SAN DIEGO COUNTY’S RESPONSE TO HEPATITIS OUTBREAK

APHL Annual Meeting
Syreeta Steele, PhD and Tracy Basler
June 4, 2018
OUTLINE

- Hepatitis A Overview
- Hepatitis A in San Diego, CA
- Laboratory Response
- Laboratory Challenges
- Laboratory Successes
HEPATITIS A OVERVIEW

- Hepatitis A can be easily spread from person to person
- Can cause liver disease lasting a few weeks to a serious illness lasting several months
- Can cause death in some cases
- Average incubation period for the Hepatitis A virus is 28 days (range: 15-50 days)
- Hepatitis A virus can live outside the body for months, depending on the environmental conditions
WHAT ARE THE SYMPTOMS?

- Fever
- Fatigue
- Nausea
- Loss of Appetite
- Jaundice
- Stomach Pain
- Vomiting
- Dark Urine, Pale Stools, and Diarrhea
WHO IS AT RISK?

- Travelers to certain countries
- Men who have sex with men
- Injection and non-injection drug users
- Persons with clotting factor disorders
- Persons with chronic liver disease
- Homeless persons &/or those with unstable living conditions
- Household members, and other close personal contacts with high or intermediate Hepatitis A occurrences
- Persons with close ongoing contact with homeless persons and/or illicit drug users or their environment via employment or volunteer activities (during this outbreak)
Hepatitis A Cases, San Diego County
1994 - 2016

Vaccine introduced
Routine vaccination for children in high-incidence states (including California)
Routine vaccination for all U.S. children

Prepared by County of San Diego, Health & Human Services Agency, Public Health Services, Epidemiology & Immunization Services, 12/6/17
BACKGROUND IN SAN DIEGO

- Reportable in California within one working day of identification by laboratory & provider (CCR Title 17 Sections 2500, 2505)

- Surveillance noted increase in cases above baseline in early March 2017

- 11/16 to 2/17: 7-9 cases expected, 19 cases reported

- Health alert on outbreak on March 10, 2017
- 588 confirmed outbreak cases from 11/22/16 thru 5/11/18
  - 403 (68.5%) hospitalizations, 20 (3.4%) deaths
  - 402 (68.3%) male (14 MSM), 186 (31.7%) female
  - Age range 5-87 (median 43.0)

- Suspected Exposure Type
  - 198 (33.6%) homeless and illicit drug use
  - 90 (15.3%) homeless only
  - 76 (12.9%) illicit drug use only
  - 167 (28.4%) neither
  - 57 (9.7%) unknown
OTHER CASE LINKS

- Co-infections
  - 81/474 (17.1%) with hepatitis C
  - 25/474 (5.1%) with hepatitis B
- 52 non-outbreak (travel, etc) cases not included in outbreak count
- Linked cases in other CA counties, AZ, CO, KY, OH, RI, UT, WV
PUBLIC HEALTH STRATEGY

- Vaccinate
- Sanitize/hygiene
- Educate
Outbreak-associated Hepatitis A Cases by Onset Week

11/1/2016 – 5/11/2018, N = 588*

Cases by Year
2016 – 6
2017 – 570
2018 – 12

*Date of specimen collection or report used if onset date unknown; dates may change as information becomes available

Prepared by County of San Diego, Health & Human Services Agency, Public Health Services, Epidemiology & Immunization Services, 05/11/18
March 2017
First specimen goes to CDC for genotyping by Sanger sequencing methods

August 2017
Order MiSeq instrument and research screening methods to perform testing in-house

October 2017
Begin testing specimens in-house by PCR screening method. Train on the use of MiSeq.

January 2018
Begin testing specimens in-house for genotyping by NGS method using GHOST

May 2017
Research sequencing methods to perform testing in-house

September 1, 2017
Emergency Outbreak declared by San Diego County Health Officer

November 2017
Molecular scientist hired

January 23, 2018
Emergency Outbreak ended
LABORATORY CHALLENGES AND OUTCOMES

- **Staffing**
  - Capacity strained due to high volume of Zika specimens
  - Shipping specimens to the CDC and VRDL
  - Bringing on-line PCR screening assay
  - Bringing on-line NGS methods

- **Training**
  - PCR screening
  - Sequencing

- **Instrumentation**
  - Purchasing NGS equipment

- **IT and Bioinformatics**
  - Software and networking approvals through County IT
  - Novice experience in bioinformatics

- **Partnerships**
  - CDC
  - CDPH-VRDL
  - MDHHS
  - County of Alameda, CA
  - University of California San Diego
  - J. Craig Venter Institute
Determined a need to confirm by molecular methods in addition to serology methods with a short TAT

No commercial PCR assays available.

Attended AMD Day September 25-26, 2017


Performance characteristics: accuracy, sensitivity, and specificity of 96%, 98%, and 96%, respectively

Began reporting results October 30, 2017

- WGS assay produced non-uniform genome coverage, and low sensitivity prompting a move to targeted NGS approach

December 2017- Developed targeted NGS assay with help from CDPH Viral and Rickettsial Disease Laboratory and CDC

- Improved sensitivity and coverage in the region of interest
- Geneious software purchased to align reads and generate phylogenetic trees

January 2018- GHOST HAV protocol available for sequencing

- Processed 282 HAV specimen through the GHOST assay
- Analyzed using GHOST portal and Geneious Software
**GENEIOUS PHYLOGENETIC TREE**

**Hepatitis A Strain Diversity**

<table>
<thead>
<tr>
<th>Genotype IB</th>
<th>Genotype IA</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA Cluster A</td>
<td>CA Cluster A17CA300</td>
</tr>
<tr>
<td>CA Cluster B</td>
<td>CA Cluster A17CA232</td>
</tr>
<tr>
<td>CA Cluster D</td>
<td>CA Cluster A17CA79</td>
</tr>
<tr>
<td>208</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>23</td>
<td>2</td>
</tr>
<tr>
<td>A17CA300</td>
<td>Other Unique Clusters</td>
</tr>
<tr>
<td>A17CA232</td>
<td>5</td>
</tr>
<tr>
<td>A17CA79</td>
<td>10</td>
</tr>
</tbody>
</table>

**Total Specimen Tested: 282**

**Tree Legend**

- IB; CA Cluster A
- IB; CA Cluster A17CA79
- IB; CA Cluster A17CA232
- IB; CA Cluster B
- IB; CA Cluster D
- IB; CA Cluster A17CA300
- IA
- Reference Sequences
SUMMARY

- San Diego County Public Health Laboratory successfully built the capacity to respond to the local Hepatitis A outbreak and now has the ability to quickly respond to future outbreaks.
- A lot of work was completed with limited resources and a very short timeframe.
- Hepatitis A cases are back to normal levels.
- For more go to Poster 105 Titled: Next Generation Sequencing of the Hepatitis A Virus Outbreak in San Diego County