Boonshoft School of Medicine
WRIGHT STATE UNIVERSITY

INFECTIOUS DISEASES NEWSLETTER

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Thomas Herchline, Editor

LOCAL NEWS

West Nile Virus in Montgomery County

The Ohio Department of Health has recorded Montgomery County's first case of West Nile Virus (WNV) in 2018. A 68-year-old female resident was diagnosed with the disease. As of August 27, there have been 8 human cases of WNV in Ohio and one death. Last year there were 34 cases and 5 deaths in Ohio but none in Montgomery County. Approximately 80% of people infected with WNV will not show any symptoms. Up to 20% of those infected have mild symptoms such as fever, body aches, and swollen glands. Symptoms can last a few days, though in some cases, they may last for several weeks. About one in 150 people infected with WNV will develop severe illness. For more information on West Nile Virus and mosquito bites visit Public Health's Fight the Bite - West Nile Virus page.

Montgomery County Hepatitis A

Hepatitis A outbreaks have been occurring in multiple states across the U.S., including several bordering Ohio. The Ohio Department of Health declared a statewide community outbreak for Hepatitis A on June 22. As of August 27, Ohio had 286 confirmed cases. Montgomery County saw its first case in April of this year. As of August 27, there were a total of 66 cases. Public Health has conducted a total of 49 external vaccination clinics for Hepatitis A with 1290 individuals being vaccinated. These clinics targeted the Montgomery County jail, homeless populations, men who have sex with men and individuals abusing drugs. In addition, 394 vaccinations have been provided at the Public Health Clinic.

Opioid Crisis

The Community Overdose Action Team's Prescription Opioid Branch is sponsoring two clinician opioid information seminars for physicians, physician's assistants, dentists, advanced practice nurses, pharmacists, and anyone else who can prescribe opioids. The goal is to provide open dialogue and best practices on proper prescription guidelines patient monitoring, and alternative pain management. Attendance is free and CME is provided. The dates are October 17 & 18th, 5:00 to 9:00 PM at the Marriott at University of Dayton on Patterson Blvd; dinner is included. Call 937-225-5700 for more information.

GI Illness Associated with Clostridium perfringens

At least 647 people that fell ill after eating at a Chipotle in Central Ohio in July. Their illnesses were caused by a foodborne disease resulting from food being stored at unsafe temperatures. After local lab tests on food and stool samples came back negative for any potential pathogens, the Delaware County Health District sent more samples to the CDC to be tested. While the food samples tested negative for Clostridium perfringens bacteria, the stool samples revealed the toxin that C. perfringens forms in the gastrointestinal tract. C. perfringens occurs when foods aren't kept at the correct temperatures. In a health inspection, the Chipotle restaurant was found to have one critical and one non-critical violation related to pinto beans and

lettuce not being kept at correct temperatures. The restaurant threw all its food away before reopening, according to the Delaware County Health District.

EMERGING INFECTIONS NETWORK

Query: Osteomyelitis Associated with Stage IV Pressure Ulcers

There were 558 respondents (42% of EIN members with an adult ID practice). A small majority (52%) reported seeing >10 patients per year with stage IV pressure ulcers, on average. Physical exam and/or laboratory/imaging results were judged to be sufficient to confidently rule in or rule out osteomyelitis for 60% of respondents. The findings most indicative of osteomyelitis were palpable or visible bone at the ulcer base (75-79% rated "strongly"); fever was rated "minimally" predictive by 68%. In patients with uncertain diagnosis, the favored evaluations were bone biopsy and MRI. Preferred treatment for Staphylococcus arues (MRSA or MSSA) was evenly split between entirely IV vs combination of IV/oral. Initial treatment with IV followed by oral (or entirely oral) treatment was preferred for all other pathogens. In patients with no (or partial) surgical debridement, preferred length of treatment varied from < 2 weeks (11.7%), > 2weeks to 6 weeks (25.6%), >6 weeks to 12 weeks (34.4%), > 12 weeks (2.9%) or "it depends" (25.4%).

NATIONAL NEWS

New HIV Treatments

Janssen announced that it has received FDA approval for Symtuza, a once-daily, single-tablet, darunavir-based HIV-1 regimen for treatment-naive and certain virologically suppressed adults. It contains 800 mg of darunavir, 150 mg of cobicistat, 200 mg of emtricitabine and 10 mg of tenofovir alafenamide (D/C/F/TAF). The FDA approval is based on data from two 48-week, noninferiority, pivotal phase 3 studies comparing the safety and efficacy of D/C/F/TAF with a control regimen. The AMBER trial evaluated the regimen in adults with no prior antiretroviral therapy history, and the EMERALD trial included virologically suppressed adults. D/C/F/TAF was found to be effective and well-tolerated in both studies and up to 95% of trial participants achieved or maintained virologic suppression (HIV-1 RNA <50 c/mL).

Merck & Co Inc reported the FDA approved two HIV oral drugs. The drugs have been approved to treat adults with HIV-1, and no prior antiretroviral treatment. Delstrigo, a once-a-day combination tablet of doravirine/lamivudine/tenofovir disproxil fumarate, was approved with a boxed warning regarding possible worsening hepatitis B infection. Pifeltro (doravirine), is approved to be administered in combination with other antiretrovirals. In DRIVE-AHEAD, 728 participants with no antiretroviral treatment history were randomized and received at least one dose of either Delstrigo or efavirenz/emtricitabine/tenofovir disoproxil fumarate once daily. Delstrigo demonstrated sustained viral suppression through 48 weeks, meeting its primary endpoint of non-inferior efficacy compared to EFV/FTC/TDF (84% in the Delstrigo group achieved viral suppression of HIV-1 RNA <50 copies/mL vs. 81% in the EFV/FTC/TDF group). At Week 48, Delstrigo -treated participants showed statistically significant superior lipid profiles as measured by changes from baseline in LDL-cholesterol (LDL-C: -2.1 mg/dL in the Delstrigo group vs. 8.3 mg/dL in the EFV/FTC/TDF group). The rate of discontinuation of treatment due to adverse events was lower in the Delstrigo treatment group than in the EFV/FTC/TDF treatment group (3% and 6%, respectively). Clinical adverse reactions of all grades occurring in ≥5 percent of participants in the Delstrigo treatment group included dizziness (7%), nausea (5%) and abnormal dreams (5%).

New Treatment Approved for Complicated Intra-Abdominal Infections

Tetraphase Pharmaceuticals announced that the FDA has approved eravacycline (Xerava) for the treatment of complicated intra-abdominal infections (cIAIs). Eravacycline was found to be well-tolerated with high

clinical cure rates during clinical trials in patients with complicated intra-abdominal infections. Eravacycline is indicated for treating cIAIs in patients aged 18 years and older. The FDA approval was based on two phase 3 clinical trials_that found that eravacycline, a fully synthetic fluorocycline, demonstrated statistical noninferiority to ertapenem and meropenem. The commercial launch of eravacycline is expected in the fourth quarter of 2018.

INTERNATIONAL NEWS

Study reveals early impact of 3-strain oral polio vaccine withdrawal

A new analysis of global polio surveillance data covering the first 2 years after withdrawal of oral polio vaccine serotype 2 (OPV2) was withdrawn in 2016 found that Sabin 2 poliovirus (one of the three vaccine strains) in stool and sewage samples declined at 2 months after withdrawal.
After a year, however, virus detections continued because of monovalent OPV2 use to stem vaccine-derived poliovirus serotype 2 (VDPV2) outbreaks. A research team from Imperial College London, the World Health Organization (WHO), and the Bill and Melinda Gates Foundation published its findings today in the *New England Journal of Medicine*. The study included stool samples from 495,035 children with acute flaccid paralysis from 118 countries and 8,528 sewage samples from four countries at high risk for transmission (Afghanistan, Pakistan, Nigeria, and Kenya) that were collected from Jan 1, 2012, to Jul 11, 2018. In stool samples, prevalence of Sabin 2 poliovirus declined from 3.9% at the time of OPV2 withdrawal to 0.2% at 2 months after withdrawal. The detection rate in sewage samples dropped from 71% to 13% over the same period. The researchers note that nine outbreaks were reported after OPV2 withdrawal and were linked to low routine immunization coverage and low levels of population immunity. They concluded that high population immunity has helped the decline of Sabin 2 poliovirus after the OPV2 was withdrawn and has kept VDPV2 circulation to areas known for high transmission risk.

CASE CONFERENCE

Contributed by Najmus Sahar

A previous healthy 61-year-old Caucasian male was brought to the emergency department in April with a 4-day history of strange behavior. Five days prior to presentation he flew to Washington D.C. to pick up a medallion gifted to the state department and flew back in the evening when his family noticed unusual altered behavior and mentation for the first time. Patient was a Harvard graduate and an attorney by profession and a sharp person in general who now seemed a bit off and dazed to family without much improvement in the last couple of days. Patient had no other systemic complaints. No history of traveling abroad, outdoor activities, tick exposure, animal bites lately. His past medical history was significant for coronary artery disease status post angioplasty, coronary artery bypass surgery years prior, hypertension, and hyperlipidemia. His medications included aspirin, clopidogril, lisinopril, atorvastatin and carvedilol. The couple lived in Florida and was visiting family in Dayton Ohio. He smokes cigars and drinks about 6 ounces of alcohol per week. He denied any history of drug abuse including intravenous (IV) drugs.

On arrival he was hemodynamically stable and physical examination was significant only for delayed recall and poor concentration. Serum chemistry panel (BMP), Liver function panel (LFTs), complete blood count (CBC), serum ammonia level, thyroid function test and urinalysis (UA) were normal. Urine drug scree and serum toxicology screen were negative. A CT scan of the head without contrast showed no intracranial abnormalities. Lumbar puncture revealed clear CSF fluid with 25 leukocytes /uL (88% lymphocytes), 240 erythrocytes/uL, and the protein level was 94mg/dL (ref. range 15-45mg/dL). Gram stain of CSF revealed no organisms. The patient was empirically started on acyclovir for presumed encephalitis. Serum HIV and VDRL were negative. MRI scan showed edema in right fronto-temporal lobes and left frontal lobe. Electroencephalograms (EEG) showed focal slowing in the right frontal/parietal regions without any epileptic discharges. The result of CSF HSV-1 PCR was positive, which confirmed the diagnosis of HSV-1 encephalitis. He was treated with 21 days of IV acyclovir. Following therapy, he suffered from residual cognitive, behavioral, and personality changes with progressive decline. He was readmitted in June to psychiatry unit for worsening agitation, paranoia, and aggression managed with divalproex sodium and risperidone with some improvement in agitation. On neurological exam patient was oriented to self and place only. MOCA scored was 24/30 and MMSE 21/30 with both demonstrating difficulty with short term memory. Patient had impaired execution of three step commands and would make tangential connections. He was easily distracted by abstract thinking and difficult to direct back to task. Laboratory investigations including CBC, BMP, LFTs, and UA were negative. CT head without contrast showed persistent right fronto-temporal changes without any new findings. CSF analysis revealed lymphocytic pleocytosis with normal glucose and elevated protein levels. CSF BioFire FilmArray Multiplex PCR test was negative excluding HSV. MRI head revealed high single intensity changes in T1-weighted scans concerning for laminar necrosis in right fronto-temporal lobes and extensive signal intensity abnormalities in bilateral fronto-temporal lobes compatible with subacute encephalitis. EEG showed widespread slowing reaching 2-3 Hertz indicative of severe cerebral dysfunction without any seizure activity. CSF paraneoplastic antibody panel revealed positive anti-NMDAR antibodies with 1:64 titer. At that point his symptoms were attributed to HSV induced anti-NMDAR encephalitis and he started on plasmapheresis in August. He received 5 cycles with some improvement but still had significant deficits in the domains of visuospatial, executive, delayed recall, language, and orientation. Four months later in January, he was readmitted for further periodic decline of cognition and aggressive behavior suspicious for recurrence or progressive encephalitis. CSF analysis revealed normal cell count, a negative HSV PCR and positive CSF anti-NMDAR antibodies with 1:10 titer. The MRI of his brain demonstrated extensive frontal and temporal injury with ex vacuo enlargement of right temporal and frontal horns consistent with ongoing parenchymal damage. Following seven cycles of plasmapheresis with limited improvement, and progressive decline he was started on monthly IV rituximab 1000mg infusions. He received 2 doses of rituximab but was ultimately incarcerated due to violent behavior.

Discussion

HSVE induced anti-NMDAR encephalitis is more commonly seen in the pediatric population making the treatment and identification of this disorder in older patients challenging. The California Encephalitis Project performed in 2007 demonstrated that it was four times more common than viral etiologies of encephalitis in a cohort of patients under the age of 30, 65% of which were below the age of 18[3]. Relapses of HSV are seen in a minority of patients making up between 7.1%-12.5% in adults and 14.3%-26.7% in children[4]. Distinguishing anti-NMDAR encephalitis from recurrence of HSVE is important due to differences in treatment and prognosis. HSVE and non-viral encephalitis can be differentiated based on time, symptoms, PCR, MRI, and response to anti-viral treatment. Time is variable in HSVE but tends to take 4-6 weeks when autoimmune. No new MRI lesions will manifest with autoimmune disease in contrast to HSVE. Symptomology differs with HSVE characterized by focal neurological signs and abnormalities in behavior and movements. Autoimmune disease will primarily manifest with abnormal behavior in adults[5]. Our patient had persistent behavioral issues post HSVE and ultimately diagnosed with anti-NMDAR encephalitis two months after.

One prospective cohort study of 51 patients with HSVE went on to develop autoimmune encephalitis. Not all of which demonstrated antibodies to NMDA receptors and other unknown antibodies were found. Additionally, some patients (11) were positive for antibodies but did not develop a clinical disease. A significant finding showed that the development of antibodies within three weeks of HSVE was a risk factor for the autoimmune disease[6]. Symptomology is different between pediatric and adult cases with a higher prevalence of psychiatric symptoms in adults and neurologic in pediatric cases[7]. Neurologic symptoms include seizure, dyskinesias (orofacial, choreoathetoid, an abnormal posturing), autonomic instability, and central hypoventilation[8]. Psychiatric symptoms include alterations in mental status, personality, and psychosis sometimes to the point of catatonia[7].

A literature review described nine adult cases with all patients over the age of 18. These cases clearly demonstrate the prominence of psychiatric symptoms and absence of movement disorders. Only one case reported the presence of dyskinesia[9]. Common psychiatric symptoms included confusion, irritability, and several having suicidal ideation. The response to therapy and outcome was variable. Cases with better outcomes had only minimal residual changes in personality, outbursts, aphasia, and memory. Different treatment options were utilized. One patient had almost complete resolution of symptoms with no treatment[10]. IV methylprednisolone was utilized in six of the ten patients and used alone in four patients. First line therapy involves steroids, IVIG, and plasmapheresis alone or in combination. Second line involves rituximab and cyclophosphamide. One study of 501 patients with anti-NMDAR encephalitis secondary to all etiologies (including teratoma) demonstrated a 53% improvement with first line therapy, 81 % of which had a favorable outcome at 24 months. Of the 47% that did not improve, 57% of this group was given the second line therapy of which 78% having a favorable outcome[7]. The study demonstrates that this disease process can be treated, however, the age, gender, and etiology of the encephalopathy in our case makes this treatment algorithm perhaps not as applicable. However, a similar case report was presented in which the an elderly woman responded positively to IVIG, rituximab, and lastly a 3 month regiment of cyclophosphamide with only mild personality changes continuing post treatment[9]. Extended long term patient outcome following treatment is not available.

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Bug of the Quarter

By: W. Grant Starrett, M.D.

For this edition of "Bug of the Quarter" we will be testing your knowledge of those organisms reviewed in the last two years. A few organisms from more remote newsletters are included. Please match the description with the correct organism, and resist googling unless you are desperate! Answers may be found at the end of the newsletter. See previous editions of the newsletter for a brief explanation.

Matching

I.	*Exophiala*	A. most commonly isolated anaerobic GPC in specimens
II.	*Weeksella virosa*	B. cutaneous facultative anaerobe resembling *staphylococcus*
III.	*Agrobacterium*	C. ubiquitous algae
IV.	*Myroides odoratus*	D. bacteremia and proctocolitis in male HIV patients
V.	*Bifidobacterium*	E. GNB found in soil/water, resistant to all *B*-lactams
VI.	*Finegoldia magna*	F. tinea nigra
VII.	*Rothia*	G. gram-negative rod, genitourinary commensal of women
VIII.	*Rhodotorula rubra*	H. rare cause of CAPD peritonitis, also causes plant tumors
IX.	*Priopionibacterium acnes*	I. false positive Aspergillus antigen test
X.	*Helcococcus*	J. anaerobic gram-positive rod, dental caries, probiotic
XI.	*Prototheca wickerhamii*	K. aerobic but occasionally misidentified as *Actinomyces*
XII.	*Helicobacter fennelliae*	L. anaerobe, under-recognized cause of device infections

Infections Within Prisons

Emma Carin Statt, UD Pre-medical Student

Infectious diseases are disproportionately affecting individuals in the prison population. The underfunding and overcrowding of prisons make prisoners much more susceptible to infection, which is continually perpetuated by laws and policies regarding healthcare of incarcerated populations. The lack of adequate infection control and treatment in prisons are serious issues due to the amount of people working and interacting with individuals in prison as well as the eventual release of most prisoners back into the community, along with the ailments they may have acquired while incarcerated. Because of this, infections prevalent in the incarcerated population can easily be spread beyond the walls of prison.

According to the Bureau of Justice Statistics, approximately 1 in 38 adults in the US were under some form of correctional supervision at the end of 2016 (Kaeble & Cowhig, 2018). The correctional population is made up of persons in prison, in jail, on probation, or on parole. While the total population under correctional supervision has decreased in the past decade, the US still comprises roughly 25% of the world's incarcerated population despite only making up 5% of the world's total population (Beyrer et al, 2016). According to an article published in "Clinical Infectious Diseases", "While incarcerated, inmates interact with hundreds of thousands of correctional employees and millions of annual visitors" (Bick, 2007). With the number of individuals either involved with or a part of the correctional population, infection within those facilities can quickly spread to a large amount of people in non-incarcerated communities.

As compared to the non-incarcerated population, "newly incarcerated inmates have an increased prevalence of HIV, Hepatitis B, Hepatitis C, syphilis, gonorrhea, chlamydia, and *Mycobacterium tuberculosis"* (Bick, 2007). From the same article, it states that while in prison, inmates have an increased risk of contracting blood-borne pathogens, STDs, MRSA, and airborne pathogens. The frequently unsanitary and overcrowded conditions highly contribute to the likelihood of contracting and spreading infectious diseases. Beyond those factors, injection drug equipment sharing, tattoo needle sharing, lack of HIV education, and lack of condoms available facilitate the spread of blood-borne pathogens and sexually transmitted diseases.

In studies done by the Canadian Medical Association, it was found that within the inmate population in Ontario between 2003 and 2004, the prevalence of HIV was 11 times higher and the prevalence of HCV was 22 times higher than the surrounding non-incarcerated population. During the same time in Quebec, it was found that the inmate population had prevalence of HIV and HCV at 19 times and 23 times, respectively, as the surrounding non-incarcerated population (Elliot, 2007). One of those studies sought to connect the prevalence of HIV and HCV within the prisoners to certain risk factors. The biggest risk factor was injection drug use. It found that, "the prevalence of HIV infection was 7.2% among the male injection drug users and 0.5% among the male non-users. Among the women, the rate was 20.6% among the injection drug users, whereas none of the non-users were HIV positive. The prevalence of HCV infection was 53.3% among the male injection drug users and 2.6% among the male non-users; the corresponding values among the women were 63.6% and 3.5%" (Poulin et al, 2007) Another substantial risk factor was unsafe tattooing practices; it was found that 37.9% of male inmates and 4.8% of female inmates had received a tattoo while in prison, with a large portion reporting the use of non-sterile equipment (Elliot, 2007).

In the same article by the Canadian Medical Association, it states that, "after an exhaustive review, the Public Health Agency of Canada [found] evidence from numerous jurisdictions that prison needle-exchange programs decreased needle-sharing practices among prisoners, did not undermine safety and security, and did not lead to increased drug use among prisoners" (Elliot, 2007). A World Health Organization review of 55 European needle exchange programs found that there was no reported increase in drug use or unintended consequences, such as using needles as a weapon (Glauser, 2013). By offering needle-exchange programs,

prisons can reduce the spread of blood-borne pathogens without compromising the health and safety of staff and other prisoners.

Racial disparities in HIV treatment and prevention combined with discriminatory policing and justice system practices are large contributing factors in why African American male prisoners are 5 times more likely to have HIV than their white counterparts (Rubenstein et al, 2016). In US women, both in and outside prison, the rate of new HIV infections in 2014 were 34.8/100,000 for African American women, and only 1.8/100,000 in white women (Beyrer et al, 2016). African Americans are incarcerated six times more, and Hispanics three times more, frequently than non-Hispanic white Americans (Beyrer et al, 2016). The health disparities seen within the general population are disproportionately affecting the incarcerated due to the enlarged proportions of ethnic and racial minorities living in prisons.

The over-crowding of jails and prisons is often discriminatory as well. As stated in the article by Rubenstein et al, "Once arrested, racial and ethnic minorities, key populations, and socially marginalized groups…often lack legal counsel, are not considered for pretrial release or alternatives to detention, or are denied release on inappropriate grounds, and do not receive a speedy trial". The article goes on to state, "Long pretrial incarceration, lengthy sentences, lack of or ineffective parole and probation procedures, and failure to provide for compassionate release keep many people incarcerated for excessively long periods of time, increase risk of HIV infection and pose barriers to accessing treatment" (Rubenstein et al, 2016).

Infections in jail and prison populations are important to consider in the grand scheme of both public health and infectious diseases. The incarcerated community is still part of the community, and many will return to the surrounding communities with the illnesses they were exposed to in prison. Additionally, the amount of prison visitors and employees exposed to those same illnesses is cause for concern, as they are the immediate connection from the incarcerated population to the surrounding communities. Working to reduce the overcrowding of jails and the discrimination seen in justice systems will help reduce the health disparities seen in prisoners. Implementing infection control and preventative measures, such as needle exchange programs and education on communicable diseases, will elevate the health of the incarcerated population and in turn will protect and improve the health of the surrounding communities as a whole.

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Bug of the Quarter: Answers

Organism	Answer	Newsletter Ed.
Exophiala	tinea nigra	8/17
Weeksella virosa	gram-negative rod, genitourinary commensal of women	2/18
Agrobacterium	rare cause of CAPD peritonitis, also causes plant tumors	11/16
Myroides odoratus	GNB found in soil/water, resistant to all *B*-lactams	2/12
Bifidobacterium	anaerobic gram-positive rod, dental caries, probiotic	2/17
Finegoldia magna	most commonly isolated anaerobic GPC in specimens	5/15
Rothia	aerobic but occasionally misidentified as *Actinomyces*	5/17
Rhodotorula rubra	false positive Aspergillus antigen test	2/11
Propionibacterium acnes	anaerobe, under-recognized cause of device infections	2/16
Helcococcus	cutaneous facultative anaerobe resembling *staphylococcus*	11/17
Prototheca wickerhamii	ubiquitous algae	2/13
Helicobacter fennelliae	bacteremia and proctocolitis in male HIV patients	5/18