HIGHLIGHTS - WINTER 2018

APUA HEADQUARTERS NEWS

APUA testifies before Canadian House of Commons

On Nov. 21, 2017, APUA program manager, Jane Kramer, represented APUA before the Canadian House of Commons' Committee on Health, which convened in Ottawa by videoconference. It was the committee's seventh and final meeting on antimicrobial resistance and this one sought an international perspective. The other witnesses were Dr. Timothy Evans from the World Bank; Willo Brock from the TB Alliance and Dr. Gerard Wright from McMaster University.

The 2-hour hearing was attended by about two dozen Members of Parliament, 11 of whom are on the Committee on Health, as well as several dozen associate MPs. Each witness was given 10 minutes for commentary, followed by a period of questions and answers.

APUA's remarks pointed them toward WHO's template for developing a national action plan and its advantages and deficiencies; a definition of antibiotic stewardship and the need to educate and persuade prescribers about evidence-based prescribing, together with a description of APUA's international country-based chapters and their value of communication among professionals; discussion of incentives for encouraging development of new medicines and rapid diagnostics; and finally, the need to acknowledge that consumer preference is causing poultry producers to depart from antibiotics for growth promotion, but as the middle class grows in the BRIC countries, their preference for meat in their diets will boost consumption of antibiotics for growth promotion. We concluded noting that, as a leader in social responsibility, Canada can be the world's model to manage the complex interplay that causes AMR through its national health system, its scale and diversity, advanced science, commercial enterprises and agriculture—in short, its rich culture.

APUA supports restored congressional funding for AMR

In October 2017, APUA joined concerned healthcare providers, scientists, patients, and public health and industry stockholders in its support for rejecting the deep cuts in antimicrobial resistance (AMR) spending proposed by the U.S. President's budget request. The letter, addressed to members of the Committee on Appropriations asked for continued, high priority, bi-partisan support for AMR that "reflects the U.S. commitment to infection prevention, antimicrobial stewardship, surveillance and innovation." Specifically, the letter recommended at least $520M for BARDA, $214M for CDC, $5.127B for NIH, $1.35B for USAID and $33.93B for the Department of Defense, as well as robust funding for several U.S. agricultural departments.

In January, 2018, APUA joined forces once again with mutually concerned stakeholders in a letter to U.S. Senate and House members who are considering reauthorization of the Pandemic and All-Hazards Preparedness Act (PAHPA). The letter describes the threat that AMR poses to national security, noting that 3,300 American soldiers in Iraq and Afghanistan became severely ill from multi-drug resistant *Acinetobacter* alone, and that weaponized, resistant plague and anthrax organisms, if released in a bioterrorist attack, could injure or kill millions. The letter points out that current support of antimicrobial R&D is insufficient to deal with these events and urges inclusion of new R&D incentives in the crafting of the upcoming PAHPA reauthorization bill.

APUA CHAPTER NEWS

APUA-Nepal Newsletter issued

APUA-Nepal chapter leader K.K. Kafle has communicated that a new edition of the *APUA-Nepal Newsletter* has recently been released (Vol 14, No. 1, 2017). This latest issue, which focuses on isolates of eight pathogen species, from urine, pus and blood collected from three municipal hospitals, compares the mean

percentages of pathogen antimicrobial susceptibility between two time periods: 2007 + 2009 vs. 2013 + 2016.

Uruguay reactivates chapter; new publication issued

APUA-URUGUAY was active between 1990 and 2003 and accomplished its specific objective of requiring medical prescription for antibiotic purchase. Unfortunately this requirement has become lax and in need of reinforcement. Additionally, Uruguay has encountered severe dramatic rises in antimicrobial resistance, and like other countries, had achieved some control of MRSA, only to be undermined by outbreaks of *C. difficile* diarrhea and pan-resistant agents within hospital infection control wards. Likewise, MRSA soft tissue infections have escalated among healthy young persons.
In light of these issues and the urgent need to develop national regulations as proposed by the Global Action Plan, a group of 10 professionals under the leadership of Dr. Maria Hortal have organized to reactivate the Chapter with the following objectives:

- Reorganize the internal structure with regular meetings
- Improve awareness and understanding of antimicrobial resistance and its mechanisms;
- Broaden knowledge through surveillance and research;
- Reduce the incidence of infection by improving hygiene and use of available vaccines
- Optimize the use of antimicrobial agents in order to preserve their efficacy

In 2018, the Chapter plans to hold three conferences on antimicrobial resistance at three Montevideo hospitals and a workshop for post graduate candidates at the Children's Hospital.

APUA applauds this renewed commitment towards rebuilding the APUA-Uruguay chapter and addressing continuing challenges.

Dr. Hortal also notes the recent publication of the article: *Increasing resistance to antimicrobials: an international alert* by T. Camou, and P. Zunino, which provides updated information, explaining the reasons why antimicrobial resistance is a complex phenomenon that affects not only people, but also agricultural and livestock production and the development and economy of countries. It discusses antibiotic pressures and mechanisms for the selection of resistance mutants and the goals and strategies of the Global Action Plan to control antimicrobial resistance.

The English abstract and full Spanish text can be found at Revista Medica de Uruguay (2017; 33 (4):277-84)

ANTIBIOTIC RESISTANCE IN THE NEWS

POLICY DEVELOPMENTS

National "AMR action plans" are now prevalent

In a November 2016 global survey conducted by the world's leading health organizations (WHO, FAO, OIE), 142 countries responded to questions concerning the development and progress of country-based antimicrobial resistance (AMR) action plans that are geared towards addressing the emerging AMR crisis. The self-assessment questionnaire also included queries on progress in human health, animal health, crop production, food safety and the environment The findings showed that over 90% of the world's population now resides in a country which has undertaken a national action plan. While 29 countries (including the U.S., Australia, South Africa, Brazil and several EU nations) have either approved or implemented an operational plan, few countries have identified funding sources to support such plans. About two-thirds have plans in various stages of

development, but 20 countries have no action plan—largely low-income nations located in Africa, Latin America and Southeast Asia. The vulnerability of these countries to the devastating impacts of AMR is a real concern.

WHO guidelines call for end to routine antibiotics in farm animals

In Nov 2017, the WHO released guidelines for the use of medically important antimicrobials in food-producing animals. The guidelines were directly informed by the findings of a recent systematic review (The Lancet Planetary Health) that commonly show a 10-15% reduction in antibiotic-resistant bacteria in food animals following interventions to restrict antibiotic use. The meta-analysis was based on review of 81 studies in animals and 13 studies in humans that described antibiotic resistance outcomes. For human studies, interventions resulted in a 24% reduction in AMR and were most pronounced in those with direct exposure to food-producing animals.

WHO now strongly recommends complete restriction of all growth-promoting antibiotic and prophylactic use in the absence of diagnosis, as well as overall reduction of all medically important antibiotics in food animals. WHO guidelines provide a recommended list of "drugs of least importance" to human health and also recommendations to restrict quinolones, 3rd-generation cephalosporins, macrolides, ketolides, glycopeptides and polymixins. Under these guidelines, healthy animals would only receive antibiotics when illness is diagnosed within the same flock, herd or fish population.

The WHO recommendations appeared concurrently with an article in Environmental Health Perspectives which showed that children of industrial hog farm workers were more prone to carrying antibiotic-resistant bacteria than those in other communities. The study adds to a growing body of evidence that demonstrate exchange of antibiotic-resistant bacteria between livestock and human handlers and household members—in this case, MRSA. Among hog farming families, 14% of the children carried MRSA and 23% carried other MDR

staph. The frequency was 6% and 8% respectively for children of workers in other occupations.

EU defines indicators for assessing antimicrobial consumption and antimicrobial resistance (AMR)

Pursuant to the EU's adoption of its Action Plan on AMR in June 2017, the EU Commission on Health and Safety has developed a scientific opinion containing proposed sets of indicators to help individual EU member nations measure their progress in reducing antimicrobial use and AMR. The proposed indicators would measure consumption of both total and specified antimicrobials in humans, and also measure certain parameters of antibiotic sales in food-producing animals.

Measurements of AMR in humans would evaluate the following:

- MRSA and 3rd-generation cephalosporin-resistant *E. coli*,
- *Klebsiella pneumoniae* resistant to aminoglycosides, fluoroquinolones and 3rd-generation cephalosporins,
- *Streptococcus pneumoniae* resistant to penicillin and *S. pneumoniae* resistant to macrolides, and
- *K. pneumoniae* resistant to carbapenems

The proposed indicators for AMR in food-producing animals would focus on *E. coli*—in particular, proportions containing ESBL-/AmpC, resistance to 3 or more antimicrobial classes, and resistance to ciprofloxacin.

The panel recommended review every 5 years in order to assess progress in addressing the antibiotic resistance crisis.

WHO releases guidelines for preventing carbapenem-resistant infections

For the first time ever, The World Health Organization has developed global guidelines for the prevention and control of serious carbapenem-resistant healthcare associated infections. This group is comprised of the gram negative, carbapenem-resistant *Enterobacteriaceae, Acinetobacter baumanii* and *Pseudomonas aeruginosa.* Also known as CRE-CRAB-CRPsA, this group is hard to

treat and causes high mortality. Following review of the latest evidence, leading experts have derived eight recommendations to support early recognition, infection prevention, and control of these agents.

International Call to Action aims to galvanize momentum; fill gaps

In October 2017, international actors across the One Health agenda convened a first-of-its-kind "Call to Action on Antimicrobial Resistance (AMR)" in Berlin to galvanize momentum on AMR. Recognizing the seriousness of the AMR problem, and that commendable steps to address it were already underway, the committee agreed that there are still gaps in current international efforts that merit further action. The roundtable resulted in a set of ten underpinning principles that stress a multi-sector, international and united commitment to action with sustained financing; support of innovative and practical solutions, such as new therapeutics, diagnostics and vaccines; maintenance of a patient-centered approach that stresses equity in antimicrobial accessibility; the mapping and monitoring of international actions; and support of future 'Calls to Action' to maintain and increase momentum.

PAVE award aims to spur development of new antimicrobials

A robust pipeline of antimicrobials is urgently needed to counter the current threat posed by antimicrobial resistance. The "calls for action" issued by multiple international organizations have included a recommendation for "pull" incentives—i.e., economic, or market entry rewards that would provide large cash awards on approval of a new antibiotic that treats high priority pathogens. A major barrier to this approach is the limited availability of public funds, as an estimated $1-2 billion would be needed to assure sufficient return on an investment. Other proposals advocate a "transferable exclusivity voucher" (TEV) that extends patent rights for 6-12 months, avoids direct government financing, and is funded by higher drug prices in alternative therapeutic areas. Added to these incentives is the newly proposed, U.S.-based Priority Antimicrobial Value and Entry (PAVE) Award. It is crafted as a limited market entry reward that would provide early funds to augment public and private payments, but would phase

down over a period of 5 years. Continuation would be tied to antibiotic availability and performance rather than volume, e.g., effective stewardship and collection of clinical data. The model attempts to restructure payments to better reflect high-value, long-term antimicrobial use. The PAVE award is seen as part of a comprehensive strategy that also includes the "push" incentives currently used by CARB-X and BARDA for preclinical and clinical research.

Hong Kong adopts action plan for addressing AMR

In July 2017, Hong Kong adopted a Strategy and Action Plan on Antimicrobial Resistance for 2017-2022. The plan responded to a survey of Hong Kong residents that showed 49% of Hong Kong residents took antibiotics in the previous 12 months. In what was described as "an horrendous prevalence of drug resistant bacteria", 47% and 48% of hospital blood samples contained antibiotic-resistant *E. coli* or MRSA respectively (compared with 2% and 11% respectively for the UK). In a country where private practitioners have no obligation to share prescription records with the government, the action plan will develop prescription guidelines for primary care doctors and enhance surveillance of drug resistance.

New guidelines issued for infection prevention in young athletes

Approximately 10% of all time lost during organized sports is due to contact related infections: *Staphylococcus aureus*—both MRSA and MSSA (methicillin-susceptible staph), Group A *Streptococcus*, and herpes simplex virus (primarily type 1), among other viruses, mites, lice and yeast. Subsequent to a recent review on the risk of acquiring organized sports-related infections, the American Association of Pediatrics has issued new guidelines (*Infectious Diseases Associated with Organized Sports and Outbreak Control*) outlining the risk factors for infection transmission in contact sports: skin-to-skin contact, shared equipment, environmental exposures and physical trauma. The guidelines urge program managers to implement protocols for the proper cleaning of shared equipment and to instruct athletes on proper hygiene practices.

ADVANCES IN NOVEL ANTIMICROBIALS

The antibiotic pipeline: what lies ahead?

❖ In 2016, the U.S. initiated the *Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X)*, with a 5-year budget of $455 million. The 254 global requests for the funding of antimicrobial projects have now been analyzed by Ursula Theuretzbacher and team, revealing a reasonable estimation of the scope of global innovation for the antibiotic pipeline. The analysis (*Market watch: Innovation in the preclinical antibiotic pipeline*) noted a good diversity of approaches, with more than 50 small-molecule, preclinical projects focused on a WHO "priority pathogen"—in particular, the extensively resistant gram-negative bacteria. The authors found a "promising trend of innovative projects," largely submitted by small companies, but note that the momentum must be supported aggressively to counteract the high attrition rate that occurs among novel approaches.

❖ In November, the European BEAM Alliance (Biopharmaceutical companies from Europe innovating in AntiMicrobial Resistance Research) released a position paper noting the innovative efforts and role played by small and medium sized enterprises (SMEs). The group of 40 biopharmaceutical companies has derived a list of 10 guidelines for supporting SME-driven innovation, among which are incentive mechanisms, dedicated regulatory pathways, R&D prizes, tax incentives, and education to attract interest. The BEAM Alliance will convene a Berlin Conference in Mar 2018 for exploring best business strategies.

❖ Meanwhile, in October 2017 the CDC awarded $9 million in additional funds to spur innovative approaches towards combating antimicrobial resistance and identifying knowledge gaps. The funds came from its Antibiotic Resistance Solutions Initiative and will support 25 research centers. The newly funded projects are detailed here.

Closthioamide—a new class of antibiotic for gonorrhea?

Neisseria gonorrhea is the agent for about 78 million infections worldwide annually and carries an array of antibiotic resistance genes that urgently require new antibiotic treatments. Closthioamide, a new class of antibiotic with a highly

unusual structure, was first discovered in 2010 by UK scientists in London who remain "cautiously optimistic" following promising early laboratory results with the novel drug. It has yet to be tried in animals or humans, but has shown marked efficacy against 97% of hospital isolates from various body sites, including drug-resistant forms. While still far from use in the clinic, the drug could potentially be produced synthetically, thereby avoiding the typical production pitfalls of mass fermentation in bacterial vats.

Nitric oxide emerges as new superbug therapy

In the U.S., chronic infections related to biofilm formation are responsible for half a million or more deaths per year—at an estimated cost of over $94 billion. In the lungs of cystic fibrosis (CF) patients, aggregates of *Pseudomonas aeruginosa* form antibiotic-tolerant biofilms, resulting in long-term morbidity and mortality. In response to new approaches to mitigate *P. aeruginosa* biofilms, UK-based scientists have tested nitric oxide (NO) as an adjunct therapy to antibiotic treatment. Subsequent to in vitro experiments which showed that NO exposure could disperse biofilms in CF sputum, the researchers have reported testing a group of 12 CF patients receiving IV antibiotics that were also supplemented with inhaled, low-dose (10ppm) NO for 7 days. The study successfully demonstrated that the mean biofilm mass and thickness were significantly decreased with NO plus antibiotics when compared with antibiotic treatment alone. Importantly, no side effects were noted. Though small, the study provides the first clinical proof-of-concept for NO adjunct therapy in CF patients.

More recently, U.S.-based AIT Therapeutics has concluded a similar phase-2 clinical trial using nitric oxide in conjunction with antibiotics to treat cystic fibrosis patients colonized with nontuberculous mycobacteria or NTM (*Mycobacterium abscessus*)—a group of rapidly growing bacteria that become refractory to treatment due to long-term antibiotic therapy. NTM patients typically require 1-2 years of antibiotic "cocktails" that have limited efficacy and high risk of adverse effects. Life expectancy is generally <5 years. AIT's 21-day trial of NO treatment (160ppm) resulted in a 65% reduction in bacterial load at day 81 and sustained

improvements in the 6-minute walk test. The clear benefits of NO treatment demonstrated in the trial may ultimately lead to extended, at-home treatment for a broader array of patients with chronic lung disease.

Mushrooms viewed as untapped source of new antimicrobials

The antibacterial compound pleuromutilin was first isolated in the 1950s from the mushroom *Clitopilus passeckerianus*. Subsequently, derivative compounds were found to be even more potent—particularly against MRSA and extremely drug-resistant TB (XTB)—exhibiting a novel mode of action that lacked the ability to develop cross-resistance. But producing these chemical derivatives has proven difficult. Renewed interest in this class of antibacterials has led University of Bristol scientists to create a novel platform for the development of new, potent modifications that could be used to refortify our antibiotic arsenal. They identified the seven core genes responsible for the production of pleuromutilin in its original mushroom host (*C. passeckerianus*) and rebuilt the pathway in an industrially useful fungus—the ascomycete, *Aspergillus oryzae*. The new synthetic platform opens the door for tapping many previously unexplored mushrooms as new hosts for natural compounds that can be altered and ultimately harvested in alternative ascomycete hosts.

Bacteriocins find practical applications in targeting resistant pathogens

Bacteriocins are a class of heat-stable antibacterial proteins that are derived from bacteria. Unlike conventional antibiotics, which are indiscriminate "carpet bombers", bacteriocins are attractive as potential therapies (*The 'Post-Antibiotic Apocalypse' Can Be Prevented. Here's How*) because they act as guided missiles to attack a very specific target and thus minimize impacts on the bacterial microbiome. Their use has been largely restricted to food preservation and agricultural applications, but University of Massachusetts scientist Margaret Riley envisions new ones. To counteract rapidly rising resistance among urinary tract infections, she is urging the Department of Defense to develop a bacteriocin-laced wipe for female soldiers. The once-a-day wipes would target the most common UTI pathogen, *E. coli*, without harming the vaginal microbiome. She also envisions

bacteriocins as anti-tuberculosis agents and is working on a bacteriocin-containing spray for testing in mice. Riley is likewise studying a bacteriocin-laden aerosol to address respiratory disease in chickens. Another target for her team is tackling the antibiotic-resistant biofilms that colonize cystic fibrosis patients.

Meanwhile, the Maine-based (U.S.) ImmuCell corporation is pursuing a bacteriocin-based drug directed at the common bovine ailment, mastitis. Riley hopes to see antibiotics restricted to use in emergency rooms, while bacteriocins become utilized in other medical settings where known pathogens can be identified.

ANTIMICROBIAL STEWARDSHIP

Pre-op antibiotics cleared for low risk surgeries

There are nearly 50 million surgeries performed in the US, with an estimated 157,500 surgical site infections incurred annually. For certain low-risk surgeries, the choice of using antibiotics pre-operatively is left to the discretion of the surgeon. While some feel strongly about the benefits of pre-op prophylaxis, others refrain from ordering short-course antibiotics out of concern for breeding resistant bacteria.

To assess the potential risk for post-operative antibiotic-resistant infection, a team of Columbia University researchers in New York examined a cohort of 689 surgical patients who developed an infection within 30 days of surgery. From that group, 550 had received antibiotic prophylaxis and 338 had an infection that was moderately or fully resistant to one or more antibiotic classes. The risk for a resistant infection was the same: 47% for those with no prophylactic antibiotic, and 49% for those with. The risk was not affected by other factors such as previous antibiotic exposure or infection, but was only higher if associated with a previous antibiotic-resistant infection. According to lead author, Daniel Freedberg, "…the best clue is past history of resistant infection." The findings are reassuring for those choosing to use antibiotics preoperatively to decrease infection risk.

Benefits of stewardship interventions diminish over time, but "peer-comparison" remains durable

In a clinical intervention (reported in 2016) conducted by researchers at the University of California, 248 clinicians from the Boston and Los Angeles areas were randomized to receive 0, 1, 2 or 3 antibiotic stewardship interventions for 18 months. Two of the interventions (one that asked physicians to justify their reason for prescribing an antibiotic—i.e., "accountable justification"; and one that compared their prescribing practices with "top performers" [i.e., peer comparison] showed dramatic reductions in improper prescribing for acute respiratory infections (nonspecific URI, acute bronchitis and influenza). A third intervention, which offered alternative, non-antibiotic treatments in lieu of a prescription, did not significantly impact antibiotic prescribing. After removal of the intervention, prescribing practices were followed up with observation for 12 months in order to assess the persistence of the interventions. While overall inappropriate prescribing continued to drop in the following year, the impacts of the interventions were diminished—by 1.4% for suggested alternatives, by 4.1% for accountable justification, and by 1.5% for peer comparison. Still, the peer comparison group outperformed the control group. The reasons are not yet clear, but mimic other studies in which peer comparison-induced improvements were sustained.

The study emphasized the importance of applying behavioral interventions for the long-term.

ANTIBIOTIC RESISTANCE/EPIDEMIOLOGY

Ampicillin resistance may have emerged from early penicillin use in livestock

A retrospective examination of the emergence of ampicillin resistance by Pasteur Institute scientists has revealed an unexpected finding. The research team gathered and tested 288 historical strains of *Salmonella typhimurium* collected between 1911 and 1969 from animals, humans and food in four continents. Their assays of antibiotic susceptibility and whole genome sequencing revealed

ampicillin resistance in 3.8% of human samples—several years before ampicillin was first released for human use in Europe (1961) and before the first outbreak of ampicillin resistance in *S. typhimurium*. Interestingly, the emergence occurred on different plasmids in France and the UK, indicating independent acquisition by different bacterial populations. The findings suggest that ampicillin resistance emerged from the antibiotic pressures exerted by the earlier widespread growth-promotion use of penicillin G[3] (benzylpenicillin) in livestock. Study director Francois-Xavier Weill has suggested that "antibiotic residues in farming environments, such as manure, soil and waste water may have had a much greater impact on the spread of ampicillin resistance than previously thought."

The authors urge re-evaluation of antibiotic use in animals and implementing a "One Health" approach to addressing resistance, including international surveillance of both humans and animals.

EU survey finds increasing livestock-associated MRSA (LA-MRSA) among humans

A European Center for Disease Prevention and Control (ECDC) survey shows more frequent detection and geographical dispersion of LA-MRSA in humans since 2007. The 2013 survey queried 28 reference labs from 28 EU/EEA countries and identified LA-MRSA in 3.9% of human samples from the 19 countries that performed MRSA typing. In five countries—Belgium, Denmark, Spain, the Netherlands and Slovenia—10% or more of isolates were LA-MRSA. The report emphasizes LA-MRSA as a "One Health" issue, and one that demands periodic monitoring and systematic mapping of potential reservoirs and transmission pathways to better target control measures.

Despite varying restrictions imposed on food animal antibiotics in Europe and the U.S., such use continues unabated in low and middle income countries, especially in intensive fish and shellfish farms.

Antibiotic side effects: new worries over IBD and infant gut microbiomes

Antibiotic overuse is linked to a higher risk for irritable bowel disease (IBD) by creating a disordered gut microbiome. A new concern has arisen over antibiotic use in teenage girls and pregnant women—i.e., additional risks for inheriting colitis, a form of IBD. The genetic component of IBD composes only 10% of a person's risk, but new studies in mice have now demonstrated an association with antibiotic consumption, and that this risk may be passed on to offspring. When healthy pregnant mice received gut flora that had been exposed to antibiotics, their pups were also born with a disordered microbiome—even though neither generation had directly been exposed to antibiotics. According to Martin Blaser, director of the Human Microbiome Program at NYU Langone Health, the findings "add to the evidence that antibiotic overuse may cause health complications even beyond antibiotic resistance."

In other research at McMaster University in Ontario, investigators have observed profound effects of antibiotic administration on the baby gut microbiome at birth. Approximately 25-30% of pregnant women test positive for Group B streptococcus and a majority of these opt for antibiotic treatment during labor to prevent transmission to the infant. The Scientific Reports study of 74 mother-infant pairs show a delay in the gut bacteria maturation – primarily expansion of the primary infant gut colonizer, *Bifidobacterium* and a persistence of *E. coli*. The delay in expansion was also observed in C-section babies exposed to antibiotics, but these effects largely disappeared after 12 weeks. According to lead researcher Jennifer Stearns "Early life microbial colonization and succession is critically important to healthy development …it's still unclear what these findings mean for infant health, especially since early infancy is such an important developmental time."

Skin microbiome negatively impacted by antimicrobials

A University of Pennsylvania study has provided proof of principle that topical antibiotics create long-term impacts on the skin microbiome. Experiments performed in hairless mice with topical mupirocin, triple antibiotic ointment (bacitracin, neomycin, and polyB) or with the antiseptics, alcohol or povidone

iodine, produced immediate shifts in bacterial populations that persisted for several days. Triple antibiotic ointment produced the most profound effect, and surprisingly, antiseptics the least—primarily a decrease in commensal staph species. Subsequent experiments showed that the elimination of resident staph species permitted colonization with *Staphylococcus aureus*, while skin pre-colonized with resident staph reduced *S. aureus* colonization. The findings are directly relevant to the use of mupirocin prophylaxis to remove *S. aureus* from the nares and other body sites, and suggest a need to monitor recipients for possible invasion or infection by other pathogens.

UK calculates drop in lifespan due to AMR

For the first time, the UK Office for National Statistics predicts a drop in life expectancy due to the problem of antibiotic resistance. Under 2010 projections, the lifespan of a baby girl born in 2016 was estimated at 83.7. New calculations revise this down to 82.9. (males = 79.9 and 79.2 respectively). By 2060, the projected lifespan is a full two years shorter.

This "cohort" life expectancy measure takes into account anticipated medical advances as well as societal changes. Opinions on anticipated improvements in medical science are less promising, and routine infections could become deadly within 20 years, resulting in "less optimistic views" that had to be considered in the new evaluation. This is the first time that antibiotic resistance is believed to factor into the downward revision.

Go here to see a map of projected global life expectancies.

Inappropriate dental use of antibiotics may be increasing *C. difficile* infection

The U.S. Centers for Disease Control has identified *C. difficile* infection as one of the top three most urgent antibiotic resistance threats, leading to nearly half a million infections and 15,000 deaths annually. A CDC research team has conducted interviews of 1626 people diagnosed with community-acquired C. diff in Minnesota between 2009 and 2015. While 57% of these patients had received

an antibiotic in the previous 12 weeks, 15% of them were prescribed by a dentist. Fully 1/3 of these dental prescriptions were not mentioned in the patient's medical chart.

The findings led to several observations by CDC epidemiologist Stacy Holzbauer. First, dentists are often left out of the conversation. The extent of their prescribing practices for prophylactic infection prevention and for other reasons amounts to 24.5 million prescriptions per year, but medical doctors often fail to ask, or are not informed of these antibiotic sources. Secondly, adverse events such as diarrhea are seldom reported back to the dentist, so feedback is lacking for outcomes. Less than half of dentists actually consider antibiotic sequelae when prescribing these drugs. Third, those patients receiving antibiotics by dentists tended to be older and also more likely than others to receive the antibiotic clindamycin, which has a known association with *C. difficile* infection (50% for clindamycin; 10% for other antibiotics).

Dental prescriptions for antibiotics number about 26 million annually—about 10% of total antibiotic prescriptions generated by pharmacies. While the American Dental Association formerly recommended prophylactic antibiotics to prevent infection in heart conditions and in knee and hip replacements, this is no longer true for most cases; and dentists may not be aware of this change. The American Dental Association now recognizes that the risks associated with taking antibiotics (e.g., C. diff) actually exceed the risk of infection in these conditions.

INFECTION PREVENTION

FDA issues new guidelines to ensure safer, less contaminated mattresses

Recent studies have demonstrated a three-fold higher risk of contracting MRSA or *C. difficile* infection if you occupy a hospital bed where the previous patient had either of those infections. The culprit was found to be the hospital mattress, which, although typically swabbed down with chemical disinfectants, is often not sufficiently clean to prevent patient infection. In recognition of the role that these fomites play in the chain of infection transmission, the FDA has recently

issued new recommendations for keeping hospital mattresses safe for use. The four-point guidelines (Keeping Patients Safe from Contaminated Mattresses) recommend the following: 1) developing an inspection plan, 2) regular inspection inside and out for stains, damage and wear 3) removal and replacement of damaged covers and 4) routine cleaning and disinfection.

Wireless "electric bandage" disrupts stubborn biofilms

Bacterial biofilms are a major complication in wound treatment, and antibiotic resistant biofilms occur in at least 75% of infections. The problem has prompted exploration into wireless electroceutical dressing (WED), which harnesses the power of electrochemistry. The technology utilizes silver and zinc printed in fabric, which when moistened, generates a weak electrical field with anti-biofilm properties. Researchers at Ohio State University have now completed the first pre-clinical study in pigs and demonstrated successful infection prevention immediately following wound induction (2 hours) and disruption of an established biofilm (7 days post wound induction). WED accelerated functional wound closure by restoring skin barrier function. The new technology is now being tested on burn wounds in humans.

DIAGNOSTICS

Study shows four simple tests can help identify pneumonia and reduce antibiotic use

Approximately 60% of European patients with lower respiratory infection currently receive antibiotic prescriptions, even though most of these infections are viral and recovery can be expected without intervention. About 1 in 20 of these patients will actually have pneumonia, but so far the diagnosis has proved notoriously difficult. A new study in the European Respiratory Journal has analyzed 28,883 UK patients with acute cough who were examined clinically for a variety of symptoms and followed for 30 days. Ultimately, four simple assessments were found to be useful for diagnosing pneumonia when corroborated with a chest X-ray: temperature above 100F (37.8C); crackling

sounds in one or both lungs, a pulse rate over 100 bpm and blood oxygen saturation under 95%. Other patient characteristics underlying illness, such as age, smoking status, shortness of breath and sputum color did not provide useful information.

Of the 115 patients with verified pneumonia, 99 (81%) had exhibited at least one of the above symptoms—with the highest sensitivity achieved when all four variables were considered (83.5%). While blood oxygen is not a routinely used test, pulse oximeters are widely available, making the four diagnostic tests easy and inexpensive to adopt. According to lead author Michael Moore, eliminating antibiotics in persons without one or more of these signs would result in a "substantial reduction in unnecessary prescriptions for this condition."

EVENTS AND PUBLICATIONS OF INTEREST

Coming soon!...

WEBINAR: "*Nudging" Clinicians to Reduce Inappropriate Antibiotic Prescribing* with Dr. Mark Friedberg, a senior scientist at the RAND Corporation. **Wednesday, February 28, 2018** from 11:30 to 12:30pm. Sponsored by The New England QIN-QIO

Superbugs & Superdrugs 2018. **March 19-20**, **2018** London, UK—Tackling the scientific, regulatory and economic challenges in order to combat antimicrobial resistance

Challenges and new Concepts in Antibiotics Research, an international symposium at the Institut Pasteur, Paris. **March 19 -21**, **2018.** http://www.amr-2018.org/#scientific-program

15th Annual Global Health & Innovation Conference, **April 14-15, 2018** Yale University, New Haven, Connecticut

ECCMID- 28th European Congress of Clinical Microbiology and Infectious Diseases, **April 21-24, 2018** Madrid, Spain

Nasal methicillin-resistant *Staphylococcus aureus* screening in patients with pneumonia: a powerful antimicrobial stewardship tool by EA Smith et al in Amer J Infect Cont. 2017, 45:1295-6

Infection Control

No-touch disinfection methods to decrease multidrug-resistant organism infections: a systemic review and meta-analysis by AAR Marra et al in *Infect Cont Hosp Epidemiol* 2018, 39:20-31. Provides evidence that ultraviolet light no-touch disinfection technology may be effective in preventing CDI and VRE infection.

Know your ozone: It's good, bad and bacteria-blasting, a blog by Erik Lief, Oct 16, 2017, the science behind ozone and its use for disinfection in hospitals, healthcare facilities and locker rooms.

Hand Hygiene 2017: the State of the State-- a webinar with Sue Barnes, presents hand hygiene in U.S. healthcare, successes and challenges, including a bundle approach to support optimal compliance.

Eradication of MRSA throat carriage – a randomized trial comparing topical treatment with rifampicin-based systemic therapy by AK Lindgren et al in *Int J Antimicrob Agents* Aug 2017Provides evidence that a combination of rifampicin and clindamycin or trimethoprim-sulfamethoxazole is more effective in eliminating pharyngeal MRSA carriage compared to topical treatment with mupirocin.

Centers for Disease Control and Prevention Guideline for the prevention of surgical site infection 2017 by SI Berrios-Torres et al in *JAMA Surg* 2017, 152:784-791

Patient engagement with surgical site infection prevention: an expert panel perspective by E Tartari et al in *Antimicrob Resist and Infect Cont* 2017 6:45. Experts evaluate options for empowering patients with information for SSI prevention.

Epidemiology

Prevalence *of Staphylococcus aureus* and of methicillin-resistant *S aureus* (MRSA) along the production chain of dairy products in north-western Greece by P Papadopoulos et al in *Food Microbiol* 2018, 69: 43-50. Epidemiology of MRSA in humans, animals, equipment and products involved in the dairy production chain.

Air pollution alters *Staphylococcus aureus* and *Streptococcus pneumoniae* biofilms, antibiotic tolerance and colonization by SJK Hussey in *Environ Microbiol* 2017, 19:1868-1880. First-time report of how black carbon drastically changes the development of bacterial biofilms—increasing antibiotic and proteolytic tolerance.

Diagnostics

Antibiotic Resistance Action Center Resources: Diagnostic Tests and Antibiotic Resistance, Developed in partnership with AdvaMedDx, the site carries downloadable visuals and fact

sheets for patients and professionals that highlight how diagnostic tests can be utilized to help combat antibiotic resistance.