Boonshoft School of Medicine
WRIGHT STATE UNIVERSITY

INFECTIOUS DISEASES NEWSLETTER

February 2018
Thomas Herchline, Editor

LOCAL NEWS

ID Fellows

Dr Alpa Desai will be on Research in February, at Miami Valley Hospital in March, and on Transplants in April. Dr Luke Onuorah will be at the VA Medical Center in February and March, and at Miami Valley Hospital in April. Dr. Najmus Sahar will be at Miami Valley Hospital in February and March, and at Children's in April.

EMERGING INFECTIONS NETWORK

EIN Query: Asymptomatic Clostridium difficile Carriage

The overall response rate was 687 of 1,321 (52%) of physicians with an adult infectious disease practice. Multiple different tests were used at the various hospitals; 64% rely on NAAT testing, either alone or in combination with GDH EIA, toxin EIA or a GI Panel. The majority (56%) reported seeing more than 10 symptomatic patients in the previous 6 months. Only 3% of respondents reported that their hospital routinely tested for asymptomatic carriage.

The full report is at: http://www.int-med.uiowa.edu/Research/EIN/FinalReport_AsymptomaticCdiff.pdf.

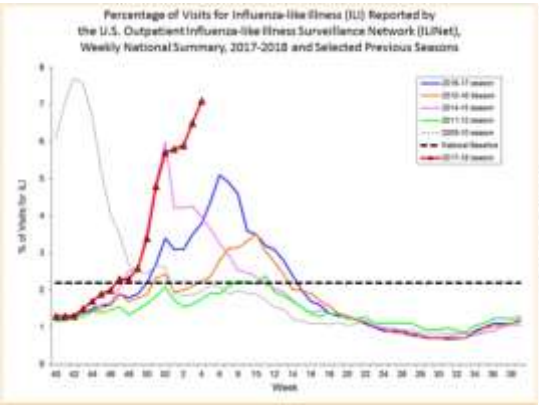
NATIONAL NEWS

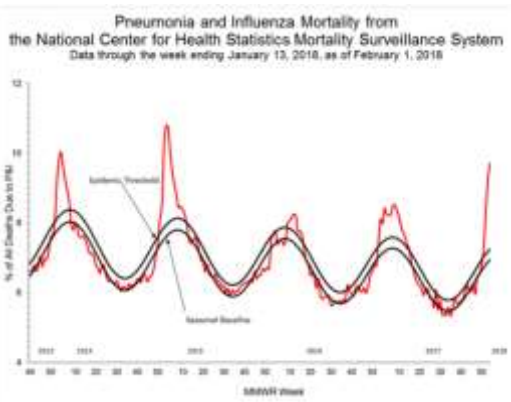
Contributed by Alpa Desai, MD

Flu season one of the worst in a decade

Per the latest weekly update from the U.S. Centers for Disease Control and Prevention every state except Hawaii and Oregon continue to experience widespread flu activity, with the more virulent H3N2 strain continuing to dominate. For the week ending January 27, 2018 the proportion of people seeing their health care provider for influenza-like illness (ILI) was 7.1%, which is above the national baseline of 2.2% and is the highest ILI percentage recorded since the 2009 pandemic. Per latest CDC update since October 1, 2017, 14,676 laboratory-confirmed influenza-associated hospitalizations have been reported through the Influenza Hospitalization Network (FluSurv-NET). This translates to a cumulative overall rate of 51.4 hospitalizations per 100,000 people in the United States. The highest hospitalization rate is among people > 65-year-old followed by adults aged 5-64 year and young children aged 0-4 year. The proportion of deaths attributed to influenza and pneumonia sharply increased to 9.7% for week ending January 13,2018. A total of 53 influenza-associated pediatric deaths for the 2017-2018 season have been reported to CDC. The unique characteristics of the H3N2 strain make that misery even more pronounced. This virus has

lower vaccine effectiveness. CDC continues to recommend influenza vaccination for all persons 6 months of age and older as flu viruses are likely to continue circulating for weeks.





Multistate Outbreak of *Salmonella* Infections Linked to Coconut Tree Frozen Shredded Coconut

As of January 12, 2018, 24 people infected with the outbreak strains of *Salmonella* I 4,[5],12:b:- and 1 person with *Salmonella* Newport have been reported from 9 states. One ill person infected with the outbreak strain of *Salmonella* has been reported from Canada. Whole genome sequencing (WGS) showed that isolates from people infected with *Salmonella* I 4,[5],12:b:- are closely related genetically. Illnesses started on dates ranging from May 11, 2017 to November 4, 2017. Ill people range in age from 1 year to 82, with a median age of 19. Among ill people, 19 (76%) are male. Six people (24%) report being hospitalized. No deaths have been reported. Epidemiology, laboratory and traceback evidence indicates that coconut tree brand frozen shredded coconut is the likely source of this multistate outbreak. The frozen shredded coconut linked to this outbreak was used as an ingredient in Asian-style dessert drinks served at restaurants. CDC recommends that retailers not sell, restaurants not serve, and consumers not eat recalled Coconut Tree Brand frozen Shredded Coconut. This investigation is ongoing.

Multistate Outbreak of Multidrug-Resistant *Campylobacter* Infections Linked to Pet Store Puppies

Epidemiology and laboratory evidence indicated that contact with puppies sold through Petland stores were a likely source of this outbreak. A total of 113 people with laboratory-confirmed infections or symptoms consistent with *Campylobacter* infection were linked to this outbreak. Illnesses were reported from 17 states. Ill people ranged in age from less than 1 year to 86, with median age of 27. 22% people were hospitalized. No deaths were reported. *Campylobacter* bacteria isolated from clinical samples from people sickened in this outbreak were resistant to commonly recommended, first-line antibiotics. Using whole genome sequencing (WGS), they identified multiple antimicrobial resistance gene and mutations in most isolates from 38 ill people and 10 puppies in this outbreak. The 12 isolates tested by standard methods were resistant to azithromycin, ciprofloxacin, clindamycin, erythromycin, nalidixic acid, telithromycin, and tetracycline. In addition, 10 were resistant to gentamicin, and 2 were resistant to florfenicol. This outbreak investigation is over. Illnesses could continue to occur because people may be unaware of the risk of *Campylobacter* infections from puppies and dogs.

INTERNATIONAL NEWS

Contributed by Luke Onuorah, MD

Detection of active TB in HIV-negative patients with a urine test

A urine test that accurately detects active tuberculosis in patients who are not co-infected with HIV has been developed by researchers. Lance A. Liotta MD, PhD, codirector of the center for applied proteomic and molecular medicine at George Mason University along with his colleagues stated in the *Science Translational Medicine* Journal that their new test increases the sensitivity of lipoarabinomannan (LAM) detection by up to 1,000 fold. A previously developed test is available for HIV-positive patients with active pulmonary disease. They were able to increase the sensitivity by using a copper complex reactive dye, RB221, embedded in open-mesh hydrogel nanoparticle cages to trap LAM in urine.
The researchers report that the new test detected TB infections in the Peruvian patients with a greater than 95% and a specificity greater than 80% when compared with controls. Larger cohort studies are needed to validate the test.

Primaquine provides most effective malaria prophylaxis

Researchers reached the conclusion that Primaquine should be the drug of choice for chemoprophylaxis for *Plasmodium falciparum and P. vivax* in areas where they co-circulate. They conducted a retrospective observational study that included Israeli rafters who had visited Ethiopia's Omo River, a malaria-endemic area over an 11-year period. The chemoprophylaxis agents used were atovaquone-proguanil, doxycycline, mefloquine and primaquine. Prophylaxis failure rates for early and late malaria were 56.7% for atovaquone-proguanil, 52.2% for doxycycline, 49% for mefloquine and 5.5% for primaquine. Sixty-two travelers out of 252 developed malaria. Of these cases, *P. vivax* was the pathogen responsible for 57 cases (91.9%) and *P. falciparum* was responsible for the remaining cases. The study also recommends a longer follow-up of greater than one month for returning patients, as approximately half of the cases for patients who took atovaquone-proguanil, doxycycline, and mefloquine were late-onset malaria - occurring after a month. **(Meltzer E, et al. *Clin Infect Dis.* 2017; doi:10.1093/cid/cix1077.)**

African Union makes commitment to vaccination

On Jan 31,2018 at the 28th African Union Summit, heads of state from across Africa adopted a Declaration on Universal Access to Immunization in Africa, in which they endorsed the Addis Declaration on Immunization, a historic and timely pledge to ensure that everyone in Africa – no matter who they are or where they live – has access to the vaccines they need to survive and thrive. The WHO Regional Office for Africa applauded this landmark commitment to immunization. The WHO recognizes that Africa has the fastest growing population of young people in the world. The better the head start they are given, the greater the chances that they go on to lead productive lives. It is expected that international funding for vaccination programs will decline, hence it is important that African countries demonstrate the political will needed to make access to vaccines available to all.

High level of worldwide antibiotic resistance, new data show

On January 29, 2018 in Bangkok the WHO released for the first time released surveillance data on antibiotic resistance. It revealed a high level of resistance to a number of serious bacterial infections in both high- and low-income countries. The WHO instituted the Global Antimicrobial Surveillance System (GLASS) in 2015. Its first report revealed a widespread occurrence of antibiotic resistance among 500 000 people with suspected bacterial infections across 22 countries. The most frequently reported resistant bacteria were

Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, Steptococcus pneumoniae ans *Salmonella spp.* WHO is encouraging all countries to set up good surveillance systems for detecting drug resistance that can provide data to this global system. To date, 52 countries (25 high-income, 20 middle-income and 7 low-income countries) are enrolled in WHO's Global Antimicrobial Surveillance System. For the first report, 40 countries provided information about their national surveillance systems and 22 countries also provided data on levels of antibiotic resistance.

Outbreak of Monkey pox in Nigeria

From 4 September through 9 December 2017: 172 suspected and 61 confirmed cases of Monkey pox have been reported in different parts of the country Nigeria. One death was reported in a patient living with HIV not receiving anti-retroviral therapy. Genetic sequencing results of the virus isolated within and across regions suggest multiple sources of introduction of the virus into the human population.
Monkeypox, a rare zoonosis that occurs sporadically in forested areas of Central and West Africa, is an orthopoxvirus that can cause fatal illness. The disease manifestations are similar to human smallpox (eradicated since 1980), however human monkeypox is less severe. The disease is self-limiting with symptoms usually resolving within 14–21 days. Treatment is supportive. This is the first outbreak in Nigeria since 1978.

CASE CONFERENCE

Contributed by Najmus Sahar, MD

A 76 years-old Caucasian male with past medical history significant for both Hodgkin's and non-Hodgkin's Lymphoma on chemotherapy , CHF, CAD s/p CABG, and DM II presented with sudden onset right knee pain on the day of presentation. Pt had a fall on left knee 4-6 weeks ago without any obvious injury or twisting at the time of fall. On presentation he had intermittent sharp pain in left knee, aggravated by putting weight on the knee with mild swelling and redness. He had no associated fever, chills, nausea, vomiting, rashes or any other swollen joints. Patient had been recently diagnosed with community acquired Pneumonia by PCP and was on levofloxacin for the last 1 week.

Vitals on admission temperature 97.7 F, BP 150/76, pulse 112 BPM, RR 18 per minute, SpO2 92%.on physical examination left knee had no redness but significant warmth and small joint effusion. ROM was limited due knee pain. Basic metabolic panel revealed glucose of 239 but is otherwise unremarkable, CBC with WBC of 7.4 c/mm3and hemoglobin of 14.1 gm/dl. CT PE protocol showed no evidence of pulmonary embolism he had mildly enlarged mediastinal lymph nodes as well as extensive mixed alveolar interstitial infiltrates throughout both lungs and large bilateral pleural effusions with increased size with compressive atelectasis in the lower lobes. X-ray of the right knee showed degenerative change but no evidence of fracture or malalignment per radiologist.

Arthrocentesis revealed cloudy fluid with WBC 33400 with 98% neutrophils, 2% monocytes and no lymphocytes. Gram stain was negative for any organism. No crystals noticed. Routine cultures were negative. AFB cultures came back positive on day five; MTB and MAC DNA probes were negative. Speciation showed Mycobacterium abscessus /chelonea complex. Susceptibilities were requested but not yet available.

Discussion

Genus mycobacterium includes Mycobacterium tuberculosis (MTB), Mycobacterium laprae, and Nontuberculous mycobacteria (NTM). Unlike M. tuberculosis and M. laprae, NTM are opportunistic pathogens and are widely distributed in environment and inhabit soil and water [2]. NTM can cause disease in immunocompetent host mostly manifested as skin and soft tissue infections, and in immunocompromised patients with localized or disseminated disease [2]. NTM are classified into rapid growing mycobacteria (RGM) that usually grows in 3-7 days versus slow growing mycobacteria (SGM) which may take over 3 weeks to grow (on solid media) [1]. RGM related SSTI may manifest as localized abscess at the site of dermal piercing, single or multiple indurated papules or abscesses after mesotherapy, furunculosis after pedicure, and papular rash after tattoo formation [2]. Cases of cosmetic tourism related post-surgical wound infection with M. abscessus have been a new area of interest in plastic surgery word. Patient usually presents 4 weeks after their cosmetic surgery abroad that includes abdominoplasty, liposuction, breast augmentation/reduction and rejuvenation procedures, with surgical wound dehiscence and infection, requiring extensive wound debridement and prolong antibiotic courses [3]. Making the diagnosis is challenging due to negative bacterial cultures, requirement of special media and circumstances for the growth of mycobacterial. Appropriate cultures from drainage material or tissue biopsy are the key. Once culture positive, NTM should be identified to species level to discriminate between pathogen versus contaminant. Molecular methods including DNA probes and sequencing are much faster for identification. Susceptibility for RGM is important to avoid development of resistance.

Macrolides are the back bone of therapy for SSTI related to these organisms. For minor SSTI, sometimes I&D are curative. For more serious infections prolong courses of antibiotics including macrolide (clarithromycin/azithromycin) plus IV medications (amikacin, cefoxitin or imipenem) are tailored for 4-6 weeks along with surgical interventions as needed [1].

References

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2. SH Wang, P Pancholi. Mycobacterial skin and soft tissue infection Current infectious disease reports, 2014 – Springer.
3. SS Cai, K Chopra, SD Lifchez. Management of mycobacterium abscessus infection after medical tourism in cosmetic surgery and a review of literature Annals of plastic surgery, 2016 - journals.lww.com.

New Antimicrobial Summary: Vabomere

By Dr. Katelyn Booher, D.O.

The combination of meropenem and vaborbactam (Vabomere) was FDA-approved as of August 29, 2017 for complicated urinary tract infections (cUTI) as well as pyelonephritis due to certain multi-drug resistant (MDR) gram negative bacteria in those 18 years of age or older. Vabomere is dosed as 4 grams total (meropenem 2 grams and vaborbactam 2 grams) every 8 hours intravenously over 3 hours, for up to 14 days. In the setting of renal impairment (GFR below 50 mL/min/1.73m^2) the dose does need to be reduced appropriately. The drug is supplied in vials containing 1 gram of meropenem and 1gm of vaborbactam. Contraindications are known hypersensitivity reactions to meropenem, vaborbactam, or anaphylactic reactions to beta-lactams, per the package insert. Usage of meropenem/vaborbactam in patients with penicillin allergies, including anaphylaxis, could be argued on the basis published data reflecting a low cross-reactivity (0.9-11%) between meropenem and penicillin (1-3). Similar to other beta-lactams, hypersensitivity reactions can occur, and meropenem has been associated with seizures and other central nervous systemic effects. It is important to note that meropenem will reduce serum concentrations of valproic acid when administered concurrently with valproic acid or divalproex sodium, potentiating risk of breakthrough seizures.

If confirmed sensitive to meropenem/vaborbactam, the antibiotic is indicated for *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter cloacae species* complex based on clinical and *in vitro* data; other gram negative data is based on *in vitro* research only. While meropenem is a bactericidal drug that acts by cell wall synthesis inhibition, vaborbactam is a non-suicidal beta-lactamase inhibitor that protects meropenem from degradation by some serine beta-lactamases (such as carbapenemases). Meropenem/vaborbactam was shown to have *in vitro* activity against Enterobacteriaceae which produced certain beta-lactamases and extended-spectrum beta-lactamases including KPC, TEM, SHV, CTX-M, CMY, and ACT. Metallo-beta lactamase- or oxacillinase-producing bacteria are not considered sensitive to Vabomere, however. In summary, meropenem plus vaborbactam will provide an option for treatment MDR gram negative urinary tract infections, particularly *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter cloacae species* complex, where high level resistance precludes the use of other antibiotic choices.

1. Atanasković-Marković M, Gaeta F, Medjo B, Viola M, Nestorović B, Romano A. Tolerability of meropenem in children with IgE-mediated hypersensitivity to penicillins. Allergy. 2008;63(2):237-240. doi: 10.1111/j.1398-9995.2007.01532.x.
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Bug of the Quarter

By: W. Grant Starrett, M.D.

This article reviews the more obscure organisms which are less commonly isolated in clinical specimens. Please contact me at wgstarrett@premierhealth.com if you come across an isolate that may fit in this category.

Organism: *Weeksella virosa*

Clinical Data:

A 59 year-old female with history of multiple sclerosis (MS) and latent tuberculosis infection presented in outpatient referral from her neurologist for a positive Quantiferon test. Testing was performed because she was being considered for alemtuzumab treatment for relapsing, remitting MS. The patient was a registered nurse who reported that she converted her PPD in the early 1980's while working at a local hospital. Several of her coworkers converted at the same time, and she was treated with isoniazid, rifampin and vitamin B6 for about a year. She had been taking rituxan for her MS for the last six years, and was also diagnosed with Crohn's disease by biopsy within the last five years. She complained of fatigue but denied respiratory or gastrointestinal symptoms, and had actually been gaining weight. The patient proceeded with alemtuzumab treatments along with antiviral and pneumocystis prophylaxis. Four months later she presented to a local hospital with weakness and was admitted due to concern for a flare-up of her multiple sclerosis. A urine culture was obtained due to intermittent urinary retention and incontinence, and the culture grew *Weeksella virosa* as well as some contaminants. Imaging and exam findings were not consistent with progressive MS, and she was discharged with supportive care.

Taxonomy

Kingdom: Bacteria
Phylum: Bacteroidetes
Class: Flavobacteriia
Order: Flavobacteriales
Family: Flavobacteriaceae
Genus: *Weeksella*
Species: *virosa*

Associated Diseases:

1. Urinary tract infection
2. Bacteremia/sepsis
3. Peritonitis
4. Pneumonia

Description:

Weeksella virosa is an aerobic, gram-negative rod that is primarily isolated from the urogenital tract of women. It was initially described as a nonsaccharolytic *Flavobacterium* in 1970 and has previously been designated CDC Group IIf and *Flavobacterium genitale.* The organism is oxidase and indole positive and generally does not grow on MacConkey agar. It produces mucoid, slimy colonies that may be mistaken for *Klebsiella*. This genitourinary commensal is rarely pathogenic, but infections of the urinary tract, peritoneum, lung and bloodstream have been described. The organism appears to be more prevalent in females and in patients with comorbities such as end-stage renal disease, obesity, liver disease and diabetes mellitus. *Weeksella* infections may be treated with most penicillins and carbapenems as well as trimethoprim/sulfamethoxazole.

Resources:

1. Koneman's Color Atlas and Textbook of Diagnostic Microbiology, 6th ed.
2. Manoguran M, *et al.* Pneumonia and sepsis due to Weeksella virosa in an immunocompromised patient. Infect Dis in Clin Practice. September 2004; vol. 12, Issue 5; 286-287.
3. Murray, *et al.* Manual of Clinical Microbiology, 7th edition.
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