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The Florida Lab Link

Hepatitis A in Florida, 2018-2019

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Hepatitis A is a contagious infection of the liver caused by the hepatitis A virus (HAV). The virus is transmitted via the fecal-oral route and can be spread directly from person-to-person through sexual contact, sharing of drugs, close physical contact or by contaminated food or water.[1] In Florida, HAV occurs most commonly in people who use injection or non-injection drugs, people experiencing homelessness and men who have sex with men.

The incubation period for hepatitis A is 15-50 days (average- 28 days). Symptoms of hepatitis A include abdominal pain, fever, nausea, vomiting, diarrhea, jaundice, dark urine and clay-colored stool. In children younger than 6 years old, about 70% will be asymptomatic while most older children and adults will have symptoms. Symptoms can last as long as 2 months but 10-15% of persons may have prolonged symptoms for up to 6 months. The infection does not become chronic, but can relapse in 10% of infected individuals.[2]

Acute hepatitis A infection is diagnosed by serologic testing to detect IgM anti-HAV. IgM is present 5-10 days before the onset of symptoms and can persist for as long as 6 months. IgG anti-HAV indicates either a history of illness or vaccination, is present for life, and provides

(Continued on page 2)

Inside this issue:

(Continued from page 1)

immunity against the disease. Hepatitis A total antibody testing indicates that the person is positive for either IgM anti-HAV or IgG anti-HAV but does not distinguish between the two. IgG anti-HAV and hepatitis A total antibody testing are not useful diagnostic tests to identify a recent infection. Hepatitis A antibody testing is widely available at commercial laboratories.[3]

The best way to prevent hepatitis A is through vaccination. The vaccine is recommended for everyone at 1 year of age, people at increased risk of infection or severe disease or anyone who wants to obtain immunity. People with underlying liver disease and people older than 60 years of age with underlying health issues should also be vaccinated. The two-dose series is highly effective, and nearly 100% of adults are immune after receiving both doses. Because the virus is transmitted through the fecal-oral route, handwashing after using the bathroom, changing diapers, and before preparing or eating food is also important in preventing infection.[4] HAV is not killed by alcohol-based hand sanitizers.

After the introduction of the hepatitis A vaccine in 1995, rates of hepatitis A infection declined more than 95% in the United States, however, since 2017, the Centers for Disease Control and Prevention (CDC) has been tracking outbreaks of hepatitis A spread through person-to-person contact. As of August 30, 2019, 30 states have reported outbreaks with 24,952 cases and 244 deaths, primarily among persons who use drugs, persons who are experiencing homelessness and their close contacts.[5]

Florida began to see an increase in hepatitis A cases in 2018 that has continued into 2019. As of August 31, 2019, a total of 2903 outbreak cases have been reported. Seventy-eight percent of cases have been hospitalized and there have been 39 hepatitis-A associated deaths reported. The median age of a case is 39 years old (range 1-89 years). Most of the cases are male (65%) and identify as white and non -Hispanic (83%). The most common risk factor reported is drug use among 57% of cases. Recent homelessness was reported among 21% of cases. Twenty two percent of cases are known close contacts to other cases. Thirty-eight percent of cases do not have an identified risk factor.[6]

In response to the 2018 hepatitis A outbreak, the Bureau of Public Health Laboratories in Tampa (BPHL-Tampa) began to perform sequencing of hepatitis A specimens from HAV IGM-positive samples submitted to better understand the strains circulating in the state. The hepatitis A virus is part of the picornaviridae

(Continued on page 3)

(Continued from page 2)

family, which encompasses several genera of viruses including the enteroviruses genus. This means that the hepatitis A virus is more closely related to polioviruses, enteroviruses, and rhinoviruses than it is to hepatitis B, which is a hepadnavirus, or hepatitis C, which is a flavivirus. There are six HAV genotypes, and types I, II and III cause illness in humans. Types I, II and III are further classified into subtypes A and B.[7]

Like other picornaviruses, hepatitis A is a positive sense single strand RNA virus, with a 7.5kb genome. Hepatitis A virus shows a remarkable degree of antigenic conservation, to the point that only one serotype exists. This means that it is impossible to use serological methods, such as EIA or plaque assays, to differentiate between HAV isolates, however, HAV does display enough genetic variability, that molecular characterization is possible. Laboratories can use reverse transcription polymerase chain reaction (RT-PCR) to differentiate between genotypes, and they can utilize nucleic acid sequencing techniques to further characterize isolates at the strain level. This testing can be particularly useful in outbreak settings. While sequencing variable regions of the HAV genome cannot be used to track viral transmission from patient to patient, it can be used to differentiate isolates within and between larger communities.[8]

Currently, BPHL-Tampa is using Illumina reversible chain termination sequencing to help put individual specimens into the context of the statewide outbreak. The VP1/P2B region, which is the most variable region of the HAV genome, is first amplified using traditional RT-PCR. Due to the multiplexed nature of Illumina Sequencing, amplicons from each individual patient sample must then be labeled with one or more unique oligonucleotide 'barcodes' referred to as an index. This index will allow the automated sequencing platform to de-multiplex the sequencing reads and assign each read to the correct patient identifier. To improve the specificity of the de-multiplexing process, three unique indices are added to the target sequence: one on the 5' end and two sequentially on the 3' end. Once indexed, samples are sequenced using 2 x 250bp pairwise reads on the Illumina MiSeq. Raw sequencing data are converted to FASTQ format to be used in downstream analysis.[8]

For the purposes of outbreak response, BPHL-Tampa is currently utilizing the CDC Global Hepatitis Outbreak Surveillance Technology (GHOST) bioinformatics pipeline to analyze all hepatitis A isolates. Sequence data, in the form of FASTQ files, are uploaded to the GHOST server, screened by quality control algorithms and aligned to curated reference sequences. This analysis will return genotype, as well as an

(Continued on page 4)

(Continued from page 3)

outbreak strain type, for each sample. Because the hepatitis A genome is highly conserved, the minimal distance for stain types is 0. This means that a single base change in the VP1/P2B region will confer a unique strain type.[9]

BPHL-Tampa has currently sequenced 171 samples associated with the current outbreak across Florida. While this only represents a fraction of the total outbreak associated cases, some patterns are beginning to emerge. One hundred thirty-eight (80.7%) samples align to strains known to have been, or are currently, associated with outbreaks elsewhere in the United States. One hundred thirteen (66%) samples belong to genotype 1b, 56 (33%) belong to genotype 1a, and 2 (1%) belong to genotype 3a.

As of January, 2020, the outbreak of hepatitis A in Florida remains ongoing. County health departments continue to investigate cases and provide vaccinations to at risk persons and BPHL-Tampa continues to increase sequencing capacity. As additional samples are sequenced and additional data collected, strain types provided by GHOST paired with epidemiological data will help to further characterize our hepatitis A cases into distinct outbreak clusters.

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Chemical Threat (CT) Preparedness Training Update

The Chemical Threat (CT) laboratory coordinators continue to reach out to the health and medical community by offering training for CT preparedness at hospitals and county health departments (CHDs). This training covers chemical threat awareness and the collection of clinical specimens after a chemical exposure event. Hospital and CHD staff play an important role in the response to a chemical exposure event when clinical specimens are collected for analysis. **NEW**: We now offer a **one-hour** course that covers both chemical agent awareness and post-exposure clinical specimen collection and shipping. This training is provided at no cost and can be presented at your facility for your convenience. Training manuals and "hands-on" exercise materials will be provided. This training is recommended for physicians, nurses, epidemiologists, emergency department personnel, phlebotomists, hospital and health department laboratory personnel and others who may collect clinical specimens. Contact Angela Ren at (813) 223-2293 (Angela.Ren@FLHealth.gov) or Michelle Latona at (904) 791-1525 (Michelle.Latona@FLHealth.gov) for more information.

Laboratory Response Network (LRN) Training—Biological Defense

The Bureau of Public Health Laboratories is currently offering an LRN sentinel laboratory training course at your facility. This training follows the American Society for Microbiology (ASM) Sentinel Level Clinical Laboratory Protocols for Suspected Biological Threat Agents and Emerging Infectious Diseases. Scheduling the training at your facility is a relatively easy process. Determine when you would like to have the training and how many people will be attending. A time will be set up that is convenient for all. The training materials are provided as well as the biodefense reference manuals for your laboratory.

The training syllabus includes: an overview of the LRN; biosafety risk assessment and biosafety for the clinical laboratory; the ASM protocols for ruling out potential bioterrorism agents and how to refer a sample to the state LRN Public Health Reference Laboratory when a bioterrorism agent cannot be ruled out; and an introduction to the CDC Select Agent Program.

Please contact Leah Kloss at (813) 233-2278 (Leah.Kloss@FLHealth.gov) to schedule a class for your facility.

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