Feature Articles

Update: Continued Pressure from ESBLs in Resistant Gram-Negatives by Karen Bush, PhD (Indiana University)

Surveillance of Klebsiella and Acinetobacter in Cuba by Dianelys Quiñones Pérez, MD, PhD (Member, APUA-Cuba, Tropical Medicine Institute "Pedro Kouri", Cuba)

C. difficile Update: APUA One-on-One with Dr. Arjun Srinivasan by Arjun Srinivasan, MD (U. S. Centers for Disease Control & Prevention)

Policy Update: GAINing Ground on Resistance by Hemal Shah, PharmD, Dayo Jagun, MBBS, MPH, & Sherwood Gorbach, MD (Optimer Pharmaceuticals & Avalere Health)

Control of Norovirus in Healthcare Settings by JM Soto Beltran PhD, & Samantha Broaders PhD (Clorox Healthcare)

APUA Headquarters in Action

APUA at WHO's Technical Consultation on Surveillance
APUA Webinar on Stewardship - Pace Credit Available
APUA comments on Antimicrobial Animal Drug Sales and Distribution Reporting
APUA co-signs letter in Financial Times
APUA signs Joint Statement on Antibiotic Resistance
APUA advocates for consumer involvement in US FDA meetings on antibiotic use in livestock

APUA Chapter Reports

APUA-Abu Dhabi, UAE—electronic ABR Surveillance
APUA-India—"Outcomes" Conference
APUA-Nepal—Multi-hospital ABR Report
APUA-Cuba—Publication on MRSA

Obituary: Professor Iwan Darmansjah

Letters to the Editor: Antibiotics in the environment

Policy Updates: Accelerating Antibacterial Development; Regulating Antibiotic Use in Livestock

News and Publications of Note

Resistance Problems Around the World

Successful Interventions

Upcoming Events

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Vol. 30 No. 3

Happy Holidays from all of us at APUA!
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Letters to the Editor*  

**Ecological Impacts of Antimicrobial Misuse**

To the Editor:

There are several parts necessary to an approach for controlling the accelerating loss of antimicrobial drugs, drugs which are not being replaced by the pharmaceutical industry. Briefly, however, there are at least two main branches to this approach or effort and coordination of these necessary branches, then, will be critical to accomplishment of this goal. One branch is that of conserving the existing stocks of these tools through prudent usage, the other is to understand and then diminish the reasons for their destruction, including the acceleration in the resistance and virulence of the pathogens themselves. This acceleration is, in part, related to facilitating the transfer of genetic material. One of the principal sources of not only passing on but actually generating new genetic combinations of drug resistant organisms is seen in the processing of wastewater (sewage). Through-put of resistance via sewage treatment sees the waterways and drinking water of this nation becoming reservoirs of resistant organisms. Thus while medicine may be reducing the unnecessary use of these drugs in an effort to stem their loss in efficacy, sewer plants are spewing these organisms into the environment, and doing so at hyper-industrial volumes.

Dr. Amy Pruden's work has brought focus upon the environmental routes for generating and transferring genetic material (antibiotic resistance genes) as contaminants of emerging concern. Her work includes potential mitigation strategies to limit the spread of antibiotic resistance genes via environmental pathways and to treat water to remove genetic material. Her basic research mission is to build fundamental understanding of complex microbial communities in environmental systems in order to improve engineered approaches for meeting public health and water sustainability goals. Without this understanding, medicine will be fighting an uphill battle and at some point, many of the elective surgeries will become too risky due to the potential for unstoppable infections. It need not reach this stage but grasping both aspects of the approach to the loss of antimicrobial drugs warrants serious understanding.

Sincerely,

Edo McGowan, M.D., Ph.D.

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**Triclosan Mania**

To the Editor:

I noticed today that new paper towel dispensers have been installed throughout the high school where I work. They feature a big "Microban" sticker on the front. I'm not sure if antibiotics are in the towels themselves or in the dispenser's plastic. Do you have information on this product? Is this product at all effective in minimizing bacteria populations? I'm preparing to teach a college course on environmental toxins and am starting with this contact to gather information for the course.

Dr. Douglas J. Buege

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Response from the APUA Editorial Staff:

A little investigation reveals that the incorporation of Microban (triclosan) is within the dispenser itself, and not the paper towels (see www.kcprofessional.com). The incorporation of Microban into products is widespread. In this case, the rationale is to protect the surface from sustained contamination by microorganisms, primarily yeast, molds and fungi. The use of Microban in plastics is generally intended to prevent long-term disintegration and discoloration from these microorganisms, especially in damp or highly contaminated environments. Since this particular dispenser is a "touchless" model (except for the emergency feed knob), it would not be expected to become very contaminated with skin bacteria through contact, so the Microban does not really serve to prevent bacterial cross-contamination between users, but rather to protect the life and appearance of the dispenser itself. This makes sense in a lot of cases where rapid deterioration can occur due to high humidity (e.g., in lawn furniture), but the logic in this case is less clear. We suspect it has more to do with the psychology of selling an item that suggests it is "more hygienic". We would tend to question whether the life of the dispenser is actually enhanced by use of this product.

The incorporation of triclosan into hundreds of products means this chemical eventually ends up in landfills and the environment in general. While there is evidence that some environmental bacteria can degrade this biocide, trace quantities have been detected in rivers, streams, wastewater, seawater, fish bile, aquatic biota, breast milk and blood plasma, and thus there are some concerns over environmental contamination and whether it can contribute to the selection of antimicrobial resistance over time.

*APUA welcomes letters to the Editor. Please send us your thoughts and questions. Names will be published but not addresses. All letters may be edited for style and length.
Update: Continued Pressure from ESBLs in Resistant Gram-Negatives

Karen Bush, Ph.D.
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Multidrug-resistant gram-negative bacteria represent one of the scourges of modern medicine. The more antibiotics that are used against them, the more resistant the pathogens seem to become, with few therapeutic options remaining for effective treatment regimens.[1] Of the various resistance mechanisms that have been described in these organisms, production of β-lactamases is perhaps the most well-studied.[2] These enzymes are responsible for the inactivation of β-lactam antibiotics such as penicillins, cephalosporins, monobactams and carbapenems, with a wide spectrum of specific hydrolysis profiles demonstrated among the different classes, or groups, of enzymes.[3] Although much attention has been paid recently to the carbapenemases (the enzymes that inactivate carbapenems as well as penicillins and cephalosporins), the more widespread β-lactamases are the extended-spectrum β-lactamases, or the ESBLs. Major resistance problems are related to carbapenemase production, in that the organisms tend to be highly resistant to multiple classes of antibiotics.[4] However, carbapenemase-mediated resistance often appears in geographical pockets, often with sporadic occurrences.[5]

In contrast, ESBLs, which also appear in multidrug-resistant pathogens, are ubiquitous. Recent surveillance studies have reported ESBL-producing *Klebsiella pneumoniae* at frequencies of 43% in Korean long-term care facilities,[6] 70% in patients with intra-abdominal infections in India,[7] and 46% and 55% in Latin American and African intensive care units, respectively.[8] ESBL-producing *Escherichia coli* from these same studies were reported at frequencies of 45% in Korea [6] and 79% in India, [7]. Not only are ESBLs found in hospital and community infections, but also in environmental isolates. In a study of *Aeromonas* spp. isolated from the Seine River in Paris in 2009, 71% of the strains were shown to produce clavulanic acid-inhibitable ESBLs.[9]

ESBLs were defined in 1995 by Bush, Jacoby & Medeiros as enzymes that had “…hydrolysis rates for the extended-spectrum β-lactam antibiotics, ceftazidime, cefotaxime, or aztreonam…10% that for benzylpenicillin…” [10] Although most of these enzymes are cataloged as functional group 2be (molecular class A) β-lactamases, ESBLs also include a few functional group 1 (class C) cephalosporinases and group 2d (class D) “oxacillinases.”[3] ESBLs specifically do not include carbapenemases, in order to differentiate carbapenem-susceptible ESBL-producing organisms.

![Figure 1. Increase in ESBLs since 1990.](image)

The total numbers of TEM and SHV β-lactamases are shown, together with the number of TEM-derived and SHV-derived ESBLs as defined in reference 13. All CTX-M-β-lactamases are assumed to be ESBLs.
from carbapenemase-producing pathogens that are resistant to carbapenem therapy.\[11\]

ESBLs initially were derived from the common plasmid-encoded TEM and SHV β-lactamases, with major outbreaks identified in the late 1980s in Western Europe and the United States.\[12\] Until the mid 1990s, all TEM-1, TEM-2 and SHV-1 variants demonstrated strong ESBL characteristics. However, over time, more TEM and SHV mutants have been identified with non-ESBL properties, as demonstrated in the Figure, such that less than half the TEM variants and about a quarter of the SHV variants have defined ESBL hydrolytic abilities.\[13\] It is likely that additional ESBLs will be disclosed among those enzymes already identified in the TEM and SHV families as investigators complete full biochemical analyses of variants that have been identified to date only on the basis of an amino acid sequence.

Unexpectedly, a new family of β-lactamases, the CTX-M enzymes originally identified in Japan in 1986 and Germany in 1989 \[14\] began to spread promiscuously at the same time TEM and SHV variants were identified globally.\[15\] It is believed that CTX-M β-lactamases originated from a chromosomal enzyme in \textit{Kluyvera} spp.\[15\] This family of enzymes was initially notable by showing hydrolytic preference for cefotaxime, but later variants may also display sufficient ceftazidime hydrolysis to cause high level resistance.\[15\] By 2009, the number of CTX-M ESBLs had exceeded the number of TEM-ESBLs or the SHV-ESBLs. Of the currently known 133 CTX-M variants, CTX-M-14 and CTX-M-15 have become the most prevalent ESBLs in Asia, the United States and Europe.\[16\-17\] CTX-M-15 is frequently produced by the \textit{Escherichia coli} virulent clones ST131-O25:H4-B2 and ST405-0102:H6-D, strains that are now distributed throughout the world.\[18\] Recent reports indicate that non-hospital, non-human sources may serve as reservoirs for some of these TEM-, SHV- and CTX-M-ESBLs, suggesting that these enzymes are well-established in our environment and will not be easily eradicated.\[19\]

Treatment of infections caused by ESBL-producing bacteria has become more difficult as multiple β-lactamases are frequently produced by gram-negative bacteria causing serious hospital-acquired infections. Although carbapenems are often the treatment of choice, many carbapenemases are now produced in concert with ESBLs, yielding highly drug-resistant pathogens. \[20\], thus leaving only drugs. Drugs like colistin, fosfomycin, temocillin or tigecycline , used either as monotherapy or in combination, may serve as therapeutic options for some infections caused by these multidrug-resistant gram-negative bacteria, \[21\-22\]. ESBL-producing urinary tract infections are particularly responsive to non-b-lactam-containing agents such as fosfomycin. \[23\] However, periodic in vitro testing is essential before long term treatment regimens are continued, as resistance may arise at any time during therapy.

Several strategies to combat multidrug resistant gram-negative bacterial infections were recently evaluated by a panel of opinion leaders during a Gram -Negative Resistance Summit. \[24\] Factors such as empiric combination therapy, pharmacodynamic optimization of dosing regimens, limitation of antibiotic exposure, and active surveillance combined with infection control were all deemed to be part of a packaged strategy that may serve to provide optimized therapy and a decrease in the spread of multidrug-resistant pathogens.

Optimistically, there are now β-lactam-β-lactamase inhibitor combinations in late clinical development that may provide some relief from ESBL-producing gram-negative pathogens.\[25\-26\] In vitro data appear promising, but clinical data are still needed to provide convincing proof of efficacy in infections caused by ESBL-producing pathogens. With the increasing proliferation of novel ESBLs, it is important for us to
continue to search for new therapeutic approaches to tackle those highly resistant gram-negative bacteria.

References
Surveillance of *Klebsiella* and *Acinetobacter* in Cuba

Dianelys Quiñones Pérez, M.D, Ph.D
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In recent years, worldwide dissemination of extended-spectrum β-lactamase (ESBL) and carbapenemase-producing gram-negative pathogens has been reported, mainly associated with hospital outbreaks, and resulting in increased length of hospital stay, costs, and mortality. *Klebsiella pneumoniae* and *Acinetobacter baumannii-calcoaceticus* complex are important reservoirs of antibiotic resistance genes, some of which are related to ESBL and carbapenemase production. The successful treatment of infections due to these pathogens has become problematic because of widespread resistance to currently available therapies. These facts justify the establishment of continuous surveillance programs for monitoring antimicrobial resistance trends globally.

The National Workshop on Antimicrobial Resistance (sponsored by The Cuban Society of Microbiology and Parasitology, the European Society of Clinical Microbiology and Infectious Diseases and the Pan-American Association of Infectology), took place in Havana, Cuba from November 7-10, 2012. The main objectives were to analyze: a) resistance as a phenomenon and the major factors contributing to its increasing prevalence; b) surveillance activities and needs; and c) strategies for response. A topic of high-interest was the problematic gram-negative bacteria.

The report from the National Surveillance Program (2010-2012) on *Klebsiella* spp. (n= 448) and *Acinetobacter* spp. (n=500) in Cuba revealed high resistance rates to a variety of antimicrobials (Table 1), primarily in the *Acinetobacter baumannii-calcoaceticus* complex and *K. pneumoniae*, which caused 95% and 96.4% of infections by these bacterial genera, respectively.

The most frequent infections caused by *Klebsiella* spp. were: bloodstream (23.4%), lower respiratory tract (18%), and urinary tract (13%). *Acinetobacter* spp. were associated with infections of the lower respiratory tract (38.6%), bloodstream (31.1%), and skin and soft tissue (13.1%). Community-acquired infection was demonstrated in 23.4% of patients infected with *Klebsiella* spp, but in only 1.6% of those infected with *Acinetobacter* spp.

*Klebsiella* spp. showed the highest resistance rates for third-generation cephalosporins, aztreonam, gentamicin, tetracycline, nitrofurantoin and ciprofloxacin. Fifty-two per cent of isolates were ESBL-producers, which accounts for the cephalosporin, aztreonam and other antibiotic resistances exhibited. Unfortunately, the plasmids carrying these ESBL genes often carry resistance determinants that also target fluoroquinolones, aminoglycosides, tetracyclines and trimethoprim-sulfamethoxazole. Several ESBL types were detected in Cuban isolates of *Klebsiella* spp. (CTX-M = 82%, TEM = 70% and SHV = 30%). Thirteen percent of ESBL-producers caused community-acquired infection. These results agree with those previously reported in other countries and corroborate the wide spread of ESBL genes in *Klebsiella* spp. This pathogen is an important genetic

“Several ESBL types were detected in Cuban isolates of *Klebsiella* spp. (CTX-M = 82%, TEM = 70% and SHV = 30%). Thirteen percent of ESBL-producers caused community-acquired infection.”
reservoir for the easy acquisition of these resistance genes by other species in the same ecological environment (e.g., E. coli). Carbapenems (imipenem and meropenem) showed better in vitro activity in the characterized isolates. These antimicrobials are recommended as first-line therapy for severe infections caused by ESBL-producing Enterobacteriaceae and so are very useful in Cuba.

In contrast, Acinetobacter is usually associated with multiple antibiotic resistance, and few effective therapeutic agents remain for many strains of this organism. Reports from the National Surveillance Program in Cuba confirm this and reveal high resistance rates for the majority of antimicrobials tested. Table 1 shows significant percentages of resistance to third-generation cephalosporins, β-lactam/inhibitor combinations, aminoglycosides, ciprofloxacin and carbapenems. Seventeen percent of Acinetobacter isolates were metallo-beta-lactamase (MBL)-positive, as detected by EDTA synergy test with imipenem or meropenem disks. Colistin, doxycycline, tetracycline and rifampin were the most active agents in vitro (Table 1).

Polymyxins have been available for more than 50 years but their clinical use was interrupted for their adverse effects—mainly nephrotoxicity (acute tubular necrosis) and neurotoxicity (dizziness, weakness, facial paraesthesia, vertigo, visual disturbances, confusion, ataxia and neuromuscular blockade). However, over the last decade the emergence of MDR gram-negative bacteria and the lack of new antimicrobials have led to a revival of polymyxins, especially colistin. This antibiotic has been reinstated as a key therapeutic option for carbapenem-resistant organisms, particularly A. baumannii, P. aeruginosa, and carbapenemase-producing Enterobacteriaceae. It is very important in countries with limited resources where tigecycline is not available. Therefore, according to our results, colistin should be considered as a treatment option for the control of infection by multi-drug-resistant A. baumannii in critically ill patients. Careful monitoring of the incidence of resistance will be necessary as usage of this agent increases.

The high level of antimicrobial resistance was often associated with resistance to at least three antimicrobial families (multi-drug-resistant or MDR; Klebsiella spp. = 53%, Acinetobacter spp. = 57%). Some Acinetobacter baumannii-calcoaceticus complexes showed extensive drug-resistance (XDR=32%), which includes MDR with carbapenem resistance, or pan-drug resistance (XDR strains with resistance to colistin = 2%) because tigecycline is not available in Cuba.

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<td>Piperacillin-tazobactam</td>
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<td>Rifampim</td>
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Table 1. Antimicrobial resistance of Acinetobacter and Klebsiella causing infection in Cuba (2010-2012).
Conclusions: This report highlights *Klebsiella pneumoniae* and *Acinetobacter baumannii-calcoaceticus* complex with important resistant phenotypes in Cuban hospitals. Although carbapenem and MBL resistances are very low in *Klebsiella* spp.—at least by phenotypic testing—these findings demand immediate molecular studies to detect emerging genetic determinants involved in the resistance to carbapenems. Colistin represents a potentially useful antibiotic in the treatment of MDR *Klebsiella* and *Acinetobacter* in Cuba. The surveillance results are providing useful guidance to hospital stewardship teams in generating informed antimicrobial formulary decisions as well as to physicians in the selection of empiric and follow-up antimicrobial agents.
**C. difficile** Update: APUA One-on-One with Dr. Arjun Srinivasan of the U.S. C.D.C.

**Arjun Srinivasan, M.D.**
Associate Director for Healthcare Associated Infection Prevention Programs
U. S. Centers for Disease Control and Prevention, Atlanta, Georgia

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Q. *Clostridium difficile* infections (CDIs) are linked to 14,000 deaths in the US each year. In recent years, what has been the trend in the incidence of CDIs and in their severity?

Recent years have seen a rise in both the frequency and severity of CDIs, with sharp increases in serious outcomes like colectomy and death. Much of this increase has been attributed to the rise of the epidemic strain of CDI.

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Deaths Caused by *C. difficile* Infections*

* Age-adjusted Rate of *C. difficile* as the Primary (Underlying) Cause of Death.

Source: CDC National Center for Health Statistics, 2012

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Q. Who is most at risk for developing a CDI?

Antibiotic exposure remains the single most important risk factor for CDI. Even short courses of antibiotics place patients at an increased risk for CDI - a risk that persists for up to a month after the antibiotics have stopped. There are well described cases of healthy patients getting CDI after even single doses of antibiotics.

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Q. What can patients do in order to prevent incidence and recurrence of CDIs?

One of the most important things patients can do to protect themselves is to avoid seeking antibiotics in situations where their healthcare providers feel antibiotics are not needed. Reducing exposures to unneeded antibiotics will reduce the risk of CDI.

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Q. What can doctors and nurses do to prevent the spread of CDIs?

Healthcare providers can work on efforts to improve the use of antibiotic prescribing. We know that many antibiotics are given to patients who don’t need them. This holds true in both in-patient and out-patients healthcare settings. Healthcare workers must also follow contact precautions and hand hygiene recommendations when they care for patients with CDI. Finally, we all need to be supportive of the efforts of environmental services staff who play a key role in maintaining a safe healthcare environment.

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Q. What steps can health care facility administrators take to curb the rising rates of CDIs in healthcare facilities nationwide?

Facility administrators should support efforts to
improve antibiotic use in their facilities. To be effective, antibiotic stewardship programs and interventions require both moral and financial support for facility administrators. I believe that every facility in the country should be taking steps to improve antibiotic use and facility administrators can play a key role in making this happen.

Q. What evidence do we have that Antimicrobial Stewardship Programs can have an impact on CDI incidence?

There have been several published studies showing drops in CDI following the implementation of antibiotic stewardship efforts. Many of these studies are summarized on the CDC’s Get Smart for Healthcare Website in the annotated bibliography.

Q. What are some of the obstacles in the successful prevention of CDIs in the hospital setting?

We still see limited implementation of efforts to improve antibiotic use in most facilities. There is clear evidence to suggest that improving the use of antibiotics will reduce CDI, but there is less evidence to suggest that interventions to improve antibiotic use are being widely implemented.

Q. CDIs are becoming increasingly common in the community setting and in long-term care facilities. What can be done at the state and community level to address this issue?

State and local health departments are playing an increasingly active role in efforts to prevent healthcare associated infections, including CDI. Indeed, CDI is a perfect example of an HAI where public health can play a key role as patients with CDI often move between various healthcare facilities. Because they sit at the nexus of all healthcare facilities, health departments are ideally positioned to help facilities work together on coordinated efforts to combat CDI.

How C. difficile Spreads

George, a 68-year-old man, goes to the doctor's office and is diagnosed with pneumonia. He is prescribed antibiotics, drugs that put him at risk for C. difficile infection for several months.

One Month Later
George breaks his leg and goes to a hospital. A healthcare worker spreads C. difficile to him after forgetting to wear gloves when treating a C. difficile infected patient in the next room.

Two Days Later
George transfers to a rehabilitation facility for his leg and gets diarrhea. He is not tested for C. difficile. The healthcare worker doesn't wear gloves and infects other patients.

Three Days Later
George goes back to the hospital for treatment of diarrhea and tests positive for C. difficile. He is started on specific antibiotics to treat it. Health care workers wear gloves and do not spread C. difficile. George recovers.

Source: CDC, 2012
In 2009 the U.S. Department of Health and Human Services (HHS) developed a National Action Plan to Prevent Healthcare-associated Infections (HAIs). In doing so, HHS acknowledged the significant burden placed by HAIs on the healthcare system. [1] These infections affect almost 2 million Americans, leading to 99,000 deaths every year, with the majority of these infections due to antibiotic-resistant organisms. [1] Antibiotic resistance, a major contributory factor to the incidence of healthcare-associated bacterial infections, has become more of a public health threat in recent years, complicated by the emergence of antibiotic-resistant bacterial strains and lack of incentives to develop new antibiotics. Antibiotic resistance has been associated with increased patient mortality, longer hospital stays, and increased healthcare costs of as much as $34 billion per year. [2-6]

In recognition of the public health significance of antibiotic resistance, many stakeholders including the Centers for Disease Control and Prevention (CDC) have called for a variety of interventions including increased surveillance, establishment of antibiotic stewardship programs, and development of new diagnostics, vaccines and antibiotics.[2,7,8] In July 2012, the Generating Antibiotic Incentives Now (GAIN) Act was signed into law as part of the Food and Drug Administration (FDA) Safety and Innovation Act (also known as PDUFA V). The GAIN Act creates incentives for drug manufacturers to seek FDA approval for new antibiotics needed to treat a select number of drug-resistant pathogens through extended market exclusivity, priority reviews and fast-track status. [9] While the GAIN act may encourage investments in new antibiotics, it does not address inherent challenges that may discourage adoption of new antibiotics by providers. Hospitals are paid based on a fixed, pre-determined rate for each inpatient hospitalization. Although the Medicare system has encouraged efficiency and controlled overall costs, the system may make it more difficult for hospitals to adopt new technologies because technologies are launched without adjustments to payment levels.

An existing pathway created by Congress - the New Technology Add-on Payment (NTAP) - has the potential to realign incentives to adopt new technologies. The NTAP policy provides temporary additional financial payments to hospitals for medical technologies that demonstrate a “substantial clinical improvement” over standard of care and meet specific cost thresholds. These add-on payments are provided during the initial years after a new technology is first introduced and cover the period of time required for the Medicare program to accumulate enough data to reset the payment rates to reflect the added costs of the new product.

DIFICID®, an oral medication indicated for the treatment of Clostridium difficile-associated diarrhea (CDAD) in adults 18 years of age and older, recently received NTAP designation. [10] The case of NTAP designation for DIFICID® is notable because C. difficile infections are among those targeted by the GAIN Act and one of the HAIs most often associated with antibiotic overuse. [11] While this is only the second time NTAP

“The increased financial incentive to use...antibiotics that may obtain future NTAP designation must be accompanied by evidence-based application of antibiotic stewardship principles.”
status has been granted to a drug in the ten-year history of the policy, it represents a potential pathway through which access could be enhanced for more critically needed medications, including antibiotics.

The increased financial incentive to use DIFICID® and other antibiotics that may obtain future NTAP designation must be accompanied by evidence-based application of antibiotic stewardship principles. This will ensure alignment of three incentives: to bring innovative antibiotics to market, provide patient access to needed antibiotics and to preserve the effectiveness of these antibiotics over a sufficient period of time. We offer a few recommendations on how to guarantee optimal public health outcomes with regards to antibiotic resistance.

**Policymakers**

To further enhance existing programs aimed at combating antibiotic resistance, policymakers should take deliberate steps to align regulatory, reimbursement and public health goals on the issue of HAI reduction. For example, Congress should consider linking any antibiotic designated by the GAIN Act to eligibility for additional Medicare payments.

**Professional Societies, CDC, Public Health Organizations**

Clinical and public health experts should be convened to develop, validate and disseminate simple protocols for antibiotic selection to support FDA-approved indications. These protocols will support rational use of antibiotics through clinical decision support for health care providers. While we recognize that these protocols should be tailored to local resistance patterns, they will drive standardization of care according to broad evidence-based principles of antibiotic use.

**Healthcare Facilities**

Finally, healthcare providers should consider establishing antibiotic stewardship programs that leverage existing delivery infrastructure for ease of implementation. In particular, we believe that electronic decision support systems should be used to operationalize validated antibiotic selection protocols.

**References**


10. Medicare Program; Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long-Term Care Hospital Prospective Payment System and Fiscal Year 2013 Rates; Hospitals’ Resident Caps for Graduate Medical Education Payment Purposes; Quality Reporting Requirements for Specific Providers and for Ambulatory Surgical Centers; Final Rule. Federal Register 77 (August 31, 2012): 53350.

Noroviruses (formerly described as “Norwalk-like virus”) are a group of non-enveloped viruses (approximately 27-35nm in diameter) with a single-stranded RNA genome, classified into the genus *Norovirus* of the family *Caliciviridae*. [1] Norovirus is the most common cause of epidemic gastroenteritis in the United States, causing >90% of non-bacterial and ≈50% of all-cause epidemic gastroenteritis worldwide. [2-4] Infection with norovirus can cause anything from mild and self-limited disease to severe gastroenteritis, especially among young children, the elderly and hospitalized patients. [3] It is also characterized by low grade fever and body aches, and thus the term “stomach flu” is used to describe the illness, although there is no biologic association with influenza. [1] Each year, norovirus causes about 21 million illnesses and contributes to approximately 70,000 hospitalizations and 800 deaths. It is estimated that healthcare and lost productivity due to foodborne illness costs up to $2 billion [2].

Noroviruses are highly contagious, with an estimated infectious dose as low as 10-18 viral particles. [5, 6] There are many different types of noroviruses and people of all ages can become infected during outbreaks. It is possible to develop immunity to specific types of norovirus, but little is known about how long immunity lasts, which may explain in part why people can get infected many times during their lifetime. [7]

The lack of a cell culture system for growing norovirus and the limited animal model has represented a challenge to understanding viral transmission; [5] however, a number of studies have demonstrated the importance of some key factors in transmission. Norovirus transmission may include: person-person transmission via the fecal-oral route, direct transmission from close contact with infected persons or contact with a contaminated surface, and by consumption of fecally contaminated food or water [1, 5]. Norovirus may have a possible route of indirect zoonotic transmission to humans through the food chain from infected pigs and cows. [8] Evidence exists for dissemination of infectious particles, especially during the process of vomiting that results in droplets contaminating surfaces or entering the oral mucosa and being swallowed. [2, 5] Table 1 shows characteristics that may contribute to the ability of norovirus to cause outbreaks in humans. [5] Norovirus outbreaks have occurred in various community and healthcare settings, including cruise ships, hotels, restaurants, public gathering places, rehabilitation centers, hospitals, and long term-care facilities. [9-12] Although norovirus is identified as a cause of community-associated gastroenteritis, systematic studies have

<table>
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<th>Table 1. Microbiologic and Epidemiologic Characteristics of Norovirus [5].</th>
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<tr>
<td>Large human reservoir of infection</td>
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<tr>
<td>Widespread host susceptibility</td>
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<td>Strain-specific immunity is short lived (weeks to months)</td>
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<tr>
<td>Multiple routes of transmission (fecal-oral, foodborne, waterborne, aerosols)</td>
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<tr>
<td>High infectivity</td>
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<td>Very low inoculating dose (&lt;10 virions)</td>
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<td>Stable in the environment</td>
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<td>Prolonged shedding</td>
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<td>No vaccine available</td>
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reported that healthcare facilities including nursing homes and hospitals are the most commonly reported settings of norovirus outbreaks in the US and other industrialized countries. [13, 14] It has also been shown that norovirus outbreaks in these settings spread rapidly, have high attack rates and are extremely difficult to control. [12, 15]

The risk factors for norovirus outbreak in healthcare settings include: enclosed living conditions, reduced levels of personal hygiene resulting from fecal incontinence, cognitive impairment, and immobility, which facilitate the transmission of the virus. Additionally, norovirus can be introduced from the community into healthcare settings by staff, visitors, or by contaminated food products. [1] Figure 1 shows the role environmental and fomite contamination play in norovirus transmission in healthcare settings. During the period of 2001-2003, the number of gastroenteritis outbreaks caused by norovirus increased worldwide, affecting many healthcare systems. [1, 16] The US provides care to approximately 3.3 million residents’ nursing homes and 31% of acute gastroenteritis outbreaks occurred in these settings. Norovirus is implicated in 86% of etiological confirmed outbreaks. [14, 17]

Environmental contamination with norovirus has been implicated in a number of outbreaks and surfaces such as staff telephones, toilet seats, toilet door handles, bed rails, and dining tables. Elevator buttons were among the most contaminated surfaces. [5, 12, 18] In 2003 an outbreak of acute gastroenteritis was reported among residents of a 240-bed veteran’s long-term care facility. Fifty-two per cent of residents and 46% of employees became sick, reporting an attack rate of 34%. [12] One of the largest norovirus outbreaks occurred in 2010 in Clark County, Nevada and involved eight long-term care facilities, where 31% of residents and 11% of staff became ill. The attack rate ranged from 17-55%; however, no deaths were reported. [19] The ability of norovirus to persist on inanimate surfaces from 8 hours up to 7 days and its relative resistance to inactivation by many common disinfectant products likely contributes to the high number of outbreaks. [5, 20]

Control of norovirus in the healthcare environment should include: isolation of the affected from the unaffected—especially staff members who are employed at, or have interaction with, multiple facilities; proper hand hygiene, including washing of hands with soap and water among healthcare personnel, patients and visitors; use of gowns and gloves; and disinfection of high-touch patient surfaces and equipment. [19, 21-4] The use of chemical disinfectants is one of the key approaches to interrupt norovirus spread from contaminated environmental surfaces. [1] It is widely acknowledged that simple detergent cleaning is not sufficient; however, wiping surfaces first with a detergent and then applying sodium hypochlorite (bleach) at a concentration of 1,000 – 5,000 ppm (1:50–1:10 dilution of household bleach 5.25%) has been shown to be effective in the disinfection of environmental surfaces. [25-6] More recently, hydrogen peroxide has also shown efficacy against norovirus [27] and has been proposed for routine environmental control of noroviruses. [28] Other commonly used disinfectants such as quaternary ammonium compounds or alcohols are not as effective against norovirus. [21, 22, 29] The CDC recommends that alcohol-based hand sanitizer can be used in addition to hand washing to prevent norovirus infection. In healthcare settings, only EPA-registered disinfectant products with specific claims for efficacy against norovirus should be
used, and personnel performing environmental services should adhere to the manufacturer’s instructions for dilutions, application, and contact time. [1] Agents registered as effective against norovirus by EPA are available on the EPA website.

Since there is no vaccine to prevent norovirus and no drugs to treat it (antibiotics are not effective against norovirus) [24], infections will continue to emerge in healthcare facilities in the coming years and it is therefore imperative to develop and adhere to stringent education and infection control practices. Surveillance, isolation, hand hygiene and disinfection of surfaces in healthcare settings play an important role in disrupting the transmission of norovirus and are key factors in reducing occurrence and severity of outbreaks.

References

“The ability of norovirus to persist on inanimate surfaces from 8 hours up to 7 days and its relative resistance to inactivation by many common disinfectant products likely contributes to the high number of outbreaks.”
nosocomial pathogens persist on inanimate surfaces? A systematic review. 2006. Infect Dis. 6:130
APUA-Abu Dhabi, UAE Update

The APUA Abu Dhabi chapter (lead: Dr. Mohammed Abuelkhair, HAAD) was established by the Health Authority – Abu Dhabi (HAAD) in February 2010 and several working groups were created to address the various aspects of judicious antimicrobial use, e.g. antibiotic consumption monitoring, antimicrobial resistance surveillance, education and awareness, community outreach, and scientific research.

The Antimicrobial Resistance Surveillance working group (lead: Dr. Jens Thomsen, HAAD) has developed and now implemented as a pilot the first electronic surveillance system for antimicrobial resistance for the Emirate of Abu Dhabi, the AD ARS (Fig. 1). This is also the first antimicrobial resistance surveillance system in the United Arab Emirates, and the second such system on the Arab Peninsula, after Oman.

Aims & Objectives: The AD ARS is designed to help the Health Authority – Abu Dhabi (HAAD), Abu Dhabi Health Services Company (SEHA) and local healthcare providers in making informed decisions regarding therapeutic guidelines and prescription policies for antimicrobials, antimicrobial stewardship programs, and infection prevention and control programs. For further aims & objectives please refer to Text Box 1.

Currently all 61 local public healthcare facilities, including 7 major public hospitals, are reporting AMR surveillance data quarterly to AD ARS, located at the Health Authority – Abu Dhabi, where the data are centrally analyzed and reported back to the concerned community (Fig. 2):

Results & Findings: A wealth of quality data from 2010-2012 is available for analysis and includes information on 48,000+ clinical isolates from 19,000+ patients with 466,000+ susceptibility tests conducted per year (Fig. 3).

Selected findings include the following (preliminary results, for discussion):

Figure 1: The Abu Dhabi Antimicrobial Resistance Surveillance (AD ARS) System and Network.

Text Box 1 - AD ARS Objectives:

- Improving clinical effectiveness of empiric antimicrobial therapy for patients with infectious diseases and hospital-acquired infections
- Providing the necessary resistance data for assessing the relationship between local antimicrobial consumption and development of antimicrobial resistance
- Supporting targeted awareness and education activities for physicians, pharmacists and the general public
- Conducting cluster and outbreak analysis
- Exchanging AMR surveillance data with other emirates and countries in the region and beyond with a view to facilitate the creation of a nation- or even Gulf Cooperation Council (GCC)-wide AMR surveillance system
reported in only 0.6% (n=2) of E. faecalis isolates, but in 24.0% (n=12) of reported E. faecium isolates; the overall VRE rate is 3.6%.

- In *Escherichia coli* and *Klebsiella pneumoniae* a particular concern is the emergence of carbapenem resistant strains. Imipenem resistance: *E. coli* = 0.4%, *K. pn.* = 1.6%; meropenem resistance: *E. coli* = 0.2%; *K. pn.* = 1.3%;

- *Pseudomonas aeruginosa*: Multidrug-resistance is very frequent (64.8% of isolates);

- *Acinetobacter baumannii* (1,649 isolates) and *Stenotrophomonas maltophilia* (204 isolates) are highly resistant to most relevant classes of antimicrobials, and multidrug-resistance is very common (71.6% and 80.3%, respectively).

A comprehensive first report is expected in early 2013.

More than a third of all *Staphylococcus aureus* isolates are already resistant to beta-lactam antibiotics (MRSA rate: 34.3%, n=730 isolates);

- To date, 15.6% of *Streptococcus pneumoniae* isolates are resistant to penicillin G, and *S. pneumoniae* is highly resistant to macrolides (erythromycin: 49.1%). Resistance to ceftriaxone (0.8%) and fluoroquinolones (0.7-1.6%) is still rare. Multidrug-resistance is prevalent in 20.0% of all isolates;

- For *Enterococci*, resistance to vancomycin has been

### Figure 2: Public healthcare facilities participating in AD ARS, Abu Dhabi Emirate, United Arab Emirates.

- Figure 2: Public healthcare facilities participating in AD ARS, Abu Dhabi Emirate, United Arab Emirates.

- Figure 3: AD ARS 2011 data base, Abu Dhabi Emirate, United Arab Emirates.

### APUA-India Update

APUA-India co-sponsored the first “International Conference of Pharmacoeconomics and Outcomes Research” on November 22-23, 2012 in New Delhi. The conference was organized by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) and was attended by more than 300 scientists and professionals. APUA-India President, Dr. Jawahar S. Bapna, a member of ISPOR-India’s National Advisory Board, was a speaker and participated in a symposium on “Preserving Antibiotics for Future Generations.” The conference program is available on the ISPOR website.

Attendees of the ISPOR conference in New Delhi, November 2012 including APUA-India members
APUA-Nepal Update

APUA-Nepal has developed, printed and distributed a poster (left) on improving community awareness for display in hospitals and private drug sellers. It warns about the dangers of antibiotic resistant bacteria, advises patients to complete their prescribed dose of antibiotics, to avoid antibiotics for viral infections, and to take antibiotics only after obtaining a prescription. The 2012 APUA-Nepal Newsletter, with sensitivity patterns of common Nepalese hospital isolates, is now available on the APUA website.

APUA-Cuba Update

APUA-Cuba President Dr. Moisés Morejón-García has published a review article (in Spanish) in Dermatología Peruana titled “Methicillin-resistant Staphylococcus aureus: A current problem.”

In early November 2012, APUA-Cuba members presented at the National Workshop on Antimicrobial Resistance attended by more than 160 specialists, mostly microbiologists and infectious disease specialists from different disciplines. Among the presentations was one by Dr. Quiñones, details of which can be found on page 7.

On November 24th, APUA-Cuba members presented five of eight lectures at a “Nutrition and Sepsis” course organized by the Cuban Society of Surgery’s Clinical Nutrition Section at the Hospital Universitario Manuel Fajardo in Havana. The close linkage between malnutrition and poor outcomes in septic patients has prompted APUA-Cuba to integrate the issue of protein energy malnutrition into its multidisciplinary approach.

On December 14, APUA-Cuba held its annual summary meeting, Balance del año and discussed the 2012 accomplishments of its 9 regional sub-chapters (4 of which were established in 2012) as well as a specialty sub-chapter—APUA-Cuba: Veterinary Medicine. In 2012, APUA Cuba has grown by approximately 600 members, bringing the total to over 1,700.

APUA-Cuba Annual Meeting, December 2012.

Obituary

It is with great sadness that we inform you of the passing of one of APUA’s esteemed long-time supporters, Dr. Iwan Darmansjah (APUA Scientific Advisory Board Member) on October 21, 2012. He was a Professor in the Department of Pharmacology and Therapeutics as well as a member of the Medical Faculty at the University of Indonesia in Jakarta. He was a member of the WHO Expert Panel on Drug Policy and Management, the WHO-SEARO Advisory Panel on Drug Evaluation, and Chairman of the International Union of Pharmacology’s Clinical Pharmacology Section. His tireless efforts have generated admiration and respect from his colleagues and others concerned with the prudent use of antibiotics.

Professor Iwan Darmansjah
APUA at WHO’s Technical Consultation on Surveillance

The World Health Organization (WHO) held a meeting titled “Consultation on Strategies for Global Antimicrobial Drug Resistance (AMR) Surveillance” in Geneva, Switzerland on December 18-19, 2012. APUA was invited to attend, and Lisa Tapert, APUA’s new Director of Program Development represented the organization. Also present were representatives from APUA-South Korea, APUA-Russia, APUA-Senegal, and APUA-Bangladesh. The purpose of the meeting was to review the scope of existing international networks for antibacterial resistance surveillance, identify capabilities, methods, and data needed to develop appropriate surveillance and identify current gaps and challenges for improving and expanding such surveillance.

APUA Webinar on Stewardship—PACE Credit Available

APUA recently presented a one-hour webinar entitled "Containing Health Care Associated Infections through Antibiotic Stewardship" in conjunction with the Tufts Medical Center. This webinar described the nature of antimicrobial resistance, identified trends of major resistant infections, and delineated the important components of successful antimicrobial stewardship. The targeted audience is infectious disease pharmacists, physicians, and laboratory personnel. This webinar is free to view and PACE credit is available until May 13, 2013.

APUA comments on Antimicrobial Animal Drug Sales and Distribution Reporting

APUA joined other public health organizations in commenting on the US FDA’s Advanced Notice of Proposed Rulemaking (ANPR). In a joint letter to the FDA, suggestions were made for improving the way veterinary drug use data is collected, aggregated, and distributed to the public. Based on the advocacy from these organizations, over 25,000 Americans also joined in the petition.

APUA co-signs letter in Financial Times

The November 13th edition of the Financial Times features a letter from APUA and other leading international health care organizations advocating for new antibiotic development as well as strong antibiotic stewardship of existing antibiotics. The letter can be viewed on the APUA website or the Financial Times website (free account needed).

APUA signs Joint Statement on Antibiotic Resistance

On November 13, the Centers for Disease Control and Prevention (CDC), the Center for Disease Dynamics, Economics and Policy (CDDEP) and the Robert Wood Johnson Foundation (RWJF), in collaboration with APUA and more than twenty other leading health care organizations, released The Joint Statement on Antibiotic Resistance. This statement coincided with CDC’s “Get Smart About Antibiotics Week.”

APUA advocates for consumer involvement in meetings on antibiotic use in livestock

The U.S. Food and Drug Administration (FDA)’s Draft Guidance #213 asks drug makers to voluntarily end the sale of antibiotics for livestock growth promotion and feed efficiency. Along with the U.S. Department of Agriculture, the FDA has planned a series of public stakeholder meetings across the country to discuss increased veterinary oversight of judicious antibiotic use in food animal production. Large animal veterinarians and producers are expected to attend. While the participation of these groups is critical, it is equally important that the public health community and consumers be represented at these meetings. APUA has signed on to a joint letter to the FDA urging the agency to actively involve public health and consumer stakeholders in the upcoming meetings, to finalize Guidance #213 and to issue a formal proposed rule regarding the Veterinary Feed Directive changes by the end of 2012.
GAP sues FDA over antibiotic sales data; DATA Act proposed in US Congress

The Animal Drug User Fee Act (ADUFA) mandates that drug companies provide basic information about antibiotic sales to the U.S. Food and Drug Administration (FDA). The FDA then shares a limited summary of these data with the public, but withholds almost all of what companies report. The Government Accountability Project (GAP) submitted a Freedom of Information Act request for this data to the FDA in February 2011. Upon denial, GAP appealed to the Public Health Service, which includes the FDA. Following a one-year delay, the appeal was denied in September 2012. A lawsuit has followed.

Recently, Representative Waxman of California proposed a bill titled the “Delivering Antibiotic Transparency in Animals (DATA) Act.” It could provide the FDA with more important information about the types, purposes, and quantities of antibiotics being fed to livestock.

FDA creates Antibacterial Drug Development Task Force; White House Advisory Board issues Report

As committed in the recent GAIN Act, the US FDA has created a new Antibacterial Drug Development Task Force, a multi-disciplinary group of 19 FDA scientists and clinicians. The goals are to: explore novel scientific approaches for antibacterial drug development; identify issues related to unmet medical needs for antibiotics; evaluate existing FDA guidances related to drug development; and use existing collaborations to work thought leaders to explore new approaches.

Following the FDA’s announcement, the President’s Council of Advisors on Science and Technology issued a report on Sept. 25 detailing a plan to double the yearly production of new drugs over the next decade. The report makes specific recommendations to improve drug development and evaluation, and effectively monitor benefits and risks.

The EU passed a non-binding resolution to tackle resistance

Resistant bacteria cause 25,000 deaths a year in the EU, Iceland and Norway. The European Center for Disease Prevention and Control (ECDC) recently released a Surveillance Report showing that more than a third of the European Union countries demonstrate increasing resistance to multiple antibiotics in both Klebsiella pneumoniae and Escherichia coli over the last four years. A summary of antibiotic consumption in Europe was also released in November.

On December 11th, the EU Parliament passed a non-binding resolution drafted by Anna Rosbach (ECR, DK) calling for urgent action in developing new drugs, better stewardship of existing ones and improved use in animal husbandry. More information can be found on the Parliament website.

Expert panel finds novel TB drug effective

On November 28, a non-FDA medical expert panel (Anti-Infective Drugs Advisory Committee) evaluated the efficacy and safety of bedaquiline, a new type of tuberculosis drug—the first in over 40 years. While the panel of 18 members unanimously deemed the drug effective, 7 members felt more evidence was needed to address the drug’s safety. The FDA will decide on the drug’s approval by Dec. 29, 2012. Although the agency usually follows the advice of the advisory committee, it is not obligated to do so.

CDC updates plan to combat antimicrobial resistance

The 2012 update of the Public Health Action Plan to Combat Antimicrobial Resistance lists the projects that the Federal Agencies in the Interagency Task Force on Antimicrobial Resistance are considering in the areas of surveillance, prevention and control, research and product development.
Origin and spread of \textit{C. diff.} mapped; Europe conducts CDI prevalence study

A new study published in \textit{Nature Genetics} reveals how two closely related strains of \textit{Clostridium difficile} developed resistance to antibiotics and spread around the world.

The European multi-centre, prospective bi-annual point prevalence study of \textit{C. difficile} infection in hospitalized patients with diarrhea (EUCLID) was launched this month. With 20 European countries and approximately 500 hospitals involved, this is the largest study of the prevalence of \textit{C. difficile} infection (CDI) ever conducted in Europe. A full report and analysis of the findings are expected in mid-2013, when the true prevalence of CDI will become known for the first time. Currently, it is thought to be widely under-estimated.

PEW releases bibliography on antibiotic resistance and food animal production

A new bibliography published by PEW Charitable Trusts lists the latest scientific and economic literature linking the routine use of antibiotics in food animals and the crisis of human antibiotic resistance. Thanks to over 30 years of research in this area, there is scientific consensus that antibiotic use in food animals contributes to resistance in humans.

CDC and PEW conduct joint survey on public knowledge about antibiotics

Modeled after APUA's 2006 telephone survey of over 900 US adults, a new poll by CDC and PEW Charitable Trusts, which surveyed over 1,000 adults via phone and focus groups, found that only 25% of respondents had heard “a great deal” about antibiotic resistance, one-third a “fair amount” and a full 41% “very little or nothing at all.” Although almost 90% of Americans knew that antibiotics are effective for treating bacterial infections, more than a third also incorrectly believed viral infections such as the common cold or the flu can be treated with antibiotics. This percentage shows a decrease from the time of the APUA survey, when approximately half of respondents believed antibiotics could cure viral infections. For more information, see the US News article.

Tufts study estimates $4-6 billion spent annually on extraneous clinical trials data

A new study at the Tufts Center for the Study of Drug Development (CSDD) shows that one in five procedures performed during the later stage of a clinical trial collects data which are not related to the core endpoints and add more than $1 million in cost per trial. These extraneous data are related to the supplementary secondary, tertiary and exploratory endpoints and are being collected to “interpret findings, guide development decisions, support adherence to protocol authoring templates and design practices, and anticipate requests from regulatory agencies, purchasers, and payors.”

Given the total number of active Phase II and III clinical trials regulated by the US FDA, it is estimated that the pharmaceutical industry spends between $4-$6 billion each year on this extraneous data. According to Professor Ken Getz of Tufts CSDD, these new findings can be used “to streamline protocol designs, improve clinical research performance, and reduce development costs.”

Call for shorter antibiotic prescriptions

In a PNAS article, researchers from the University of California Irvine pointed out the guiding principle for antibiotic treatment should be “to impose no more selection than is absolutely necessary.” A recent PLOS blog further explores this idea and the author explains, “To be clear, nobody is saying patients should decide their own dose. But there is a good argument to be made that the public health message about antibiotics, which is consistent worldwide for many diseases and drugs, deserves a second look.”
In the US, the threat of carbapenem-resistant *Enterobacteriaceae* (CRE) bacteria continues to spread as reported in a recent *USA Today* article. The first known case was reported in 2001 at a North Carolina hospital. Since then, CREs have spread to at least 41 other states.

**UTI treatments losing effectiveness in US**

According to new research from *Extending the Cure*, a project of the Center for Disease Dynamics, Economics & Policy (CDDEP), urinary tract infections (UTIs) are becoming harder to treat, with the overall share of resistant UTI-causing bacteria increasing by over 30% between 1999 and 2010. This is especially problematic as UTIs are the second most common type of infections in the United States. The highest burden of antibiotic resistant UTIs was in the East South Central and South Atlantic states. While, New England and the Pacific states had lower levels. For more information see the CDDEP website.

**First two NDM-1 hospital outbreaks reported in Canada**

New Delhi M-1 was first detected in 2008 in a Swedish traveler in India. Although individual cases have been reported in Canada since 2010, these were among people who had travelled outside the country for health care. The first outbreak occurred at William Osler Health System in Brampton, northeast of Toronto in October 2011. It involved five patients, all carrying *Klebsiella pneumoniae*, and all linked, as shown by molecular study. None of the patients in the outbreak had travelled to or been hospitalized in countries where NDM-1 is endemic and it is unclear where the bacteria had been acquired.

The second outbreak took place at Toronto's Sunnybrook Health Sciences Centre in January 2011 and was over by February 2011. During that time two patients came into the hospital with different strains of NDM-1 *K. pneumoniae*. One had received previous health care in India, but the second had not. The bacteria spread to colonize seven others and four of the patients developed infections.

**MRSA outbreak in German hospital**

The Intensive Care and Emergency Medicine Unit at the Klinikum Bremen-Mitte Hospital in Bremen, Germany reported in October 2012 that MRSA bacteria had been detected in 45 people, including patients, staff and relatives. There is evidence to suggest that the outbreak resulted from multiple strains and cannot be traced to a single source. In 2011, the same hospital had an outbreak of *Klebsiella* in the Neonatal Intensive Care Unit which resulted in the death of three children and controversy over the hospital’s hygiene practices.

**“Swine MRSA” spreads in Denmark**

In 2006, MRSA CC398, found on pig snouts and skin, was first identified as a human pathogen in Denmark. At the time, the infection mostly threatened farm workers, but has now spread to the general population. The total number of swine MRSA infections in Denmark has increased from 43 cases in 2009 to around 200 cases this year. Accused of inaction, the Danish Food and Health Ministers have met to discuss the issue. The strain has not been found in Swedish pigs but precautions are being taken to prevent the importation of the bacteria.

**ECDC experts visit Greece to discuss resistance**

The Hellenic Center for Disease Control and Prevention (KEELPNO) had requested technical support from the European Center for Disease Prevention and Control (ECDC) to help curb Greece’s increasing antimicrobial resistance problem. To discuss the issue, experts from ECDC travelled to Greece on November 29-30, 2012. According to coverage by NPR, the economic crisis in the country has severely impacted hospitals and ECDC predicts that budget shortages will lead to increases in hospital-acquired infection rates in Greece, which are already among the worst in Europe.
UV light for hospital disinfection

Researchers at Duke University Medical Center and the University of North Carolina Hospital System used short-wave ultraviolet radiation (UV-C) to nearly eliminate Acinetobacter, Clostridium difficile and vancomycin-resistant Enterococcus (VRE) in more than 50 patient rooms at the two medical facilities. Given previous findings by the University of North Carolina team that UV-C is effective at decreasing methicillin-resistant Staphylococcus aureus (MRSA) in hospital rooms, the new study lays critical groundwork for expanding a new technology for broad elimination of major hospital-acquired pathogens.

Provider education and feedback boosts stewardship

A study involving one of the nation’s largest networks of pediatric practices was able to nearly halve the inappropriate use of antibiotics through quarterly monitoring and feedback of its physicians’ prescribing patterns. Initially, about 28% of children inappropriately received a broad-spectrum antibiotic for a targeted condition. After the antibiotic primer session and a year of regular prescribing evaluations, clinicians in the intervention group reduced off-guideline use to 14%. The control group rate also declined, but only to 23%.

Simple hygiene measures help curb hospital-acquired infections

According to research first reported at IDWeek, washing intensive care unit (ICU) patients with chlorhexidine antiseptic soap for the duration of their ICU stay, in conjunction with the application of intranasal mupirocin antibiotic ointment for 5 days, lowered the number of patients harboring methicillin-resistant Staphylococcus aureus (MRSA) by more than a third, while bloodstream infections caused by MRSA and other pathogens decreased by 44%. The study involved nearly 75,000 patients in 43 mostly community hospitals in 16 states. Lead researcher Dr. Susan Huang, associate professor at the University of California, Irvine School of Medicine cautioned that results apply to ICUs only. While there is concern that even within critical-care settings, broad adoption could speed emerging antibiotic resistance, Dr. Huang stressed that widespread use of antimicrobials in patients at low risk for infection could increase resistance to these products without any benefit.

Similar results were seen in prevention of infection following colorectal surgeries at seven large US hospitals involved in a two and half year project, organized by the Joint Commission hospital regulating group and the American College of Surgeons. Interventions included having patients shower with special “germ-fighting” soap before surgery, and a change of gowns, gloves and instruments during operations to prevent hospital staff from spreading germs picked up during the procedure. Some hospitals also used special wound-protecting devices on surgical openings to prevent intestinal contamination of skin. The average rate of infections linked with colorectal operations dropped from almost 16% of patients during a 10-month phase when hospitals started adopting changes to about 11% afterward. An estimated 135 infections were prevented by the project, saving about $4 million. The average length of hospital stay for patients who did get infections dropped from 15 days to 13 days, which also helped cut costs.

The Netherlands cuts antibiotic use in food animals by half

Compared to the first half of 2009, the total sales of antibiotics for veterinary use in the Netherlands has been reduced by 51% in the first half of 2012. The 50% reduction target was originally set for 2013 but has remarkably been achieved in 2012 itself. The decline in sales of the "critical antibiotics”—fluoroquinolones and third and fourth generation cephalosporins—was 23% and 92% respectively. "We are excited about these promising results," wrote Verdaas, Minister of Economic Affairs (EZ) and Schippers, Minister of Health, Welfare and Sport (VWS) to the House of Representatives.
# Upcoming Events

**February 4-8, 2013**: Tufts CSDD “Postgraduate Course in Clinical Pharmacology, Drug Development and Regulation,” Boston, MA.


**February 21-23, 2013**: Australian Society for Antimicrobial's Annual meeting “Antimicrobials 2013,” Sydney, Australia.


**March 14, 2013**: British Society for Antimicrobial Chemotherapy’s Spring Meeting 2013, London, UK.

**April 27-30, 2013**: European Congress on Clinical Microbiology and Infectious Diseases (ECCMID 2013), Berlin, Germany.

**May 18-21, 2013**: American Society for Microbiology's ASM 2013, Denver, CO, USA.

**May 28-June 1, 2013**: Congreso de la Asociación Panamericana de Infectología (API 2013), Santiago, Chile.

**June 5-8, 2013**: International Congress of Chemotherapy and Infection (ICC 2013), Nishi-Ku, Japan.

**June 8-10, 2013**: Association for Professionals in Infection Control and Epidemiology’s Annual Conference(APIC 2013), Ft. Lauderdale, FL, USA.


**July 8-9, 2013**: Annual Global Healthcare Conference (GHC 2013), Singapore, Malaysia.

**July 27 – August 1, 2014**: International Union of Microbiological Societies 2014 Congresses, Montréal, Canada.

**August 31- September 1, 2013**: Clinical Infectious Diseases Society Conference (CIDSCON 2013), Mumbai, India.

**September 10-13, 2013**: Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC 2013), Denver, CO, USA.

**October 2-6, 2013**: Infectious Diseases Society of America (IDSA), the Society for Healthcare Epidemiology of America (SHEA), the HIV Medicine Association (HIVMA), and the Pediatric Infectious Diseases Society (PIDS)’s IDWeek 2013, San Francisco, CA.

**November 19-22**: International Conference on Infectious Disease Dynamics (EPIDEMICS 2013), Amsterdam, Netherlands.
About Us

Antibiotics are humanity’s key defense against disease-causing microbes. The growing prevalence of antibiotic resistance threatens a future where these drugs can no longer cure infections and killer epidemics run rampant. The Alliance for the Prudent Use of Antibiotics (APUA) has been the leading global non-governmental organization fighting to preserve the effectiveness of antimicrobial drugs since 1981. With affiliated chapters in more than 66 countries, including 33 in the developing world, we conduct research, education and advocacy programs to control antibiotic resistance and ensure access to effective antibiotics for current and future generations.

Our global network of infectious disease experts supports country-based activities to control and monitor antibiotic resistance tailored to local needs and customs. The APUA network facilitates the exchange of objective, up-to-date scientific and clinical information among scientists, health care providers, consumers and policy makers worldwide.
Dear APUA Colleague,

We write to wish you happy holidays and ask for your renewed partnership in "Preserving the Power of Antibiotics." For over 35 years, APUA has been a steadfast force working to ensure antimicrobial treatment effectiveness around the world. To ensure that antibiotic resistance is front and center on the public health agenda, we cannot let our guard down now. With your support we will move forward in 2013, securing adequate funding and policies to ensure effective antibiotic treatment for current and future generations.

While the antimicrobial resistance issue was largely ignored just a few years ago, we can take mutual satisfaction in our progress. With your help APUA's evidence-based advocacy has had an impact this year:

- The GAIN Act passed in the US, providing incentives for new antibiotic and diagnostics development.
- The US FDA has released progressive guidances to improve the use of antibiotics in food animals.
- The Antibiotic Stewardship Movement is now gaining traction with the promise of legislated funding and incentives.
- The WHO has renewed the antimicrobial resistance international action plan with APUA's participation.

APUA member donations provide invaluable unrestricted support for infrastructure needed to conduct APUA's activities, including:

- Production of APUA Clinical Newsletters with distribution to more than 10,000 infectious disease practitioners.
- Focused distribution of educational materials in resource-poor countries.
- A US National Stakeholder Meeting: "Improving Antimicrobial Use in Food Animal Production: Alternatives, Options and Incentives."
- A new APUA webinar: "Containing Healthcare-Associated Infections through Antibiotic Stewardship"

Your generosity is greatly appreciated as we balance the fiscal constraints of a nonprofit organization with APUA's ambitious plans in the fiscal year 2012-2013. Please send your donation to the address below or use our Paypal link. We thank you for your generous support over the years and look forward to working together closely in 2013. With your help, APUA will continue its role as a valuable source of non-commercial information on antibiotic resistance around the world.

Happy New Year and Many Thanks!

Stuart B. Levy, M.D. (President)  
Kathleen Young (Executive Director)

Suggested Donations (Tax deductible in the US):
$100: General support  
$200: Support coordination of APUA Clinical Newsletter  
$500: Support development of public education materials  
$1000: Support chapter liaison with developing country  
Other

“Preserving the Power of Antibiotics”®