Michigan Department of Health & Human Services

Michigan Hepatitis A Outbreak Update for Clinicians

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For a Clinical Webinar Event
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Disclosures

Dr. Wells has no financial interest, or any conflicts of interest, regarding the material provided in her presentation today.

Slide Material has been Adapted from:

- *Epidemiology and Prevention of Vaccine-Preventable Diseases*, National Center for Immunization and Respiratory Diseases
- Michigan Department of Heath and Human Services Communicable Disease Division materials
Outline

• Review of Hepatitis A Virus
• Hepatitis A Diagnosis and Management
• Guidelines for Hepatitis A Prevention, General
• Michigan Outbreak 2016-Present
• Guidelines for Management of Hepatitis A, Michigan 2018
• Waning Hep A Immunity in HIV, Michigan 2018
Review of Hepatitis A Virus
Hepatitis A Virus

- Picornavirus (RNA)
- Humans are only natural host
- Stable at low pH
- Inactivated by temperature of 185°F or higher, formalin, chlorine
  - Disinfection: 1 and 2/3 cups bleach in 1 gallon water (5000 ppm).
  - Allow 1 minute of contact time and then rinse with water.


MDHHS Communicable Disease Division
Hepatitis A Pathogenesis

• Entry into mouth
• Viral replication in the liver
• Virus present in blood and feces 10-12 days after infection
• Virus excretion may continue for up to 3 weeks after onset of symptoms

Hepatitis A Disease

- Highly contagious, vaccine-preventable (acute) liver infection
- Incubation Period - illness can appear 15 to 50 days after exposure
  - Average 28 days
- Illness not specific for hepatitis A
- Likelihood of symptomatic illness directly related to age
- Children generally asymptomatic, adults symptomatic

Hepatitis A Epidemiology

• Reservoir
  – human
• Transmission
  – fecal-oral
• Temporal pattern
  – none
• Communicability
  – 2 weeks before illness to 1 week after onset of jaundice


* Rates per 100,000 population; † Annual Average Incidence; Source: MMWR Supplements; February 12, 2016 / 65(1);29–41
USA Incidence of acute hepatitis A—by age group: 1990 - 2006

Source: MMWR Surveillance Summaries; March 21, 2008 / Vol. 57 / No. SS-2
Transmission

Ingestion of fecal matter, *even in microscopic amounts*, from:

- Touching objects or eating food that someone with hepatitis A infection handled
- Close, person-to-person contact with a person who is infected
- Use of recreational drugs, whether injected or not
- Sexual contact with someone who has a hepatitis A infection

Adapted from MDHHS Communicable Disease Division slides

From MDHHS Communicable Disease Hep A Slide set
Reported Cases Associated with HAV Outbreaks – United States, 2007–2017


From MDHHS Communicable Disease Hep A Slide set
Hepatitis A Diagnosis and Management
Hepatitis A Symptoms

NON-SPECIFIC!!

Fever

Fatigue

Nausea

Loss of Appetite

Jaundice

Stomach Pain

Vomiting

Dark Urine, Pale Stools, or Diarrhea

Not all people infected with hepatitis A experience illness. Most hepatitis A infections in children younger than age 6 are not accompanied by symptoms. Older children and adults are at risk for severe hepatitis A disease.

Adapted from MDHHS Communicable Disease Division slides
Risk Factors for Hepatitis A (General)

• International travelers (particularly high-risk itineraries like travel to rural areas in high-risk countries)
• Contacts of recent international adoptees from HAV endemic countries
• Men who have sex with men
• Users of illegal drugs
• Michigan Outbreak 2016-present are different!!
Occupational Risks

• Outbreaks of hepatitis A have been reported among persons working with hepatitis A-infected primates
  – This is the only occupational group known to be at increased risk for hepatitis A

• Food workers are not at increased risk because of their occupation but may play a critical role in transmission

• US serologic studies have shown no or mildly increased risk of HAV infection in wastewater workers

Serologic Testing

• Serologic testing required to confirm the diagnosis.

• Virtually all patients with acute hepatitis A have detectable IgM anti-HAV.

• Acute HAV infection confirmed during acute or early convalescent phase of infection by presence of serum IgM anti-HAV
  – IgM detectable 5-10 days before the onset of symptoms and can persist for up to 6 months

• Polymerase chain reaction (PCR)-based assays can be used to amplify and sequence viral genomes
  – These assays are helpful to investigate common-source outbreaks of hepatitis A.

Hepatitis A virus is shredding, person is contagious (spreading infection). Person shows clinical illness (symptoms).

Timeline for hepatitis A manifestations.
Serologic Testing, cont

• IgG anti-HAV appears in the convalescent phase of infection
  – Remains present in serum for the lifetime of the person, and confers enduring protection against disease**
  – Total anti-HAV measures both IgG anti-HAV and IgM anti-HAV
  – Persons with total anti-HAV positive and IgM anti-HAV negative: indicates immunity consistent with either past infection or vaccination

** Exceptions noted- will be discussed in HIV later in presentation

Medical Management

• There is no specific treatment for hepatitis A virus infection
• Treatment and management of HAV infection are supportive

Guidelines for Hepatitis A Prevention - General
Primary Prevention- Immunization

• Inactivated whole-virus vaccines
• Pediatric and adult formulations
  – pediatric formulations approved for persons 12 months through 18 years
  – adult formulations approved for persons 19 years and older

Hepatitis A Vaccine Immunogenicity

• **Adults**
  – more than 95% seropositive after one dose
  – nearly 100% seropositive after two doses

• **Children and Adolescents**
  – more than 97% seropositive after one dose
  – 100% seropositive after 2 doses (in clinical trials)

• **Hepatitis A Vaccine Efficacy**
  – **HAVRIX**
    • 40,000 Thai children 1 to 16 years of age
    • vaccine efficacy 94%
  – **VAQTA**
    • 1,000 New York children 2 to 16 years of age
    • vaccine efficacy 100%

Childhood Hep A Vaccination

• All children should receive hepatitis A vaccine at 12 through 23 months of age
• Vaccination should be integrated into the routine childhood vaccination schedule
• Children who are not vaccinated by 2 years of age can be vaccinated at subsequent visits
• States, counties, and communities with existing hepatitis A vaccination programs for children 2 through 18 years of age should maintain these programs
• New efforts focused on routine vaccination of children 12 months of age should enhance, not replace ongoing vaccination programs for older children
• In areas with without an existing hepatitis A vaccination program catch-up vaccination of unvaccinated children 2 through 18 years of age can be considered

Adult Hep A Vaccination

• Adults 19 years of age and older receive the adult formulation of hepatitis A vaccine according to licensed schedules

• Persons at increased risk for HAV infection, or who are at increased risk for complications of HAV infection, should be routinely vaccinated
  – See “Risk Factors” Slide 16
Post Exposure Prophylaxis (PEP)

- PEP can protect susceptible (unvaccinated) persons who have recently been exposed to hepatitis A:
  - Remember, the incubation period of hepatitis A is approximately 28 days (range 15-50 days)

- PEP must be given within 2 weeks after exposure to prevent infection:
  - Hepatitis A Vaccine
  - Immune globulin (IG)
Michigan Outbreak 2016-Present
Hepatitis A Outbreak in Michigan: Statewide Update
May 4, 2018

Adapted from MDHHS Communicable Disease Division slides
Michigan Hep A Outbreak

CURREN MICHIGAN OUTBREAK

<table>
<thead>
<tr>
<th>Event</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>August 2016, nine cases of hepatitis A reported in SE Michigan counties.</td>
<td>Early investigation focused on ill food workers and food establishments</td>
</tr>
<tr>
<td>No common source of infected identified; multi-modal</td>
<td>Cases included persons with substance use disorder, homeless or transient living, recently incarcerated, food workers, and men who have sex with men (MSM)</td>
</tr>
<tr>
<td>Investigations continuing, vaccination efforts ongoing</td>
<td>Outreach and education to vulnerable populations</td>
</tr>
</tbody>
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Adapted from MDHHS Communicable Disease Division slides
Reported Number of HAV cases in Michigan 2008-2018

Adapted from MDHHS Communicable Disease Division slides
Hepatitis A MI Outbreak Testing

- CDC sequencing HAV positive serum samples from representative cases (high risk cases, but no travel-related cases)
  - Fall 2016, SEMI clinical labs asked to send all HAV positive serum samples to Bureau of Labs (BOL)
  - Samples forwarded to CDC lab for sequencing
  - CDC notified MDHHS in Aug 2016 that MI cases not related to previous hepatitis A outbreaks in Virginia or Hawaii, San Diego
  - Michigan strains are unique: 1B strain 1 and 2

Outbreak Case Classification:
- Cases were classified as outbreak cases if they had the Hepatitis A1B Outbreak Strain #1 or #2

BOL began conducting whole genome sequencing Dec 2017

Adapted from MDHHS Communicable Disease Division slides
WHOLE GENOME SEQUENCING DENDROGRAM

Adapted from MDHHS Communicable Disease Division slides
Epidemiologic Summary
Counts & Demographics

Epi Summary for Hepatitis A Cases in Michigan Reported Aug 1, 2016 – May 2, 2018

- 828 Total Cases
- 537 (64.8%) Male
- 665 (80.3%) Hospitalized
- Age range, <1–90 years
- Median age, 40 years
- 26 (3.1%) Deaths

Adapted from MDHHS Communicable Disease Division slides
Confirmed Hepatitis A Case Onset by Week for the Michigan Outbreak for cases referred Aug 1, 2016 to May 2, 2018

Cases likely to increase due to 15-50 day incubation period and reporting delays

*If illness onset was not identified first lab collection date was used in place

Adapted from MDHHS Communicable Disease Division slides
Confirmed Hepatitis A by Risk Factors Reported August 1, 2016 to May 2, 2018

- 50.2% Documented Substance Use Disorder (374)
  - 8% Injection
  - 20% Non-Injection (most report marijuana use)
  - 20% Both (Injection & non-injection)
- 26.4% Coinfection with Hepatitis C (197)
- 14.6% Men Who Have Sex with Men (73)
- 13.4% Homeless or Transient Living (100)
- 7.7% Recently Incarcerated (57)
- 4.7% Food Worker (35)
- 3.0% Healthcare Worker (22)
- 2.7% Coinfection with Hepatitis B (20)

Adapted from MDHHS Communicable Disease Division slides
Relative Case Distribution by Risk Factor Status
Aug. 2016 – Feb. 2018

Adapted from MDHHS Communicable Disease Division slides
Temporal and Geographic Distribution of Outbreak Cases Patients with High Risk Characteristics

Data source: Michigan Disease Surveillance System, MDHHS.

Adapted from MDHHS Communicable Disease Division slides
TRENDS IN THE NUMBER OF CASES

828 Cases
665 Hospitalized
26 Deaths

Risk Factors

<table>
<thead>
<tr>
<th>Substance Use</th>
<th>Homeless</th>
<th>Hepatitis B</th>
<th>Hepatitis C</th>
<th>MSM</th>
<th>Correctional</th>
<th>Healthcare</th>
<th>Good Worker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feb 2011-16</td>
<td>2</td>
<td>100</td>
<td>20</td>
<td>73</td>
<td>57</td>
<td>22</td>
<td>35</td>
</tr>
<tr>
<td>Feb 2018</td>
<td>3</td>
<td>34</td>
<td>9</td>
<td>25</td>
<td>11</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Average Cases</td>
<td>7</td>
<td>6</td>
<td>6</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Source: MDSS

Adapted from MDHHS Communicable Disease Division slides
Guidelines for Management of Hepatitis A, Michigan Outbreak, 2018
MDHHS and local public health officials are working to:

• Begin case investigation within 12 h after reported to public health
• Provide guidance and data to healthcare community
• Educate the public about hepatitis A and prevention
• Encourage community agencies and healthcare providers to immunize clients with risk factors for hepatitis A
• Increase availability of vaccine and conduct vaccination clinics
• Increase vaccinations!
Hepatitis A Vaccination for Outbreak Control, MI Outbreak

- Vaccination is the cornerstone of control of community outbreaks

- Post-exposure prophylaxis alone may not effectively control outbreaks

- Targeted vaccination to the groups at highest risk are the best way to control disease spread

- Primary prevention with adequate vaccination of at-risk groups is preferable

Hepatitis A Vaccination for Outbreak Control, MI Outbreak

- Vaccination in EDs was a major success in San Diego
- Screening tools are available on our website and from your peers
- Screen for insurance status and risk group
  - Public vaccine available for Medicare, Medicaid, and uninsured
  - Risk groups: sub, homeless, liver disease, MSM, recent incarceration
- Public doses must be registered in MCIR (MAVP)
- Not required to look up the individual in MCIR before vaccinating

Vaccination and PEP, MI Outbreak

### Box A: Identifying PEP for patient based on age (years) and health status

<table>
<thead>
<tr>
<th>Age</th>
<th>&lt;1</th>
<th>1-40</th>
<th>41-59*</th>
<th>60-74*</th>
<th>75+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>IG</td>
<td>Vaccine Preferred</td>
<td>IG; vaccine if IG is in short supply</td>
<td>IG; vaccine if IG is in short supply</td>
<td>IG</td>
</tr>
<tr>
<td>Other (Box B)</td>
<td>IG</td>
<td>IG</td>
<td>IG</td>
<td>IG</td>
<td>IG</td>
</tr>
<tr>
<td>Highest Risk (Box C)</td>
<td>Consider vaccine and IG for possible longer-term protection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*When IG is unavailable or in short supply, single-antigen HAV vaccine may be used for PEP in healthy people 41-74 years of age. To read more about hepatitis A vaccine for PEP in this age group, please see: [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4643264/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4643264/).

### Box B: People who are preferred to receive IG for PEP

- Those less than 12 months of age
- Those aged 41 through 74 years (*Vaccine can be used if IG is not available)
- Those who are immunocompromised, including persons:
  - With HIV/AIDS
  - Undergoing hemodialysis
  - Who have received solid organ, bone marrow or stem cell transplants
  - Receiving high dose steroids (>2mg/kg/day)
  - Receiving chemotherapy, immunomodulators and/or biologic medications, (mercaptopurine, methotrexate, infliximab, adalimumab, etanercept, tacrolimus, mycophenolate, etc.)
  - Persons who are otherwise less capable of developing a normal response to immunization
- Those who have chronic liver disease or other chronic medical conditions
- Those whom vaccine is contraindicated
Box C: People with High Risk Indications who should be considered for receiving IG AND hepatitis A vaccine for PEP²³

- Pregnant women
- Persons with chronic liver disease
- Persons who are immunocompromised, including persons:
  - With HIV/AIDS
  - Undergoing hemodialysis
  - Who have received solid organ, bone marrow or stem cell transplants
  - Receiving high dose steroids (>2mg/kg/day)
  - Receiving chemotherapy, immunomodulators and/or biologic medications, (mercaptopurine, methotrexate, infliximab, adalimumab, etanercept, tacrolimus, mycophenolate, etc.)
  - Persons who are otherwise less capable of developing a normal response to immunization

NOTES:

²The efficacy of combined HAV/HBV (Twinrix®) vaccine for post-exposure prophylaxis (PEP) has not been evaluated so it is not recommended for PEP.

²Guidance was provided by a CDC subject matter expert with the Division of Viral Hepatitis on situations when IG and hepatitis A vaccine should be administered at the same time.

³If hepatitis A vaccine and IG are both considered then they may be administered simultaneously but at separate anatomic injection site.
MI OUTBREAK RISK FACTORS

Are you at risk for Hepatitis A?

People who are at high risk include:

- Men who have sex with men (MSM)
- People who use illegal drugs
- People currently homeless or in transient living
- People recently in jail or prison
- People with underlying liver disease*

*Note: people with underlying liver disease (e.g., cirrhosis, hepatitis B, or hepatitis C) are at increased risk of having poor outcomes if they are infected with hepatitis A.

Ask your doctor about vaccination if you are at high risk.

The best way to protect against hepatitis A is to get the hepatitis A vaccine.

Adapted with permission from the County of San Diego.
HAV cases vs. HAV doses administered to adults by month, August 2016 - February 2018

*N= 771 includes primary, secondary, tertiary confirmed or probable cases from July 2016 February 28, 2018 using MDSS
MCIR data as of March 10, 2018
Getting the Vaccine out: Partners – A Selection

**State**
MDHHS Public Health Administration  
Bureau of Epidemiology and Population Health  
Bureau of Family Health Services  
Bureau of Laboratories  
Bureau of EMS, Trauma, and Preparedness  
Bureau of Community-based Services  
Bureau of Health and Wellness  
Local Health Services  
Medical Services  
**MI Volunteer Registry**  
External Affairs and Communications  
Legislative and Constituent Services  
Michigan Department of Corrections  
Michigan Department of Agriculture and Rural Development

**Professional**
Michigan Health & Hospital Association  
Michigan State Medical Society  
Michigan Osteopathic Association  
Michigan Association for Local Public Health  
Michigan Primary Care Association  
Michigan College of Emergency Physicians  
Michigan Association of Community Mental Health Boards  
Michigan Association of Family Physicians  
Visiting Nurses Association
Partners – A selection (cont’d)

Local & Regional
Local health departments, Clinics
County Jails, Correct Care Solutions, and drug courts
Regional Healthcare Coalitions
Salvation Army Rehabilitation
Street Medicine Detroit
Neighborhood Service Organization - Tumaini Clinic
Detroit Recovery Project
Capuchin Soup Kitchen
Mariners Inn
Samaritas House
St. John Community Center
Detroit Rescue Mission
Naomi’s Nest
Elmhurst Home
Self-Help Addiction Rehabilitation (SHAR)
Community Health Awareness Group (CHAG)
Sacred Heart Rehabilitation Centers
Community Programs, Inc.
Turning Point
Meridian
Waning Hep A Immunity in HIV, Michigan 2018

Possible loss of hepatitis A virus (HAV) seroprotection noted among people living with HIV — Michigan, 2018
Potential Waning Hep A Immunity in Patients Living with HIV

• Healthcare providers have reported that people living with HIV who were previously vaccinated against hepatitis A or had positive total HAV antibody testing may be susceptible and at risk for acquiring hepatitis A virus infection
Potential Waning Hep A Immunity in Patients Living with HIV

• 2 hepatitis A cases had positive total hepatitis A virus (HAV) antibody test results upon entry into care for HIV
  – They were not offered HepA vaccination previously because of presumed immunity
  – These providers have instituted re-screening patients who have not had total HAV antibody testing in the past 5 years

• Additional patients have been identified who have seroreverted from positive total HAV antibody status to negative, including those with history of HepA vaccination.
Potential Waning Hep A Immunity in Patients Living with HIV

• Though inconclusive, these early findings are concerning for loss of seroprotection in PLWH who may be susceptible and at risk of acquiring HAV infection.

• Total HAV antibody status should be updated if testing has not been performed during the previous 5 years for patients at risk during this outbreak
  – MSM, illicit substance use, homelessness or in transient living conditions, recent incarceration, and underlying liver disease including hepatitis B or C

• If total HAV Ab testing is negative, regardless of previous vaccination history, MDHHS recommends:
  – the patient completes the monovalent HepA vaccine series
  – the provider documents a post-vaccination response at least 4 weeks after the 2nd dose
Clinician Resources- Hep A and HIV

• Clinical experts at Henry Ford Hospital are available through the HIV Consultation Program for hepatitis A questions related to HIV patients.

• Non-urgent questions can be submitted at www.henryford.org/HIVconsult, and will be responded to in 24 to 48 hours.

• For urgent questions, health care professionals should contact the 24-hour consultation line by calling 313-575-0332.
Hepatitis A Outbreak Website

In support of efforts, MDHHS has a website for the hepatitis A outbreak that has important and timely information, available at:

➢ **www.mi.gov/hepatitisAoutbreak**

- The website contains a brief case count, hospitalized cases, and deaths for an at-a-glance review that is updated each Friday.
  - Confirmed cases are also listed out by jurisdiction.
  - A Comprehensive Summary with case demographics and risk profiles is also available.
- A full listing of communication documents and educational materials available for download.
Printed Materials

Poster – Protect Yourself from Hepatitis
(updated 11/2017)

Available to order in the Clearinghouse at no cost!
(Brochure on backorder, being re-printed)

http://www.hpclearinghouse.org/
Click “Enter Here to Place Your Order”
Click “Immunizations”

Item Numbers:
IM160 – Poster
IM161 – Brochure

• Brochures translated in Arabic, Spanish, Chinese, and Bengali available at:
  www.mi.gov/hepatitisAoutbreak
Outreach Materials

Flyer – Help Stop the Spread of Hepatitis A

Flyer – Hepatitis A is in Michigan communities

Flyer – Hepatitis A is Spreading

Stop the spread. Get vaccinated today.
Questions