Boonshoft School of Medicine
WRIGHT STATE UNIVERSITY

INFECTIOUS DISEASES NEWSLETTER

November 2013

T. Herchline, Editor

LOCAL NEWS

ID Fellows

Dr Kunal Desai will be at Miami Valley Hospital November through December and at the VA Medical Center in January through March. Dr. Katelyn Booher will be at the VA Medical Center November through December and at Miami Valley Hospital January through March.

Local Disease Activity

The first case of influenza associated hospitalization for the 2013-2014 flu season in Montgomery County was reported in September. The patient is a 36 year old Miamisburg resident. She was admitted to Kettering Medical Center on September 10th with rapid onset of shortness of breath, productive cough, and fevers up to 103°F. Testing was positive for Influenza A. She had a history of travel to the Cayman Islands and became ill 2 days following her return to Dayton. Local (and national) influenza activity has remained low through October.

Montgomery County continues to receive significant numbers of refugees, primarily from Africa (Democratic Republic of Congo, Eritrea, Ethiopia and Sudan regions), Iraq and Columbia. Catholic Social Services of the Miami Valley is the resettlement agency. Public Health provides the initial medical screening and care for refugees. The initial evaluation includes a nurse visit - past and present medical problems are identified, medications reviewed, vision is screened, chest x-ray obtained and laboratory testing arranged to identify treatable medical conditions. Newly arriving refugee also view a DVD designed to introduce them to the health care system in the U.S. and provide an introduction to getting settled into their new home. At a second appointment, a physician performs a physical examination, reviews overseas medical documentation, and discusses the results of the testing done. Medical issues are addressed and clients are set up with primary care physicians in the community for any new or on-going health problems. Specialist referrals are sent if necessary. Thus far in 2013, PHDMC has provided medical evaluation services to 160 refugees. Common problems include latent tuberculosis, intestinal parasites, eosinophilia, and hepatitis B.

NATIONAL NEWS

Contributed by Katelyn Booher, DO

Study Demonstrates the Value of the ID Specialist

Early intervention by an ID specialist saves lives and reduces medical costs. Data of 130,000 hospitalized Medicare patients was analyzed; the study compared outcomes of those treated by an ID specialist versus those who were not. Hospitalized patients with severe infections treated by an ID specialist were 9

percent less likely to die in the hospital and 12% less likely to die after discharge. With an ID specialist involved, average ICU stays were decreased by 3.7 days, and hospital readmission within 30 days was less likely. Early ID consultation (within two days) was associated with further benefit in readmission rate and cost.

More U.S. Teens Susceptible to HSV-1, A Growing Cause of Genital Herpes

HSV-1 is becoming a significant cause of genital herpes in industrialized countries, with one study reporting nearly 60% of genital herpes infections attributable to HSV-1. A new study demonstrates that increasing numbers of U.S. adolescents lack antibodies that may offer future protection against HSV-1. Fewer teenagers have been exposed to HSV-1 during childhood than in previous years. Overall, HSV-1 seroprevalence from 2005-2010 was 54%. HSV-1 seroprevalence declined by almost 23% from 1999-2004 compared to 2005-2010. HSV-2 seroprevalence was not significantly different across any of the age groups. Declining seroprevalance may place teens at increased risk for acquiring HSV-1.

Changes to Incivek (telaprevir) product labeling

FDA approved changes to the Incivek (telaprevir) product labeling to include results from trial C211 (OPTIMIZE) to support a twice daily dosing regimen. The dosage and administration of telaprevir were updated from 750 mg three times a day to 1125 mg twice daily. Telaprevir total exposure was found to be similar regardless of three times daily versus twice daily dosing. Also, there were no differences in types of emerging variants after comparison of the two dosing options. The anticonvulsant medications carbamazepine, phenobarbital, and phenytoin were moved from the Drug Interactions to the Contraindications Section.

Tygacil (tigecycline): Increased Risk of Death

FDA notified health professionals and their medical care organizations of a new Boxed Warning describing an increased risk of death when intravenous Tygacil is used for FDA-approved uses as well as for non-approved uses. These changes to the Tygacil Prescribing Information are based on an additional analysis that was conducted for FDA-approved uses after FDA issuing a Drug Safety Communication about this safety concern in September 2010. Tygacil is FDA-approved to treat complicated skin and skin structure infections (cSSSI), complicated intra-abdominal infections (cIAI), and community-acquired bacterial pneumonia (CABP). The analysis showed a higher risk of death among patients receiving Tygacil compared to other antibacterial drugs: 2.5% (66/2640) vs. 1.8% (48/2628), respectively. The adjusted risk difference for death was 0.6% with corresponding 95% confidence interval (0.0%, 1.2%). In general, the deaths resulted from worsening infections, complications of infection, or other underlying medical conditions. Health care professionals should reserve Tygacil for use in situations when alternative treatments are not suitable.

Multi-drug Resistant Salmonella Heidelberg Infections Linked to Foster Farms Brand Chicken

As of October 29, 2013, a total of 362 persons infected with seven outbreak strains of *Salmonella* Heidelberg have been reported from 21 states as well as Puerto Rico. 38% of ill persons have been hospitalized, and no deaths have been reported. 74% of ill persons are located in California. Investigations have demonstrated that consumption of Foster Farms brand chicken is the likely source of this outbreak of *Salmonella* Heidelberg infections. On October 7, 2013, U.S. Department of Agriculture's Food Safety and Inspection Service (USDA-FSIS) issued a public health alert due to concerns that illness caused by *Salmonella* Heidelberg is associated with chicken products produced by Foster Farms at three facilities in California. On October 10, 2013, changes were implemented in processing to prevent further contamination. The outbreak strains of *Salmonella* Heidelberg are resistant to several commonly

prescribed antibiotics. This antibiotic resistance may be associated with an increased risk of hospitalization or possible treatment failure in infected individuals.

INTERNATIONAL NEWS

Cholera in Mexico

The Ministry of Health in Mexico has reported 176 confirmed cases of infection with *Vibrio cholerae* O1 Ogawa toxigenic, including one death. The cases were reported from Sept. 9 through October 23. The increased risk of diarrheal diseases is attributed to a hurricane and tropical storm that affected the region simultaneously, causing heavy rains, floods, landslides and internal displacement of populations. Most of the patients (n=157) were from the state of Hidalgo. The patients ranged in age from 3 months to 88 years. Fifty-seven of the patients were hospitalized. According to WHO, this is the first local transmission of cholera since the 1991 to 2001 epidemic in Mexico, but the current strain is different from the strain that circulated at the time. The genetic profile of the strain obtained from the patients in this outbreak is 95% similar to a strain that is currently circulating in Haiti, Dominican Republic and Cuba. Health authorities in Mexico are continuing their outbreak investigation and surveillance.

Dengue in the Americas

Dengue continues to experience a resurgence in the Americas. For the year (reported as of October 25th), the following numbers of cases have been reported in Central America: Mexico – 162,008, Cost Rica – 42,638, Nicaragua – 31,338, Honduras – 30,818. Even greater numbers have been reported in South America: Brazil – 423,672, Paraguay – 140, 787, Colombia – 102,944, Venezuela – 41, 938. In the Caribbean, the highest number of cases have been reported from Martinique – 4450, St Martin – 1940, Barbados – 981, and Jamaica – 520. The increasing dengue rates may be attributed to a number of factors including increasing density of *Aedes aegypti*, the introduction of *Aedes albopictus*, and general population growth combined with poor sanitary conditions. Dengue cases in the US continue to be predominantly acquired outside the country.

Case Conference

Contributed by Kunal Desai, MBBS

36 y/o Hispanic male with history of HIV/AIDS with absolute CD4 counts of 20/mm^3 presents with epigastric abdominal pain associated with nausea, non-bloody vomiting and multiple episodes of diarrhea for 5 days. He complains of pruritic rash mainly over torso for last 5-7 days. He denies recent travel or sick contacts. He denies recent hospitalization or antibiotic use in last 3 months. He also complains of decreased appetite. He denies fever, chills, shortness of breath, cough or chest pain. He is originally from Mexico and has lived in USA for last 12 years. He has 1 cat at home and lives with 5 other male friends. He is a heavy drinker 912-18 beers per day) and smoker. He has been off anti-retroviral therapy for several months due to his non-compliance to medical treatment. His vital signs are unremarkable on admission. Pertinent physical findings include cachectic looking male in no distress, faint erythematous macular serpinginous rash centripetal distribution, mostly over his trunk and diffuse abdominal tenderness. Laboratory data is significant for Sodium of 128. CBC showed normal WBC as well as normal absolute eosinophil counts. His chest x-ray is unremarkable. Abdominal x-ray shows mild diffuse small bowel distension. Patient continued to have GI symptoms during hospital stay. His blood cultures, stool culture, Clostridium difficle PCR, stool cryptosporidium exam and Strongyloides IGG are negative. His Stool ova and parasite exam shows numerous Strogyloides larva. Even though he did not have pulmonary symptoms, his sputum is examined for parasite and reveals numerous Strongyloides larva as well. Further history and review of old records revealed that he was treated with albendazole for 7 days and one dose of ivermectin 2 years ago for chronic Strongyloides infection. Patient is diagnosed with Strongyloides hyperinfection syndrome with SIADH. He is symptomatically better including rapid resolution of rash after 2 weeks of treatment with ivermectin. His repeat stool exam 10 days later shows no parasite.

Discussion

Strongyloides stercoralis is an intestinal helminth that infects humans through contact with soil containing the larvae. Strongyloidiasis may be prevalent in AIDS patients in the USA who emigrated from Strongyloides endemic countries [1]. Strongyloides hyperinfection syndrome refers to accelerated autoinfection, generally the result of an altered immune status and implies the presence of signs and symptoms attributable to increased larval migration. Typical risk factors for developing hyperinfection syndrome include corticosteroid or other immunosuppressive drugs, HTLV-1 infection, hematologic malignancies, organ transplant and hypogammaglobulinemia [2]. HIV is not considered a risk factor for Strongyloides hyperinfection syndrome. In all, there are fewer than 30 cases of hyperinfection occurring in HIV-infected patients in the literature [2]. The question of why HIV infection does not increase risk of Strongyloides dissemination or hyperinfection is perplexing. Based on the fact that T helper cells type 2 (Th2) activity in the HIV infected individual may be impaired to a much lesser degree, or may even be augmented, it is proposed that Th2 activity in the HIV host helps to prevent dissemination of Strongyloides stercolis [3]. Montes et al. showed that regulatory T cell counts (CD4 T cells) are increased in patients with HTLV-1 and Strongyloides stercoralis co-infection and may play a significant role in susceptibility to Strongyloides hyperinfection [4]. Thus, low CD4 counts in HIV patients and preservation of Th2 activity may explain low risk of hyperinfection syndrome in HIV patients. Strongyloides hyperinfection syndrome in an AIDS patient is considered an unusual based on available literature.

References:

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BUG OF THE QUARTER

Contributed 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: *Comamonas*

Clinical Data:

A 64 year-old female with history of hypothyroidism and gout suffered a complex humeral fracture after falling down the steps while on vacation. She underwent open reduction and internal fixation of the left humeral shaft and supracondylar fractures. While the operation proceeded, dripping was noted from a ceiling vent on the opposite side of the room as the OR table and surgical instruments. The surgeon had the fluid collected while he completed the case, and it was sent for culture. Further investigation revealed that the OR staff had requested an increase in temperature prior to the case starting, and this adjustment was made manually by the boiler room. The surgeon subsequently had the temperature lowered again. Fluid from the air handler condensate pan as well as the condensate that had been collected from the dripping ceiling vent grew *Comamonas acidovorans.* The patient recovered from her surgery without incident and is doing well.

Taxonomy

Family: *Comamonadaceae*
Genus: *Comamonas (Delftia)*
Species: *acidovorans*

Associated Diseases:

1. nosocomial infections (including bacteremia, UTI and respiratory tract infection)
2. eye and ear infections
3. endocarditis

Description:

Like most *Burkholderia* and *Stenotrophomonas*, *Comamonas acidovorans* is an aerobic, non-spore-forming, non-fermenting Gram-negative bacillus. Found worldwide in water and soil, it is an occasional cause of nosocomial infection in immunocompetent and immunosuppressed patients. Catheter-related bloodstream and urinary tract infections have been reported, as well as empyema. Endocarditis in an IV drug user and contamination of dental water systems have also been described. Originally classified as a *Pseudomonas*, it held the name *Comamonas acidovorans* until 1999 when the new genus *Delftia* was defined based upon genetic testing. Microbiologists can identify this organism based on an orange ("pumpkin-colored") indole reaction due to production of anthranilic acid from tryptone. While this incident did not result in infection, this organism is just another example of a pathogen that may be transmitted via contaminated water in the hospital (and community) setting.

Resources:

1. Horowitz H, *et al.* Endocarditis associated with Comamonas acidovorans. J Clin Microbiol. 1990 January; 28(1): 143–145.
2. Khan S, *et al.* Fatal *Delftia acidovorans* infection in an immunocompetent patient with empyema. Asian Pac J Trop Biomed. 2012 Nov;2(11):923-4. doi: 10.1016/S2221-1691(12)60254-8.
3. Koneman's Color Atlas and Textbook of Diagnostic Microbiology, 6th ed.
4. Manual of Clinical Microbiology, 7th edition.

5. Ojeda-Vargas MDM, *et al.* Urinary tract infection associated with *Comamonas acidovorans*. Clinical Microbiology and Infection. Volume 5, Issue 7, pages 443–444, July 1999.
6. Stampi S, *et al. Comamonas acidovorans* contamination of dental unit waters. Letters in Applied Microbiology. Volume 29, Issue 1, pages 52–55, July 1999

Newly FDA Approved Influenza Vaccines Available for the 2013-2014 Season

Kendal Leslie, PharmD Candidate, Ohio Northern University

Each fall millions of people flock to their primary care providers, local pharmacies, and flu clinics to receive their annual influenza vaccination. With a selection including the traditional trivalent, high dose, intradermal, and nasal spray forms all approved in the US, there is no shortage of options to choose from. There are six newly FDA approved influenza vaccines available for the 2013 – 2014 flu season alone. New vaccines include several quadrivalent formulations and egg free alternatives.

For years traditional influenza vaccines were trivalent, consisting of three strains of the influenza virus including two different strains of influenza A and a single strain of influenza B. Influenza A is further categorized into subtypes based on surface antigens hemagglutinin and neuraminidase. Vaccines provide protection by inducing both cell mediated and humoral (antibody production) immune responses. Vaccine induced antibodies are usually strain specific, meaning antibodies active against one type or subtype of virus might confer little or no protection against another type or subtype of the same virus, as well as conferring little or no protection against a different variant of the same type or subtype due to mutation. The composition of the influenza vaccine is evaluated and adjusted each year based on the strains of influenza that are predicted to circulate in the upcoming flu season. According to the Centers for Disease Control and Prevention (CDC), the protection provided by the annual influenza vaccine will last at least 6-8 months.

Prior to the 1970's, there was only one dominate strain of influenza B known as the B/Yamagata/16/88 lineage. Beginning in the mid 1970's, a new strain known as B/Victoriay2/87 lineage emerged in China. By the 1980's the B/Victoriay2/87 lineage was considered the dominate strain globally. The emergence of this new strain has complicated the selection process for trivalent vaccines as both strains have co-circulated over the past decade. In some seasons one strain would dominate, in other seasons both strains may have been prevalent. Influenza B can infect all ages; however, incidence is higher in children and young adults compared to incidence of influenza A.

The new quadrivalent vaccines contain the traditional two strains of influenza A, as well as both strains of influenza B. Including both strains of influenza B will ensure the annual vaccine matches whichever strain is dominant that flu season. Patients who will benefit most include those who will be at risk for infection due to a mismatch in the trivalent vaccine or during seasons when both influenza B lineages are co-circulating. The CDC concludes if quadrivalent vaccines had been used from 2001-2008 there would have been an estimated 2.1 million fewer cases of influenza, over 20,000 fewer hospitalizations, and 1,300 fewer deaths.

The quadrivalent influenza vaccine is available as a standard intramuscular injection and a nasal spray. Randomized controlled trials comparing Flumist Quadrivalent to the trivalent form of Flumist, show no significant difference in adverse reactions with the exception of fever in children 2-8 years. Fever did occur more often with Flumist Quadrivalent (5.1%) compared with Flumist (3.1%). Additional studies show no significant difference in adverse reactions between the quadrivalent and the traditional trivalent intramuscular injections. Both Flumist Quadrivalent and all available quadrivalent intramuscular vaccines were found to be noninferior during immunogenicity analyses. Similar to the trivalent form, Flumist Quadrivalent is approved for nonpregnant patients 2-49 years old, without contraindications. Fluarix Quadrivalent, along with Flulaval Quadrivalent are approved for patients 3 years and older, while Fluzone Quadrivalent is approved for patients 6 months and older.

In addition to the newly released quadrivalent vaccines, two additional vaccines, Flucelvax and FluBlock, have also been FDA approved for the 2013-2014 season. These new vaccines are produced with little or no egg protein. Flucelvax is a trivalent intradermal injection approved for patients 18 years and older. It is

produced using cell cultures, but is not considered egg free due to the use of seed viruses supplied by the World Health Organization (WHO), which are initially processed using eggs. Flucelvax can be used in patients with a history of mild egg allergy, specifically hives. FluBlock is a trivalent, intradermal injection, approved for use in patients 18-49 years old. It is considered to be egg free and can be administered to patients with an egg allergy of any severity.

The following recommendations for the 2013-2014 flu season come from the CDC. All persons 6 months and older, without contraindications, should receive an annual influenza vaccination. If a child age 6 months to 8 years has never received an influenza vaccine in the past, two doses, four weeks apart are recommended for their first vaccination. It is particularly important for patients with an increased risk of complications due to the flu, as well as their care providers, to receive an influenza vaccine. No product or dosage form is preferred over another. Vaccinations should begin soon after the products become available as it could take at least two weeks to reach a peak antibody response.

FDA Approved Influenza Vaccines for 2013-2014 Influenza Season			
Vaccine	**Trade Name**	**Manufacturer**	**Age Indications**
IIV3 Standard Dose	Afluria	CSL Limited	≥ 9 yrs.
	Fluarix	GlaxoSmith Kline	≥ 3 yrs.
	Flucelvax*	Novartis Vaccines	≥ 18 yrs.
	FluLaval	ID Biomedical Corp.	≥ 3 yrs.
	Fluvirin	Novartis Vaccines	≥ 4 yrs.
	Fluzone	Sanofi Pasteur	†
	Fluzone Intradermal	Sanofi Pasteur	18-64 yrs.
IIV3 High Dose	Fluzone High-Dose	Sanofi Pasteur	≥ 65 yrs.
IIV4 Standard Dose	Fluarix Quadrivalent*	GlaxoSmith Kline	≥ 3 yrs.
	FluLaval Quadrivalent*	ID Biomedical Corp.	≥ 3 yrs.
	Fluzone Quadrivalent*	Sanofi Pasteur	‡
RIV3	FluBlok*	Protein Sciences	18-49 yrs.
LAIV4	FluMist Quadrivalent*	MedImmune	2-49 yrs.
Adapted from Centers for Disease Control and Prevention: Seasonal Influenza			

* Newly approved vaccine for 2013 – 2014 season
† IIV3 Fluzone age indication based on individual product
0.25 mL single dose prefilled syringe 6-35 mos.
0.5 mL single dose prefilled syringe ≥ 36 mos.
0.5 mL single dose vial ≥ 36 mos.
0.5 mL multi dose vial ≥ 6 mos.
‡IIV4 Fluzone age indication based on individual product
0.25 mL single dose prefilled syringe 6-35 mos.
0.5 mL single dose prefilled syringe ≥ 36 mos.
0.5 mL single dose vial ≥ 36 mos.
IIV3: Inactivated Influenza Vaccine Trivalent
IIV4: Inactivated Influenza Vaccine Quadrivalent
RIV3: Recombinant Influenza Vaccine Trivalent
LAIV4: Live Attenuated Influenza Vaccine Quadrivalent

2013-2014 U.S. Trivalent Influenza Vaccine Composition
A/California/7/2009 (H1N1)–like virus
H3N2 virus antigenically like the cell-propagated prototype virus A/Victoria/361/2011
B/Massachusetts/2/2012–like virus (Yamagata lineage)

2013-2014 U.S. Quadrivalent Influenza Vaccine Composition
A/California/7/2009 (H1N1)–like virus
H3N2 virus antigenically like the cell-propagated prototype virus A/Victoria/361/2011
B/Massachusetts/2/2012–like virus (Yamagata lineage)
B/Brisbane/60/2008–like virus (Victoria lineage)

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Upcoming Events

November 2013		
13	Journal Club	MVH 6NW
13-17	American Society of Tropical Medicine & Hygiene	Washington DC
27	Case Conference	MVH Maxon Parlor
December 2013		
11	Journal Club	MVH 6NW
18-22	World Confrence on Infectious Diseases	Chennai, India
	Case Conference (Cancelled)	
January 2014		
8	Journal Club	MVH 6NW
29	Case Conference	MVH Maxon Parlor
February 2014		
5	Journal Club	MVH 6NW
26	Case Conference	GDAHA
March 2014		
	Journal Club (TBA)	
26	Case Conference	GDAHA
April 2014		
2	Journal Club	MVH 6NW
10-12	ACP Internal Medicine 2014	Orlando, FL
30	Case Conference	GDAHA
May 2014		
	Journal Club (TBA)	
10-13	European Congress of Clin Micro & Inf Dis	Barcelona, Spain
28	Case Conference	GDAHA
6-10	European Society for Paediatric ID	Dublin, Ireland
June 2014		
4	Journal Club	MVH 6NW
7-9	APIC	Anaheim, CA
25	Case Conference	GDAHA
September 2014		
6-9	ICAAC	Washington, DC
October 2014		
8-12	IDSA/ID Week	Philadelphia, PA