Boonshoft School of Medicine
WRIGHT STATE UNIVERSITY

INFECTIOUS DISEASES NEWSLETTER

Aug 2017
T. Herchline, Editor

LOCAL NEWS

ID Fellows

Dr Alpa Desai will be at the VA Medical Center in August, and at Miami Valley Hospital in September and October. Dr Luke Onuorah will be at Miami Valley Hospital in August, at the VA Medical Center in September, and at Miami Valley Hospital in October. Dr. Najmus Sahar will be at MVH in August through October.

NATIONAL NEWS
Contributed by Luke Onuorah, MD

Infections Following Intra-Articular Injections

On March 6, 2017, the New Jersey Department of Health (NJDOH) was notified of three cases of septic arthritis in patients who had received intra-articular injections for osteoarthritic knee pain at a private outpatient practice. The practice voluntarily closed the next day. NJDOH, in conjunction with the local health department and the New Jersey Board of Medical Examiners, conducted an investigation and identified 41 cases of septic arthritis associated with intra-articular injections administered during 250 patient visits at the same practice, including 30 (73%) patients who required surgery. Bacterial cultures of synovial fluid or tissue from 15 (37%) patients were positive; all recovered organisms were oral flora. An infection prevention assessment of the practice identified multiple breaches of recommended infection prevention practices, including inadequate hand hygiene, inappropriate use of pharmacy bulk packaged (PBP) products as multiple-dose containers and handling PBP products outside of required pharmacy conditions, and preparation of syringes up to 4 days in advance of their intended use. No additional septic arthritis cases were identified after infection prevention recommendations were implemented within the practice. *Source: Ross K, Mehr J, Carothers B, et al. Outbreak of Septic Arthritis Associated with Intra-Articular Injections at an Outpatient Practice — New Jersey, 2017. MMWR Morb Mortal Wkly Rep 2017;66:777–779.*

Zika Virus Update

On July 24, 2017, CDC issued updated interim guidance for healthcare providers caring for pregnant women with possible Zika virus exposure. The falling prevalence of the disease, increases the likelihood of false-positive test result of IgM antibody screening tests. Furthermore, IgM antibodies which may persist for 12 weeks, are unable to distinguish between infections that occurred during an on-going pregnancy or before an on-going pregnancy, especially for women with possible Zika virus exposure before a pregnancy. These limitations should be considered when counseling pregnant women about the risks and benefits of testing for Zika virus infection during pregnancy.

- All pregnant women in the United States and U.S. territories should be asked about possible Zika virus exposure *before* and *during* the current pregnancy, at every prenatal care visit.

- Pregnant women with recent possible Zika virus exposure and symptoms of Zika virus disease should be tested to diagnose the cause of their symptoms.
- Asymptomatic pregnant women *with ongoing* possible Zika virus exposure should be offered Zika virus NAT testing three times during pregnancy.
- Asymptomatic pregnant women who have recent possible Zika virus exposure (i.e., through travel or sexual exposure) but *without ongoing* possible exposure are not routinely recommended to have Zika virus testing
- Zika virus IgM testing is no longer routinely recommended for asymptomatic pregnant women *with ongoing* possible Zika virus exposure

Source: Oduyebo T, Polen KD, Walke HT, et al. Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States (Including U.S. Territories), July 2017. MMWR Morb Mortal Wkly Rep 2017;66:781-793

Multistate outbreak of *Salmonella* Typhimurium

As of July 19, 2017, 24 people infected with the outbreak strains of *Salmonella* Typhimurium have been reported from 16 states. Ohio is not one of these states. For people whose information was available, illnesses started on dates ranging from March 17, 2017 to June 22, 2017. Ill people ranged in age from less than one year to 57 years, with a median age of 24. Seventy-five percent of ill people were female. Among 21 people with available information, six (29%) were hospitalized. No deaths were reported. Nine (69%) of 13 ill people had laboratory exposures in the week before they became ill. They reported behaviors while working in the laboratory that could increase the risk of *Salmonella* infection. These included not wearing gloves or lab coats, not washing hands, and using the same writing utensils and notebooks outside of the laboratory. This outbreak highlights the potential risk of *Salmonella* infection associated with working in microbiology laboratories. *Source: https://www.cdc.gov/salmonella/typhimurium-07-17/index.html*

INTERNATIONAL NEWS

Contributed by Najmus Sahar, MD

Yellow Fever in Brazil

The CDC is reporting an ongoing outbreak of yellow fever in Brazil. The first cases were reported in the State of Minas Gerais in December 2016, but confirmed cases have since been reported in the neighboring states of Espirito Santo, São Paulo, and Rio de Janeiro. Some cases have resulted in death. Health authorities in the affected states, with assistance from the Brazilian Ministry of Health, are conducting mass vaccination campaigns among unvaccinated residents of affected areas. Anyone 9 months or older who travels to these areas should be vaccinated against yellow fever. People who have never been vaccinated against yellow fever should not travel to areas with ongoing outbreaks. CDC no longer recommends booster doses of yellow fever vaccine for most travelers. However, a booster dose may be given to travelers who received their last dose of yellow fever vaccine at least 10 years ago and who will be in a higher-risk setting, including areas with ongoing outbreaks

Ebola in Democratic Republic of The Congo

On May 11, 2017, the Ministry of Public Health of the Democratic Republic of the Congo notified international public health agencies of a cluster of suspected cases of Ebola Virus Disease (EVD) in the Likati health zone of the province of Bas Uélé. The first report mentioned 8 suspected cases, including two deaths, with a third death reported on May 12. Testing of samples was conducted by the Institut National de Recherche Biomedicale (INRB) in Kinshasa, with two samples testing positive for Ebola Zaire by reverse transcription polymerase chain reaction (RT-PCR) test. Teams from international

agencies, including CDC, WHO, MSF (Doctors without Borders), and others, supported the Ministry of Public Health's epidemiologic, diagnostic, clinical, and communications efforts to respond to the outbreak. The response faced challenging logistical obstacles, including the remoteness of the area and limited services. Mobile diagnostic laboratories provided testing of samples in the affected areas. Following a period of 42 days since the second negative laboratory diagnostic test of the last confirmed patient, WHO declared an end to the outbreak on July 2, 2017. There were a total of 8 probable or confirmed cases; 5 were laboratory confirmed; there were 4 deaths.

EMERGING INFECTIONS NETWORK

EIN Query: HIV and Aging

The overall response rate was 345 of 681 (51%) of adult ID practitioners who have reported an interest or practice in HIV medicine. Of these, 294 reported caring for HIV-infected patients in the past year; only these respondents were included in the remaining survey questions. A small majority (53%) reported providing primary care for the majority of their patients. A slightly higher number (57%) reported that their clinic provided multidisciplinary support to patients (mental health,case management, etc). On average, 37% of patients were > 50 years old. The top barriers to "healthy aging" in patients > 50 years old (in order of ranking) were multimorbidity, polypharmacy, low income/savings, and tobacco/etoh use.

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

CASE CONFERENCE

Contributed by Alpa Desai, MD

58 y/o Indian female, who has been living in Dayton, Ohio for 30 years, presented to ID clinic 2 days after returning back from India after short stay of 4 weeks with an unexplained fever. She went to small town in northern part of India for small ritual ceremony 2 weeks after her arrival to India. Patient reported that she developed high-grade fever, dysuria, malaise and weakness. She reported that she used appropriate mosquito prevention measures, drank bottle water and ate cooked home food. She reported that she played holi (Hindu festival of color) with well water and rose. Her symptoms started 2 days after enjoying the festival of holi. She went to local hospital where she was admitted for possible UTI and started on some antibiotic. Patient's dysuria resolved after starting antibiotic but continued to spike fever. Urine culture was negative. Blood cultures were not done at the local hospital. Patient was transferred to Tertiary care hospital in Delhi due to persistent fever despite being on antibiotic for 5 days.

Her work up was unrevealing at Tertiary care hospital. Basic blood tests include CBC, and BMP were normal. LFT was mildly elevated with AST-91, ALT. ESR – 67. HIV ELISA, viral hepatitis serology, malaria antigen and smear were negative. Urine and Blood culture were negative. CT of the chest and abdomen showed multiple nodular infiltrates with surrounding ground glass haziness in bilateral lung filed associated with mediastinal and supraclavicular lymphadenopathy and hepatomegaly but normal spleen. She underwent bronchoscopy with trans-bronchial biopsy and supraclavicular lymph node biopsy. BAL culture, BAL MTB PCR, and BAL PCR for multiple bacterial and viral pathogens were negative. Trans-bronchial biopsy result showed acute inflammation but no granuloma, AFB/fungal stain were negative. Patient was treated with ceftriaxone and levofloxacin for about 2 weeks with some clinical improvement but continued to have intermittent low-grade fever. She was advised to travel back to USA for further work up.

After returning to USA and being off antibiotics for 2-3 days she started having high-grade fever and malaise, poor appetite and generalized weakness. In USA, basic blood work was unremarkable except ESR of 99. Blood cultures, Q fever serology, Echocardiogram were unremarkable. CT chest and abdomen showed numerous bilateral pulmonary nodules, multiple bilateral mildly enlarged supraclavicular, superior mediastinal and axillary lymph nodes, no hilar lymphadenopathy or intra abdominal pathology. Patient underwent axially node biopsy, which showed benign reactive lymph nodes (no granuloma), AFB, fungal and routine cultures as well as universal bacterial PCR were negative. Given patient CT chest finding and recent travel history to India, pulmonary melioidosis was strongly suspected. India is highly endemic for melioidosis. Patient was offered to get lung nodule biopsy but patient rather decided to start empiric treatment for melioidosis. Patient was originally started on Ceftazidime and Bactrim. Patient did not tolerated Bactrim so switched to doxycycline. Patient received total 10 days of IV ceftazidime and doxycycline followed by doxycycline monotherapy for total 3-6 months treatment. Repeat CT chest done 2 weeks after combination antibiotic therapy, showed near complete resolution of lung nodules. Her symptoms resolved completely and repeat ESR improved to 29.

Discussion

Melioidosis infection caused by *Burkholderia pseudomallei*, which is aerobic, motile, non spore forming gram negative bacteria with characteristic cornflower heads colonies and bipolar staining resembling safety pins on gram stain. It is an endemic to large part of south and east Asia and northern Australia. *Burkholderia pseudomallei*, was previously known as *pseudomonas pseudomallei* until 1992. It is environment saprophytes and is found in wet soil in particular (rice paddy field) and water. Three major routes of transmission include inhalation, ingestion and inoculation through skin from the contaminated soil. Literature reported that there are associated risk factors related to this infection include diabetes mellitus (most common) followed by alcohol abuse, chronic lung disease and chronic kidney disease (1). Mortality is significantly high in patients with chronic respiratory disease. The absence of any risk factors was strongly predictive of survival. Pneumonia was the most common clinical presentation followed by genitourinary infection, skin and soft tissue infection, septic arthritis and rarely neurological melioidosis with meningo-encephalitis, myelitis and cerebral abscesses (1). Melioidosis has characteristic of forming internal organ abscesses especially in lungs, liver, spleen, skeletal muscle and prostate. Pulmonary melioidosis could be primary infection acquired through inhalation or it could be secondary infection developed from primary non-pulmonary infection during the course of their illness (2). CT scan of chest has characteristic finding of pulmonary melioidosis with multi lobar pulmary nodules and if remain untreated then it can develop chronic cavitary lung lesion specially in upper lobe of lungs (2). *B. pseudomallei* is inherently resistant to penicillin, ampicillin, first-generation and second-generation cephalosporins, gentamicin, tobramycin, streptomycin, and polymyxin (3). Studies have reported that B. pseudomallei isolates were 100% susceptible to Imipenem/Meropenem followed by Ceftazidime 99.5%. Ciprofloxacin has activity against B. Pseudomallei but it is not reliable to treat infection given variable susceptibility. Augmentin and Bactrim has 97% susceptibility (3). Treatment of melioidosis comprises two phase 1. Acute phase (parenteral antibiotics given for >/= 10 days) and 2. Eradication phase (oral antibiotics to complete a total 3-6 months) (4). Acute phase is treated with IV Ceftazidime + co-trimoxazole or Meropenem and eradication phase is treated with either Bcatrim or doxycycline or Augmentin.

References

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4. Inglis, Timothy JJ, Dionne B. Rolim, and Jorge LN Rodriguez. "Clinical guideline for diagnosis and management of melioidosis." *Revista do Instituto de Medicina Tropical de São Paulo* 48 (2006): 1-4.

Effect of Climate Change on the Epidemiology of Infectious Diseases

Contributed by Ashley Trent (UD Student, PHDMC Intern)

Over recent years climate scientists have come to a consensus that anthropogenic climate change is occurring. According to the Intergovernmental Panel on Climate Change, global land and ocean surface temperature has increased by 0.85°C from 1880 to 2012. (Stoker 2014) The increasing global temperature is expected to cause a variety of weather and climate events in the near future. These include increasing precipitation, rising sea levels, droughts, and more extreme weather events. An often overlooked consequence of these changes is their impact on human health. The World Health Organization (WHO) has estimated that there will be $2-4 billion in direct damage costs to health by 2030. The increasing temperature, precipitation, and humidity will influence the life cycle of vectors such as mosquitos and ticks. Flooding, and extreme water events can lead to unclean water and increased displacement of vulnerable populations from tropical areas. The possibility of droughts will also lead to poorer nutrition in many populations, making individuals more susceptible to disease. Currently, most research has focused on diseases transmitted through vectors, and waterborne illnesses. Due to their significant burden to human health this review will focus on malaria, dengue, Lyme disease, and cholera.

The most well studied climate change impacts on health are vector borne diseases. Vector life cycles are highly affected by increasing temperatures, and precipitation due to the inability of arthropods to physiologically regulate body temperature. Evidence has suggested three main mechanisms responsible for increasing vector and zoonotic diseases: geographic range shifts, change in the rate of development, survival and reproduction of vectors, change in reservoirs and pathogens, and changes in biting rates. (Patz, Grabow, Limaye 2014) These changes in vectors will introduce diseases into new areas, as well as increase the rate of transmission in areas where they are already endemic. According to the WHO, if global temperatures increase by 2-3°C as predicted, there will be a 3-5% increase in the population at risk for malaria, which could mean millions of additional cases each year. (Shuman 2010) Due to its transmission through arthropod vectors, malaria is a disease that is highly sensitive to weather changes. Adult mosquitos have a narrow optimal temperature range for survival and usually thrive in tropical zones. If temperatures increase, mosquitoes will migrate to temperate areas, and higher altitudes in the tropical countries in which they are currently endemic. Increasing temperature has also been found to increase human biting rate, and mosquito development which increases vector density. Malaria is also closely linked to changes in rainfall; an increase in precipitation creates more habitats optimal for larvae development. (Ramasay, Surendran 2012)

Dengue is a rapidly spreading arbovirus, and there are currently no specific antiviral medications or vaccines to help manage the disease, making vector control an important factor in preventing transmission. *Aedes aegypti* is the primary vector for dengue transmission, this confines transmission to tropical regions because overwintering larvae and eggs of this mosquito are killed in freezing temperatures. Temperature also increases the proportion of mosquitoes that become infected because the extrinsic incubation period (EIP) of the virus shortens with increasing temperature. (Patz et al., 1998) In a study by Patz et al. (1998) a general circulation model was used to predict epidemic potential of dengue, and they found that epidemic potential increased with a small temperature rise, which indicates that fewer mosquitoes would be needed to spread dengue in vulnerable populations. Similarly, in a study by Colon-Gonzalez, et al. (2013) there was a projected increase up to a 40% in dengue incidence in Mexico by 2080 due to climate change, with other factors held constant. This is due to a decrease in the EIP of the virus, and development of the mosquito with increasing temperature.

Lyme disease is caused by *Borrelia burgdorferi*, which is transmitted by ticks, *Ixodes scapularis* and *Ixodes ricinus*, in North America and Europe. Temperature limits the northward expansion of ticks because they require a monthly average temperature to be above -7 °C. Current climate models predict

that warming temperatures will allow the ticks to expand northward into Canada. (Patz, Grabow, Limaye 2014) In addition to temperature allowing the expansion of the ticks into more northern areas, increasing temperature also directly affects transmission rates. Specifically, the length of time that a tick feeds is correlated with the transmission of the infection. As temperature increases, feeding time will lengthen as well, increasing the overall transmission rate. (Parham et al., 2015)

An additional concern of climate change is its effects on water-borne illnesses. *Vibrio cholerae* is potentially one of the most serious pathogens with close ties to changes in water conditions. According to the WHO there are between 3-5 million cases of cholera per year worldwide, resulting in 120,000 deaths. (Escobar, et al. 2015) Vulnerable populations, especially those around coastlines are at the greatest risk. Cholera is usually an opportunistic epidemic following natural disasters, and is more prevalent following both low and high levels of precipitation. During times of low precipitation, scarcity of water and poor sanitation can lead to an increase in exposure to contaminated water. This was seen in Kenya in 2009, during a drought there were 4700 cases of cholera in one month, and 119 deaths. (Shuman 2010) In addition, excess precipitation and flooding can lead to poor sanitation if sewage infrastructures are overwhelmed, leading to run off. Developed countries are also at risk even with their high water quality because cholera can be transmitted through contaminated seafood. Studies have also suggested that with the increase in seawater temperature cholera may begin to emerge in new regions. (Escobar et al. 2015)

Changes need to be adopted into current health care systems to adapt to climate change impacting infectious disease. Adaptations have been suggested by Confalonieri, et al (2015). These strategies include increasing epidemiological surveillance for emergence of infections in new areas, as well as developing warning systems for epidemics following extreme water events. In addition, they suggested disease and vector control programs to reduce the risk of infections. Finally, it is important that health systems are easily accessible, especially to vulnerable populations. Developing countries in which infrastructure and health systems are not as well-structured are especially vulnerable; if an extreme weather event occurs, these systems would be easily overwhelmed.

References

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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: *Exophiala*

Clinical Data: A 78-year-old female with history of breast cancer and chronic obstructive pulmonary disease presented in outpatient referral from a local pulmonologist for pneumonia due to mycobacterium avium complex (MAC). The patient had a chronic dry cough for about 2 years, and underwent CAT scan of the chest the previous year. A subsequent scan four months later demonstrated mild bronchiectasis with nodular patterns concerning for atypical mycobacterial infection, and she was referred to a pulmonologist. A bronchoscopy was performed, and cultures grew MAC as well as *capnocytophaga* and microaerophilic and alpha hemolytic streptococci. Fungal cultures grew *Exophiala* and *Candida albicans*. The patient reported that her cough had been more frequent since the bronchoscopy, but she denied fevers or other constitutional symptoms. She had no history of exposure to TB, although she worked in a medical facility for 5 years back in the 1980's and her annual PPD was always negative.

Taxonomy

Kingdom: Fungi
Division: Ascomycota
Class: Eurotiomycetes
Order: Chaetothyriales
Family: Herpotrichiellaceae
Genus: *Exophiala*

Associated Diseases:

1. Tinea nigra
2. Chromoblastomycosis (*E jeanselmei, E spinifera*)
3. Subcutaneous phaeohyphomycosis
4. Opportunistic infections
5. Maduromycosis
6. Hypersensitivity pneumonitis

Description:

Exophiala is a genus of dematiaceous (brown or black) fungi that produce a melanin-like pigment in the walls if its yeast and mycelial elements. It is a saprophytic fungus common in the environment, and has also been found in wet, oligotrophic locations such as dishwashers and bathrooms. Although it is an uncommon pathogen, infections with these organisms have been well described. Cutaneous and subcutaneous infections are most common in normal hosts. Examples include Tinea nigra, a superficial infection of the palms and soles caused by *Exophiala (Hortaea) wernickii* primarily in tropical and subtropical climates. Subcutaneous infections may also be caused by *Exophiala jeanselmei and Exophiala spinifera.* Deep infections usually occur in immunocompromised hosts, and include fungemia, brain abscess, and respiratory tract infections caused by *Exophiala dermatiditis, Exophiala jeanselmei,* and other species. Itraconazole, voriconazole and amphotericin B have all been used to treat infections with these organisms.

Resources:

1. Koneman's Color Atlas and Textbook of Diagnostic Microbiology, 6th ed.
2. Mandell, *et al.* Principles and Practice of Infectious Diseases, 6th edition.
3. Ramanan P, *et al. Rothia* Bacteremia: a 10-year experience at Mayo Clinic, Rochester, Minnesota. J Clin. Microbiol. **September 2014** vol. 52 no. 9, **3184-3189.**
4. **Woo, *et al.* Clinical Spectrum of *Exophiala* Infections and a Novel *Exophiala* species, *Exophiala hongkongensis.* J Clin Microbiol. January 2013, vol. 51 no. 1, 260-267.**
5. www.mycobank.org
6. **Zeng JS, *et al.* Spectrum of clinically relevant *Exophiala* species in the United States. J Clin Microbiol. November 2007, vol. 45 no. 11, 3713-3720.**

7.

Upcoming Events

August 2017		
9	Journal Club	MVH 6NW
30	Case Conference	MVH Maxon Parlor
September 2017		
13	Journal Club	MVH 6NW
27	Case Conference	MVH Maxon Parlor
October 2017		
4-8	ID Week http://www.idweek.org/	San Diego, CA
11	Journal Club	MVH 6NW
25	Case Conference	MVH Maxon Parlor
November 2017		
8	Journal Club	MVH 6NW
	Case Conference (TBA)	MVH Maxon Parlor
December 2017		
13	Journal Club	MVH 6NW
	Case Conference (TBA)	MVH Maxon Parlor
January 2018		
10	Journal Club	MVH 6NW
31	Case Conference	MVH Maxon Parlor
February 2018		
14	Journal Club	MVH 6NW
28	Case Conference	MVH Maxon Parlor
March 2018		
4-7	Conference on Retroviruses and Opportunistic Infections http://www.croiconference.org/	Boston, MA
14	Journal Club	MVH 6NW
28	Case Conference	MVH Maxon Parlor
April 2018		
18-20	Society for Healthcare Epidemiology http://sheaspring.org	Portland, OR
21-24	European Congress of Clin Micro & Inf Dis http://www.eccmid.org	Madrid, Spain
June 2018		
7-11	ASM Microbe (ASM General Meeting & ICAAC) http://asmmicrobe.org	Atlanta, GA