter Leader

The life expectancy of a child born in Nigeria today is less than fifty years. In stark contrast, a child born in Japan, for example, can confidently expect to live for at least eighty years, significantly in excess of half a life time longer than his Nigerian counterpart. This comparison, horrifying as it is, tells half of the story because no less than 94 in every 1,000 babies born in Nigeria will die before their first birthday and 138 will not be alive to celebrate their fifth birthday. Comparable figures for Japan are 2.79 years and 3.3 years respectively. There are myriad reasons why the Nigerian figures are so dismal, but perhaps the most telling statistic is that 43.1% of fatalities in third world countries as a whole are due to infections, compared with 2.67% for North America. The import of this difference is that, whilst death in the affluent countries is due mainly to chronic and degenerative changes caused by old age, most deaths in Nigeria and other tropical countries are due to infections that are likely to attack young people, and in doing so, make it impossible for them to live very long. This means however that a much brighter picture is bound to be achieved if infections were to be adequately controlled through prevention, blanket vaccination cover, improvements in social hygiene infrastructure, and of course, effective chemotherapy. The point needs to be made at this juncture that the hot and humid tropical environment is, in the absence of other considerations, one that is especially conducive to the proliferation of all forms of microbial life. Some of the most life-destroying microbes— e.g., those responsible for malaria, lassa fever, ebola, and sleeping sickness are confined to the tropics, and virtually all other infections are very strongly associated with these regions. The issue of containing these infections is compounded by the material poverty that is characteristic of countries in the tropics—a baffling level of poverty given the abundance, if not profusion, of natural resources: crude oil, solid minerals, forest products, agricultural products (and their potential) among others with which the tropics are endowed. On the contrary, conditions in these developing countries suggest that the quality of life in those countries has slipped, in some cases glaringly so.

It is with the above considerations in mind that one should contemplate the challenge of antimicrobial chemotherapy in the tropics. First, there are simply more infections to be dealt with, and with high ambient temperatures, the rate of growth and consequent microbial evolution is very high, such that the development of resistance to antimicrobial agents should be expected to be significantly higher than that found in countries situated in temperate zones. Interestingly, the possibility of this happening has received scant attention.

The introduction of antibiotics into clinical practice has had a major impact on the internal environment of the human body. As with any environment, this has led to the imposition of stiff
selective pressures, leading to the development of new variants of microorganisms, which in most cases are not biochemically nor morphologically different from those that remain sensitive. One major challenge of chemotherapy in Nigeria and other developing countries is the identification of these resistant organisms, followed by an adequate response.

Although genuinely new antibiotics are not being developed anywhere near the rate at which they are required, patients in the affluent developed countries have access to advanced anti-infective agents that are way beyond the reach of people in the developing countries. The latter have to wait for patents on new drugs to expire, and are instead treated with pharmaceutically inferior generic versions of drugs which have been heavily used in Europe and the United States before their eventual introduction into the drug markets of the developing countries. A case in point is ciprofloxacin, which because of its high cost, was very sparingly used in Nigeria before 2003 when it was still patented. Subsequently, there was an explosion in its use as no less than fifty different generic brands of the drug became available in Nigeria within a period of two years. In our laboratory study of commensal E. coli from students of the Obafemi Awolowo University in Nigeria, the prevalence of antibiotic resistance rose from low single digits to 20% in 2005. Ciprofloxacin is now regarded as the drug of choice in antibacterial chemotherapy in Nigeria, but given the extant conditions, it cannot be long before the effectiveness of this drug becomes heavily compromised, as indeed has happened to other antibiotics in the past.

The issue of acquired antimicrobial resistance has now moved out of the pages of relatively inaccessible scientific journals and has been dressed in lurid garb in large circulation newspapers, a testament to its new-found news worthiness. Many of the stories concerning the ‘superbugs’ are sensational and perhaps more disturbing than they should be, but they boost circulation figures and so will run repeatedly. Even the most respectable of these papers finds it impossible to treat this subject with the circumspection that it deserves. Stories concerning the grave challenges facing the use of antimicrobial agents in third world countries are far less sensational than the closure of a few wards caused by MRSA or Clostridium difficile in a New York or London hospital, but are sure to bring more misery, sudden death and ever increasingly lower quality of life to people in developing countries.

APUA and U.S. Regulators Consider Foodborne Hazards

The Pew Charitable Trust, together with Center for Science in the Public Interest, convened a day-long meeting on January 25, 2011 on “Managing the Risk of Foodborne Hazards: STECs (shiga toxicigenic E. coli) and Antibiotic-Resistant Pathogens.” Presenters hailed from the food and pharmaceutical industries, governmental agencies – USDA, FDA, CDC, universities, and global agencies – WHO. The purpose of the conference was to collect expert recommendations to respond to emerging foodborne pathogens and related public policy.

Dr. Elisabeth Hagen, Under Secretary for Food Safety in the USDA, delivered the opening keynote. She highlighted the uniqueness of both the challenge and opportunity posed by the problem of foodborne illness in that it is one of the few public health problems that are preventable. It is important to anticipate emerging threats. The current challenge that remains unaddressed is that posed by non-O157 STECS, which cause about 36,700 illnesses, 1,100 hospitalizations and 30 deaths annually.

She noted that a new challenge to managing foodborne pathogens is how to preserve antibiotic effectiveness. Collaboration among groups and good science are essential to the development of prevention-based policies and are at the core of all decision-making in food safety.

The focus of the morning session was antibiotic-resistant pathogens. Dr. Stuart Levy delivered a talk on “Environmental and Societal Impacts of Antibiotics.” He related that every dose of antibiotic given has a consequence. Antibiotics are powerful drugs and powerful selectors of resistance. Between 30-50% of antibiotics used is unnecessary. He cited his prospective farm study in 1975-76 which demonstrated the transfer of tetracycline resistance genes from chickens fed tetracycline-supplemented feed to farm dwellers: one-third of human fecal samples contained more than 80% of tetracycline-resistant bacteria (N Engl J Med 295: 583-588, 1976). Dr. Levy emphasized that antibiotics are societal drugs and that giving them to one person affects others and the environment. Selection density influences antibiotic resistance frequency. APUA’s Reservoirs of Antibiotic Resistance (ROAR) Scientific Network has investigated the role of commensal bacteria in resistant pathogens and its ISRAR project focused on surveillance among non-clinical bacteria in a search for new resistance determinants, with the participation of APUA Chapters in India, South Korea, Vietnam, South Africa, Turkey, Georgia, Uganda, and Bangladesh.

The afternoon session included presentations on the State of Science, Public Health Impact, Strategies for Risk Management, and Enhancing the Collaborative Response to Foodborne Hazards. Michael Taylor, of the FDA, delivered the keynote summary.
Preservation of Antibiotics for Medical Treatment Act (PAMTA) reintroduced to US Congress

On March 9, 2011, Representative Louise Slaughter (D-NY) reintroduced the Preservation of Antibiotics for Medical Treatment Act (PAMTA) targeting the non-therapeutic use of antibiotics in farm animals. Representative Slaughter first introduced this legislation in 2009. PAMTA would call for the FDA to re-examine its approvals of veterinary antibiotics. If enacted, it would remove from food animal production the non-therapeutic use of seven classes of antibiotics that are important to human health, unless animals are diseased or drug companies can prove that their use does not harm human health. Statistics from the Center for a Livable Future, an organization at Johns Hopkins Bloomberg School of Public Health, reveal that almost 29 million pounds of antibiotics are used in animals in the United States — 80 percent of the total antibiotics used in the country. The Alliance for the Prudent Use of Antibiotics, Pew, and over 300 other health, agricultural, environmental, humane, and consumer organizations are in support of enactment of legislation to remove the non-therapeutic use of medically important antibiotics in farm animals. These groups warn that the overuse and misuse use of antibiotics in food animal production is an immense threat to humans because it produces drug resistant bacteria that our current antibiotics will be ineffective against. The Bill currently has 19 co-sponsors and has been referred to the Committee on Energy and Commerce, and in addition to the Committee on Rules.

To Save Antibiotics, Make them a Separate Class of Drugs

Stuart B. Levy, M.D., President of the Alliance for the Prudent Use of Antibiotics (APUA) and Tufts University School of Medicine Professor, suggests that the U.S. Food and Drug Administration (FDA) develop a separate class of antibiotics as “societal drugs” to bring increased awareness of their unique societal effects and to provide stronger incentives for industry to develop new drugs to combat resistant infections.

“Antibiotics are different from all other drugs ... [as they] affect the treated individuals and those sharing their health facility, home, and other environments.”

“The list of cosponsors can be found at http://www.govtrack.us/congress/bill.xpd?bill=h112-965

APUA, the estimated annual cost of antibiotic resistance in U.S. hospitals is greater than $20 billion and adds 6.4 – 12.7 hospital days per patient stay.

New FDA Guidance Expected to Protect Medically Important Antimicrobials

FDA’s revised Draft Guidance #209, on “The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals,” is expected to be released for a 90-day public comment period this June. The agency’s most recent version of this guidance document, released on June 28, 2010,
concluded that “using medically important antimicrobial drugs for production purposes is not in the interest of protecting and promoting the public health.” In anticipation for the release, *The Pew Charitable Trusts*, *The American Academy of Pediatrics*, and *Keep Antibiotics Working* held a meeting to prepare for FDA’s findings and coordinate an effective response to ensure the agency maintains its commitment to reducing injudicious antimicrobial use in farm animals. APUA was among 35 groups invited to participate at the meeting this May in Washington, DC.

**APUA-Ethiopia Update**

Dr. Yilkal Asfaw, DVM, Associate Professor and Dean of the Faculty of Veterinary Medicine (Addis Ababa University) and member of the APUA-Ethiopia chapter, has offered an AMR Advocacy and Intervention presentation entitled *Antimicrobial Resistance (AMR) and Residues in Livestock and their Products - Consequences to Public Health in Ethiopia* at multiple Ethiopian venues, including the School of Pharmacy, Addis Ababa University; the Ministry of Agriculture; and the meeting of the *Ethiopian Food, Medicine, and Health Care Administration and Control Authority* held April 8-15, 2011. Dr. Yilkal is an advocate of antimicrobial resistance control and has authored or co-authored more than twenty peer-reviewed journal publications in his field of study. He was one of the investigators in the Ethiopian Antimicrobials Use, Resistance and Containment Baseline Survey.

**APUA-Nepal Update**

APUA—Nepal was featured in an Article published in the WHO Regional Forum. Dr. K.K. Kafle, the Head of the Department of Clinical Pharmacology at the Institute of Medicine, and Professor B.M. Pohkrel, the Chief Editor of the Nepal Association for Medical Laboratory Sciences co-authored "Antimicrobial resistance at different levels of health-care services in Nepal," which can be found at: http://www.searo.who.int/LinkFiles/WHD-11_RHF.pdf/

**New APUA Chapter in Ghana**

In March 2011, Ghana joined APUA’s global chapter network. The new Chapter leader is Dr. Kwaku Poku Asante, a public health physician with an interest in interventions that will reduce the burden of public health disease. Dr. Asante holds a BSc. in Medical Sciences (1997), an MD degree (2001) and a Masters in Public Health (2004) from the premier University of Ghana. He has additional training in the conduct of health research, project management, communication and research ethics.

In the last 6 years, Dr. Asante has led key research investigations into malaria, meningitis and anemia in the Kintampo North and South Districts, utilizing both qualitative and quantitative methods in evaluating health programs. Currently, he is a Clinical Research Fellow at the Kintampo Health Research Centre, Ghana Health Service and holds a Malaria Vaccine Advocacy Fellowship with the Bill and Melinda Gates Foundation/PATH Malaria Vaccine Initiative. We are pleased to welcome Dr. Asante and the new Ghana chapter to APUA’s network of 66 chapters worldwide.

**APUA-Indonesia on World Health Day**

APUA—Indonesia launched its new *National Antibiotic Guidelines* at a national meeting held on April 7—World Health Day and featured guest speaker, Dr. Hari Paraton. The guidelines were developed by Indonesia’s AMRIN (Antimicrobial Resistance in Indonesia: Prevalence and Prevention) team at the invitation of the Minister of Health for World Health Day —“Antimicrobial resistance: NO action today, NO cure tomorrow.” The meeting was designed as a platform for initiating Indonesian activities in preventing and controlling the problem of antibiotic resistance in that country.

**Pan American Symposium on Antibiotic Resistance and Appropriate Antibiotic Use** at the XV Pan American Congress of Infectious Diseases 2011, Punta del Este, Uruguay on April 9th.
APUA Celebrates 30 Years of Global Activities in “Preserving the Power of Antibiotics”!

2011 marks APUA’s 30th year as the leading global non-governmental organization fighting to preserve the power of antibiotics. Over the years, APUA has conducted numerous research projects, published reports, held Congressional briefings, established an international chapter network in 66 countries, and served as a trusted resource to policymakers, clinicians, and consumers. We hope you can join APUA chapters and friends in celebrating the 30th anniversary at the annual APUA member’s reception at the 51st ICAAC in Chicago. Also join us at APUA’s symposium, “Celebrating 30 years of APUA: Novel approaches to the containment of antibiotic resistance — a global perspective”. Find more information on our web site and in ICAAC Program. Thank you for your partnership and support.