Boonshoft School of Medicine
WRIGHT STATE UNIVERSITY

INFECTIOUS DISEASES NEWSLETTER

November 2015

T. Herchline, Editor

LOCAL NEWS

ID Fellows

Dr Shruti Patel will be at Miami Valley Hospital in November-December, and at the VA Medical Center in January.

Local Disease Activity

Pertussis cases increased during the fall; in September, there were 9 probable/confirmed cases in children ages 2 months to 12 years old and two in adults ages 18 and 49. In October, there were 10 probable/confirmed cases in children ages 2 months to 16 years old. There were no school or daycare links between cases. Reported cases are not classified as confirmed until the cough has been present for 14 days. Close contacts were appropriately treated.

There were multiple reports of enteric illness during the month of October, including Campylobacter (4 cases), Shigella (2 cases), E coli/STEC (2 cases), and one case each of Giardia, Salmonella, and Vibrio. The only links were brother/sister; there were no sensitive occupations involved.

There were two recent scabies outbreaks reported from separate assisted living communities. The index case for the first outbreak was diagnosed June 19th. Nine other residents were treated for scabies based on symptoms - none were confirmed by skin scraping. The last reported case was August 24th. The index case for the second outbreak was diagnosed July 21st. A total of 16 residents have been treated (8 confirmed cases). No reported cases since August 10th. There were no known links between these outbreaks.

NATIONAL NEWS

FDA Issues Warning Regarding Viekira Pak and Technivie

The FDA issued a warning that hepatitis C treatments Viekira Pak and Technivie can cause serious liver injury, mostly in patients with underlying advanced liver disease. As a result, the FDA is requiring the manufacturer to add new information about this safety risk to the drug labels. Patients taking these medicines are asked to contact their health care professional immediately if they develop fatigue, weakness, loss of appetite, nausea and vomiting, yellow eyes or skin, or light-colored stools. The review of adverse events reported to the FDA Adverse Event Reporting System (FAERS) database and to the manufacturer of these medicines, AbbVie, identified cases of hepatic decompensation and liver failure in patients with underlying liver cirrhosis who were taking these medicines. Some of these events resulted in liver transplantation or death. These serious outcomes were reported mostly in patients taking Viekira Pak who had evidence of advanced cirrhosis before starting treatment. Since the approvals of Viekira Pak in December 2014 and Technivie in July 2015, at least 26 worldwide cases submitted to FAERS were

considered to be possibly or probably related to Viekira Pak or Technivie. In most of the cases, liver injury occurred within 1 to 4 weeks of starting treatment. FAERS includes only reports submitted to FDA, so there are likely additional cases about which we are unaware. Health care professionals should report side effects involving Viekira Pak or Technivie to the FDA MedWatch program

Influenza Activity

The Centers for Disease Control and Prevention's (CDC) Influenza Division collects and analyzes surveillance data year-round and produces a weekly report on U.S. influenza activity from October through May. During October, overall influenza remained below baseline threshold within the United States. Pneumonia and influenza mortality also remained below the epidemic threshold. For week 41 (ending October 17, 2015), Guam reported widespread influenza activity, no states reported widespread or regional influenza activity, 4 states reported local spread of influenza, 29 states (including Ohio) reported sporadic influenza activity and 17 states reported no influenza activity. Regionally (Auglaize, Champaign, Clark, Darke, Greene, Miami, Montgomery, Preble, Shelby, and Warren counties), there were 5 cases of influenza A and 1 case of influenza B in October, with 4 influenza-related hospitalizations.

Recent Respiratory Infection Linked to Increased Risk of Stroke in Children

In a study published in the journal Neurology, researchers found that recent infection (within the past week) was associated with a 6 fold increased risk of stroke. Upper respiratory infection (common cold) was the most frequently reported infection. Strokes are known to affect approximately 11 in 100,000 children. The Vascular Effects of Infection in Pediatric Stroke study was an international study which also found that children who had received most or all of the recommended vaccines had a much lower risk of stroke compared to children who had received few or none of the recommended vaccines.

INTERNATIONAL NEWS

Ebola Virus Disease

The Ebola outbreak in West Africa continues to decline. Sierra Leone has been declared Ebola free, with the last positive test more than 42 days ago. The CDC has dropped the recommendation for active monitoring of travelers arriving from Sierra Leone. There were a total of 14,122 cases from the country. Guinea is now the only remaining country with suspected ongoing transmission (3806 cases). Liberia (10,672 cases), Nigeria (20 cases), Mali (8 cases), the United States (4 cases), Senegal (1 case), United Kingdom (1 case), Italy (1 case) and Spain (1 case) have each had cases but have been declared Ebola free.

Case Conference

Contributed by Shruti Patel, MD

A 61 year old male with history of remote trauma to his right femur and osteotomy with skin flap reconstruction was evaluated for worsening of chronic right knee arthralgia. Total knee arthroplasty was planned and as a preparation he had an arthrocentesis done with intra operative cultures which were negative after two weeks. Patient underwent right total knee arthroplasty after two month. Three weeks after surgery patient was admitted to hospital for infected wound dehiscence's and drainage from knee. I&D was done and cultures were sent. Wound VAC was applied and he was discharged home with ciprofloxacin and rifampin. Cultures grew *Serratia, Klebsiella and Fingoldia magna.* One month later in follow up, he was found to have worsening of infection and was admitted to hospital. He was afebrile without any leukocytosis. CT scan of right knee showed his wound communicating with an abscess extending to the metaphysis with suspicion for osteomyelitis. He underwent surgery for removal of right TKA with I&D and antibiotics spacer placement. He was started on broad spectrum antibiotics. 5 out of 6 intra operative cultures from this surgery grew only *Veillonella spp.* Patient was treated with moxifloxacin 400 mg daily and metronidazole 500 mg four times a day for three months. One month later he underwent I&D with multiple cultures and re implantation of antibiotics spacer. Two months later patient underwent new total knee arthroplasty. All antibiotics were stopped ten days before surgery. All intra operative cultures were negative except one culture eventually grew *Bacillus spp.* Patient received linezolid 600 mg two times a day for three weeks for *Bacillus spp.* All antibiotics were stopped after three weeks of repeat surgery. Upon one year checkup patient is still doing well without any recurrence of knee joint infection.

Discussion

Most common anaerobic bacteria causing prosthetic joint infections are *Propionibacterium acnes. Fingoldia magna* is probably second most common anaerobic bacteria causing these infections. It is gram positive anaerobic cocci which colonizes human skin and gastrointestinal tract. It was formerly known as *peptostreptococcus magnus* until 1999. It commonly affects ankles, knee and hip joints. Most common risk factors are previous trauma or surgery to affected joints and poor dentition. It is not a contaminant when isolated from sterile site and should be considered true pathogen. It is vital to go susceptibilities as it has variable susceptibilities to penicillin and clindamycin. Penicillin is recommended antibiotic of choice. Alternative antibiotics options are clindamycin with rifampin or moxifloxacin. Duration of treatment is variable and case based but should be at least 4 to 6 weeks.

This patient also grew *Veillonella spp.* which is strictly gram negative anaerobic cocci. It is part of gastro intestinal, mouth and vaginal flora. *Veillonella parvula* is most significant species which causes infection. There are total 9 cases reported so far as veillonella causing osteomyelitis in spine and other bones. There are only two cases reported so far for prosthetic joint infections. There are no guidelines about treatment for *Veillonella* prosthetic joint infections due to this being very rare cause. Our patient was susceptible to clindamycin, imipenem and metronidazole and resistant to penicillin and piperacillin/tazobactam. We have successfully treated him with moxifloxacin and metronidazole.

References

1: Al-Otaibi FE, Al-Mohizea MM. Non-vertebral Veillonella species septicemia and osteomyelitis in a patient with diabetes: a case report and review of the literature. J Med Case Rep. 2014 Nov 12;8:365.

2. Shah, Neel B., et al. "Anaerobic prosthetic joint infection." *Anaerobe* 36 (2015): 1-8.

3: Walter G, Vernier M, Pinelli PO, Million M, Coulange M, Seng P, Stein A. Bone and joint infections due to anaerobic bacteria: an analysis of 61 cases and review of the literature. Eur J Clin Microbiol Infect Dis. 2014 Aug;33(8):1355-64.

4. Levy PY, Fenollar F, Stein A, Borrione F, Raoult D. Finegoldia magna: a forgotten pathogen in prosthetic joint infection rediscovered by molecular biology. Clin Infect Dis. 2009 Oct 15;49:1244-7.
5. Felten A, Desplaces N, Nizard R, Sedel L, Lagrange P. [Peptostreptococcus magnus osteoarticular infections after orthopedic surgery. 14 cases and pathogenicity factors]. Pathol Biol (Paris). 1998 Jun;46(6):442-8.

New Antimicrobials

Contributed by: Katelyn Booher, D.O.

AVYCAZ, the combination of ceftazidime, a third-generation cephalosporin, and avibactam, a novel non-beta-lactam beta-lactamase inhibitor, was FDA-approved in the U.S. in February 2015. The combination is indicated for use in patients 18 years or older for complicated intra-abdominal infections (cIAI) in combination with metronidazole, and complicated urinary tract infections (cUTI), including pyelonephritis. Avibactam restores the activity of ceftazidime against many beta-lactamase-producing Gram-negative bacteria, including extended-spectrum beta-lactamases (ESBLs) and *Klebsiella pneumoniae* carbapenemases (KPCs). The activity of ceftazidime against *Pseudomonas aeruginosa* is also enhanced with the addition of avibactam (1,2).

Ceftazidime/avibactam should be reserved for indicated infections that are proven or strongly suspected to be due to susceptible bacteria, including treatment of cIAI due to the *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Providencia stuartii, Enterobacter cloacae, Klebsiella oxytoca, and Pseudomonas aeruginosa*. The combination is also indicated for cUTI due to *Escherichia coli, Klebsiella pneumoniae, Citobacter koseri, Enterobacter aerogenes, Enterobacter cloacae, Citrobacter freundii, Proteus spp., and Pseudomonas aeruginosa* (1,2).

Dosing of AVYCAZ is 2.5grams (ceftazidime 2 grams and avibactam 0.5 grams) intravenously over 2 hours every 8 hours. Recommended duration for cIAI is 5 to 14 days, and for cUTI, including pyelonephritis, 7 to 14 days. Renal dosing adjustment is required for creatinine clearance less than 50mL/min, and doses must be given following dialysis on dialysis days as the medication is dialyzable.

Contraindications include known serious hypersensitivity to the components of ceftazidime or avibactam, or the cephalosporin class. As with other beta-lactams, hypersensitivity reactions including anaphylaxis and serious skin reactions may occur, as well as cross-hypersensitivity in penicillin-allergic patients, *Clostridium difficile*-associated diarrhea, and seizures and other neurologic events, particularly in the setting of renal impairment. The most common adverse reactions are vomiting, nausea, constipation, and anxiety (incidence of greater than or equal to 10%).

Clinical trials support similar efficacy of ceftazidime-avibactam versus standard carbapenem therapy in cIAI and cUTI, including those due to cephalosporin-resistant Gram-negative isolates (2). Three phase I pharmacokinetic studies and two phase II clinical studies have reported safety and tolerability; the combination has been well tolerated with few serious adverse events reported (1,2).

1. Zhanel G, Lawsson C, Adam H, et al. Ceftazidime-Avibactam: A Novel Cephalosporin/Beta-lactamase Inhibitor Combination. *Drugs*. 2013;73: 159-177.
2. Mawal Y, Critchley IA, Riccobene TA, et al. Ceftazidime-avibactam for the treatment of complicated urinary tract infections and complicated intra-abdominal infections. *Expert Rev Clin Pharmacol.* 2015; 8:691-707.

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 and may be considered contaminates or colonizers. Please contact me at wgstarrett@premierhealth.com if you come across an isolate that may fit in this category.

Organism: *Hafnia alvei*

Clinical Data: A 73 year-old female with history of diabetes mellitus and obesity presented to a local hospital with diaphoresis and hypotension and was admitted for sepsis associated with left lower extremity cellulitis. Her history was significant for invasive melanoma, for which she had undergone a radical vulvectomy about six weeks prior. This was complicated by a wound infection and was successfully treated with surgical debridement and a broad spectrum antibiotic course. Significant third spacing of fluid occurred with treatment, and she had an acute exacerbation of chronic venous insufficiency in her left leg resulting in stasis ulcers following discharge. Blood and wound cultures on her current admission grew Group A streptococci, and her urine cultures grew a *citrobacter* species as well as *Hafnia alvei.* Broad spectrum antibiotics were maintained at the time of transfer to a long term acute care facility.

Taxonomy:

Division: Bacteria
Phylum: Proteobacteria
Class: Gammaproteobacteria
Order: Enterobacteriales
Family: *Enterobacteriaceae*
Genus: *Hafnia*
Species: *alvei*

Associated Diseases:

1. Nosocomial wound infections
2. Peritonitis
3. pneumonia
4. line infections
5. urinary tract infections

Description:

Hafnia alvei is a motile, enteric gram-negative bacillus that shares characteristics with *Enterobacter* and *Serratia* and does not ferment lactose. It was previously known as *Enterobacter hafniae, Enterobacter aerogenes* subsp. *hafniae*, and *Enterobacter alvei.* The organism is uncommonly isolated in clinical specimens and rarely causes infection other than in patients with multiple comorbidities including malignancy, trauma and the post-operative state. Accordingly, infections are often nosocomial including surgical wound and line infections. Recovery of this organism in pure culture from clinical specimens is unusual and may be more suggestive of infection as opposed to colonization. *Hafnia alvei* infections respond to antimicrobial agents frequently used to treat other enteric gram-negative organisms, such as broad spectrum penicillins, third-generation cephalosporins and carbapenems.

Resources:

1. Greipsson S, *et al.* Numerical taxonomy of *Hafnia alvei.* International Journal of Systematic Bacteriology 1983;44;470-475.

2. Gunthard H, *et al.* Clinical significance of extraintestinal *Hafnia alvei* isolates from 61 patients and review of the literature. Clin Inf Dis 1996;22;1040-5.
3. http://www.uniprot.org/taxonomy/569
4. Murray, *et al.* Manual of Clinical Microbiology, 7th edition.
5. Mandell, *et al.* Principles and Practice of Infectious Diseases, 6th edition.

Upcoming Events

November 2015		
11	Journal Club Case Conference cancelled	MVH 6NW
December 2015		
9	Journal Club Case Conference cancelled	MVH 6NW
January 2016		
13	Journal Club	MVH 6NW
27	Case Conference	MVH Berry 5
February 2016		
10	Journal Club	MVH 6NW
22-25	Conference on Retroviruses and Opportunistic Infections http://www.croiconference.org/	Boston, MA
24	Case Conference	MVH Maxon Parlor
March 2016		
2-5	International Congress of Infectious Disease http://www.isid.org/icid/	Hyberabad, India
9	Journal Club	MVH 6NW
30	Case Conference	MVH Maxon Parlor
April 2016		
9-12	European Congress of Clin Micro & Inf Dis	Istanbul, Turkey
13	Journal Club	MVH 6NW
27	Case Conference	MVH Maxon Parlor
May 2016		
18-21	Society for Healthcare Epidemiology http://www.shea-online.org/Education/SHEASpring2016Conference.aspx	Atlanta, GA
June 2016		
12-14	Refugee Health Conference http://www.northamericanrefugeehealth.com/	Niagra Falls, NY
16-20	ASM Microbe/ICAAC http://www.asmmicrobe.org/	Boston, MA
October 2016		
26-30	ID Week http://www.idweek.org/	New Orleans, LA