



Hepatitis A Virus: Old Things Made New

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 - Site investigator for HIV/HCV SWITCH Registry Study
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- www.cdc.gov
- Bennett JE, Dolin R, and Blaser MJ. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*, 8th Ed.

Objectives

- By the end of this lecture the learner will be able to:
 - Describe the epidemiology of hepatitis A virus (HAV) in the US, including recent epidemics in CA, KY and TN;
 - Identify the method of and risk factors for HAV transmission;
 - Recognize clinical symptoms and signs of HAV;
 - Recommend appropriate prevention strategies, including immunization and post-exposure prophylaxis.

Case

- Chuck is a 35 y/o homeless man who lives in Nashville, TN.
- He has HIV and diabetes mellitus type 2.
- He uses inhaled drugs intermittently and drinks 0-6 beers daily.
- He takes ART (emtricitabine/tenofovir + darunavir/ritonavir) and metformin.
- He presents to the emergency department due to 2 days of fever, chills, nausea, vomiting, abdominal pain.
- He has noted that his urine is dark and that his stool is a light color.

Case Cont.

- Exam reveals:
 - Overt scleral icterus
 - Jaundice
 - Diffuse abdominal tenderness with palpation
- Labs reveal:
 - CBC unremarkable
 - BMP with Cre 1.1
 - AST 1800
 - ALT 2200
 - Alk Phos 250
 - T bili 8.5
- Additional diagnostics:
 - HAV
 - IgM positive
 - IgG negative
 - HBV
 - sAn negative
 - cAb positive
 - sAb positive
 - HCV
 - Ab positive
 - RNA negative
 - HIV
 - Ab positive
 - CD4 750/30%
 - RNA <40

Chuck's Questions

- What do I have?
- How did I get it?
- What does this mean for me moving forward?
- Do other people get this, and how can it be prevented?

Overview

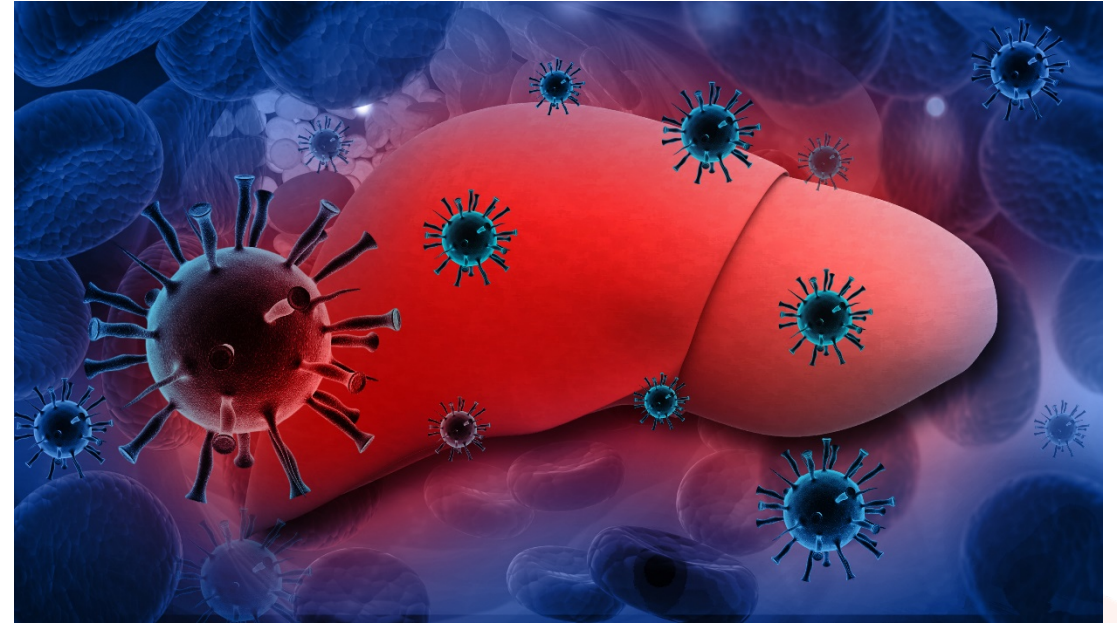
- Definition
- Epidemiology
- Clinical Manifestations and Complications
- Diagnosis, Treatment and Prevention
- Epidemics

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Hepatitis

- Hepatitis = inflammation of the liver
- Differential Diagnosis:
 - Hepatitis viruses
 - Hepatitis A (HAV)
 - Hepatitis B (HBV)
 - Hepatitis C (HCV)
 - HIV
 - Cytomegalovirus (CMV)
 - Alcohol
 - Drug and/or supplement toxicity
 - Obesity [leading to non-alcoholic fatty liver disease (NAFLD)]
 - Genetic disorders



Clinical Manifestations of Hepatitis

- Acute Symptoms and Signs:
 - Fever
 - Fatigue and anorexia
 - Nausea and vomiting
 - Abdominal pain
 - Jaundice, dark urine, and clay-colored stools
 - Arthralgias
- Labs reveal elevated aminotransferase levels and bilirubin.
- HAV causes a self-limited (although potentially severe) infection.
- HBV and HCV may both cause acute and chronic infection that increase the risk of cirrhosis, end stage liver disease, and liver cancer.

Hepatitis A Virus

- Picornaviridae family
- RNA, non-enveloped virus
- Humans are natural host
- GT 1, 2, and 3 may infect humans (1 being most common)
- Stable in environment for months
 - Inactivated at high temperatures and by some chemicals
 - Not inactivated by alcohol-based sanitizers



www.cdc.gov

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HAV Epidemiology and Risk Factors

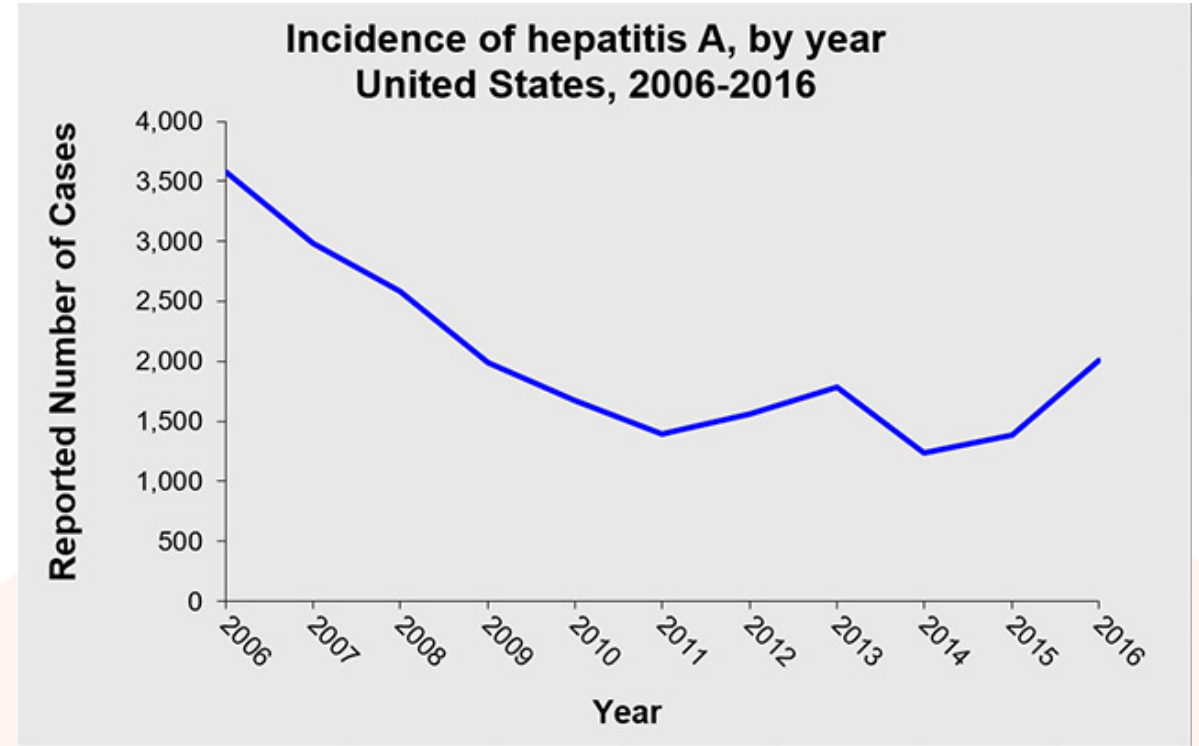
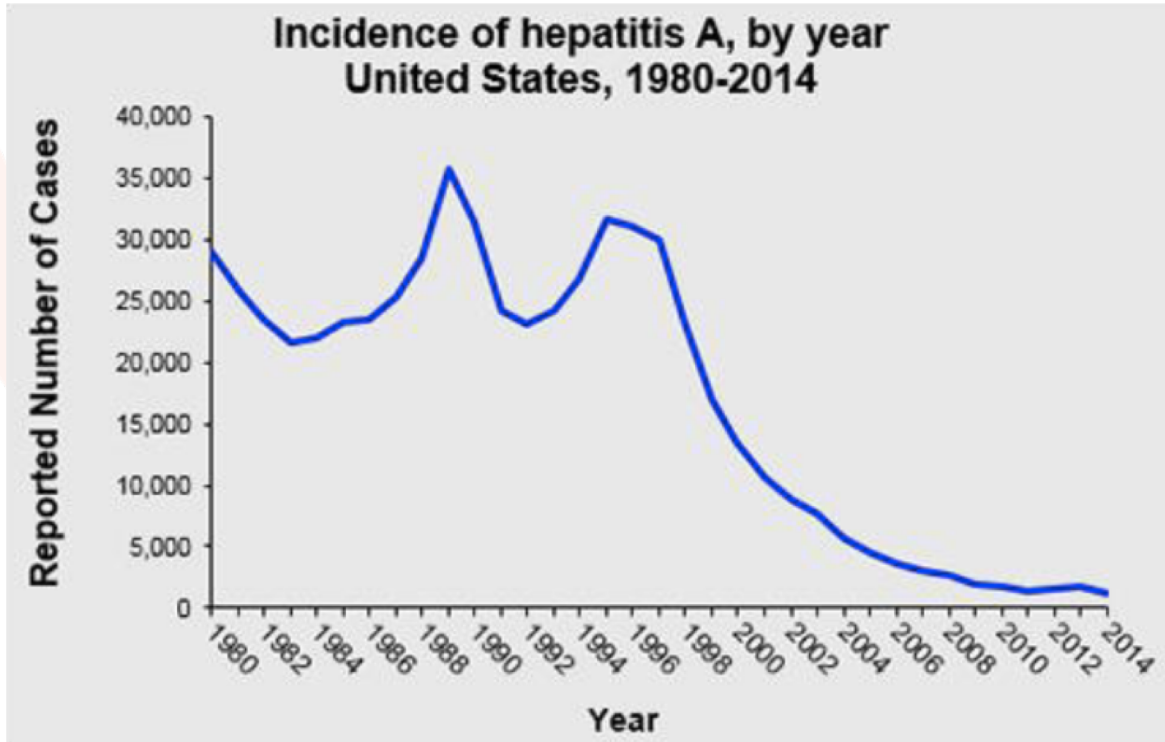
- Estimated 15,000-20,000 in the US each year
- Incubation x 1 month (15-50 days) with duration <2 months
- Transmission most common via fecal-oral route
 - Typically via contaminated food/water including undercooked/raw meat (i.e. shellfish)
 - Stool infectious for 2-3 weeks prior to symptoms (peak infectivity) and 1 week after onset of symptoms
 - Transmission has been documented with blood product transfusions

Who is at risk?

Although anyone can get Hepatitis A, some people are at greater risk, such as those who:

- Travel to or live in countries where Hepatitis A is common
- Use recreational drugs, whether injected or not
- Have sexual contact with someone who has Hepatitis A
- Have clotting-factor disorders, such as hemophilia
- Are men who have sexual encounters with other men
- Are household members or caregivers of a person infected with Hepatitis A

HAV US Epidemiology Trends



www.cdc.gov

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Clinical Manifestations of HAV

- Fever
- Fatigue and anorexia
- Nausea and vomiting
- Abdominal pain
- Jaundice, dark urine, and clay-colored stools
- Arthralgias
- Elevated aminotransferase and bilirubin
- Usually lasts 2-3 weeks but may be up to 2 months
- 20-40% of cases considered severe and require hospitalization

True or False?

- Once Chuck's initial clinical symptoms related to HAV resolve, he will have no further HAV-related issues.

Clinical Complications of HAV

- Relapsing hepatitis
- Cholestatic hepatitis
- Acute liver failure
- Autoimmune hepatitis (rare)

Relapsing Hepatitis

- Occurs in ~10% of patients (range of 3-20% in different studies)
- Initial presentation with subsequent improvement but later worsening of LFTs with or without symptoms
- Occurs 1-12 weeks later and lasts for 3 weeks – 12 months
- Relapse usually mild

Cholestatic Hepatitis

- Occurs in 5% of patients
- Prolonged elevation of bilirubin and alkaline phosphatase (i.e. >3 months)
- Symptoms include fever, weight loss, jaundice, pruritus, and/or diarrhea

Acute Liver Failure

- <0.1% of acute HAV cases, though 4.5% of acute liver failure cases
- Severe presentation with of hepatitis with coagulopathy and hepatic encephalopathy
- Occurs within 20 weeks
- More common in older adults and those with preexisting liver disease

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HAV Diagnosis



- Clinical diagnosis definition
 - Clinically consistent illness
 - Positive serologic test (IgM antibody)
- Outbreak case definitions
 - Confirmed (i.e. RNA with genotype and/or epidemiologic data)
 - Probable (i.e. meets clinical diagnosis)
 - Suspect
 - Not outbreak case (guided by genotype and/or epidemiologic data)

HAV Treatment and Prevention

- Treatment is supportive only
- Prevention may be provided by pre-exposure immunization
- Post-exposure prophylaxis may include immunization and/or immune globulin (IG)
- Use universal precautions and good hand hygiene
- Avoid untreated water, unwashed fruits and vegetables, and raw or undercooked seafood or shellfish

Who should get vaccinated against Hepatitis A?

Vaccination is recommended for certain groups, including:

- All children at age 1 year
- Travelers to countries where Hepatitis A is common
- Family and caregivers of recent adoptees from countries where Hepatitis A is common
- Men who have sexual encounters with other men
- Users of recreational drugs, whether injected or not
- People with chronic or long-term liver disease, including Hepatitis B or Hepatitis C
- People with clotting-factor disorders

Multiple Choice (In Your Mind...)

- Chuck has a 35 y/o twin brother with identical medical problems who has shared food with Chuck 10 days ago. What prophylaxis is most appropriate?
 - A. HAV vaccine
 - B. HAV IG
 - C. HAV vaccine + IG
 - D. No post-exposure prophylaxis

HAV Vaccines

- Two hepatitis A inactivated whole-virus vaccine
 - One combined hepatitis A/B vaccine
- Immunogenicity 95% in adults after 1st dose of HAV vaccine
- Vast majority (near 100%) of adults seroconvert after 2nd dose
 - Seroconversion lower in liver disease, advanced immunosuppression, and some other conditions
- >90% protected for life

HAV Post-exposure prophylaxis (PEP)

- Recommended within 2 weeks of contact with confirmed case
- Includes both immunization as well as immune globulin (IG) depending on demographic and risk factors:
 - Age 1-40:
 - HAV vaccine
 - Age >40:
 - IG +/- vaccine
 - Use vaccine if IG not available
 - Preference for IG in age >60 and definitely in age >75
 - Age <12 mo, immunosuppressed, liver disease, vaccine allergy:
 - IG

NOTE: Recent immune globulin PEP recommendations in San Diego outbreak included dosing at 0.1 ml/kg (5x higher than prior doses) due to lower concentration of anti-HAV immunoglobulins in donors.

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San Diego, CA Epidemic: Description

- Occurred in 2017
- Associated with drug use and homelessness
- Common coinfection with HBV and HCV

Jurisdiction	Cases	Hospitalizations	Deaths
San Diego	587	402	20
Santa Cruz	76	33	1
Los Angeles	12	8	0
Monterey	12	10	0
Other	17	8	0
Total	704	461	21

California Department of Public Health

San Diego, CA Epidemic: Interventions

- >160,000 vaccinations administered
 - Most (>80%) delivered to high-risk individuals
 - Novel distribution including mass vaccination events, foot teams, mobile vans, and local institutional support
- Sanitation campaign
 - Power-spraying sidewalks
 - Temporary housing tents with bathrooms and showers
- Indication for vaccine expanded beyond traditional risk factors
 - Food service workers
 - Healthcare workers
 - Sanitation workers
 - Public safety workers
 - Homeless service providers

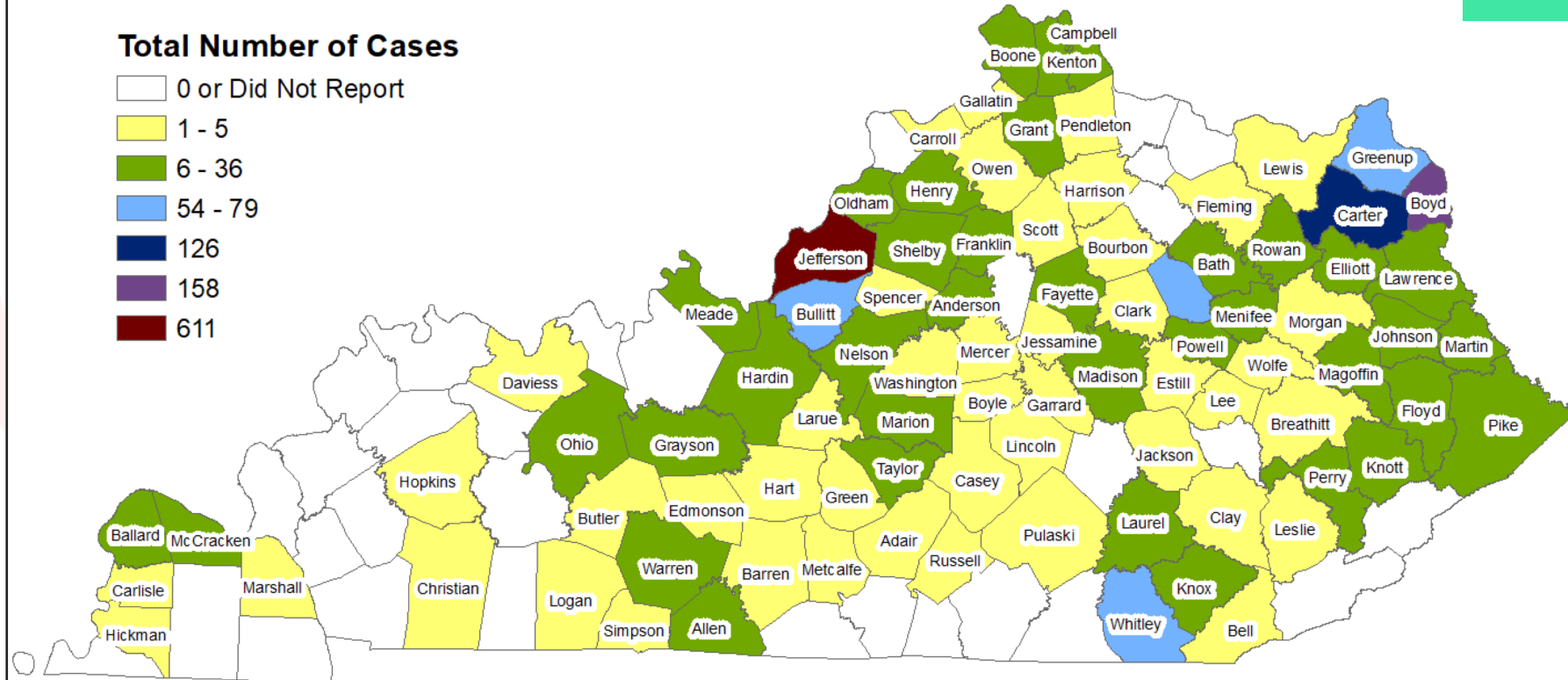
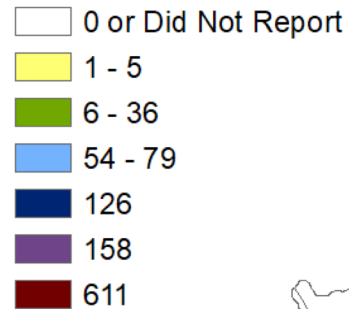
Kentucky HAV Epidemic

Counts as of September 22, 2018:

- Total Outbreak: **1,851**
- Hospitalizations: **1029**
- Deaths: **14**

KY17-089 Distribution of Outbreak-Associated Acute Hepatitis A Cases by County, August 1, 2017 - September 22, 2018

Total Number of Cases

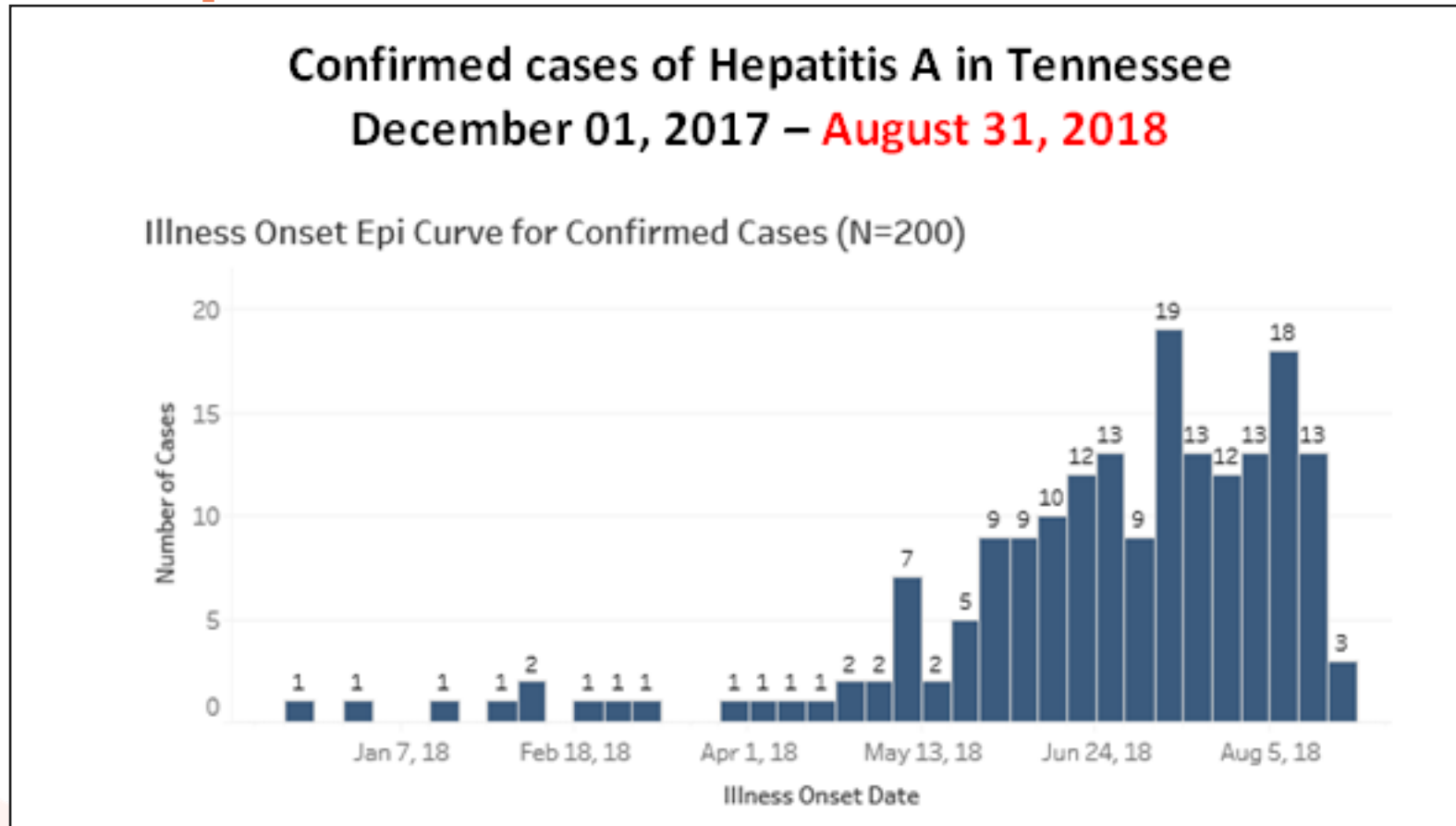


n = 89 counties with outbreak-associated cases

Counties where cases have not previously been identified: Lee.

- Associated with recreational drug use and homelessness

Hepatitis A Outbreak in TN



Hospitalizations: 144/200 (72%)

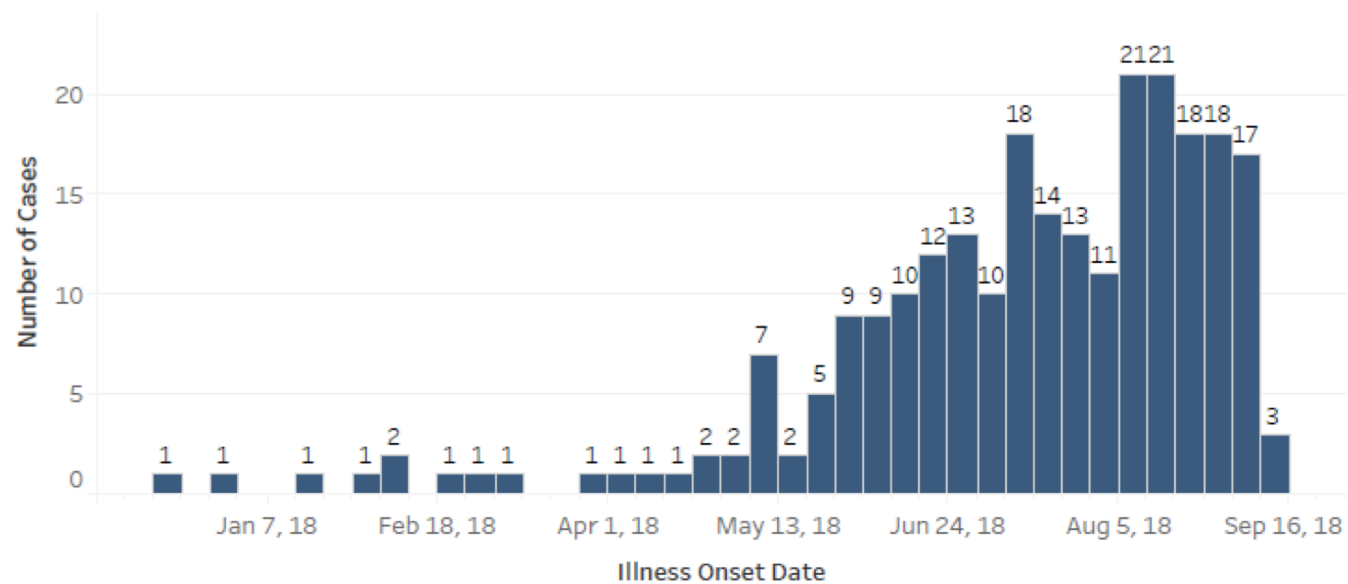
Deaths: 0

Updated Data

Hepatitis A Outbreak -- Tennessee

as of 9/21/2018 3:00:27 PM

Illness Onset Epi Curve for Confirmed Cases (N=254)



Cases by Region (N=254)

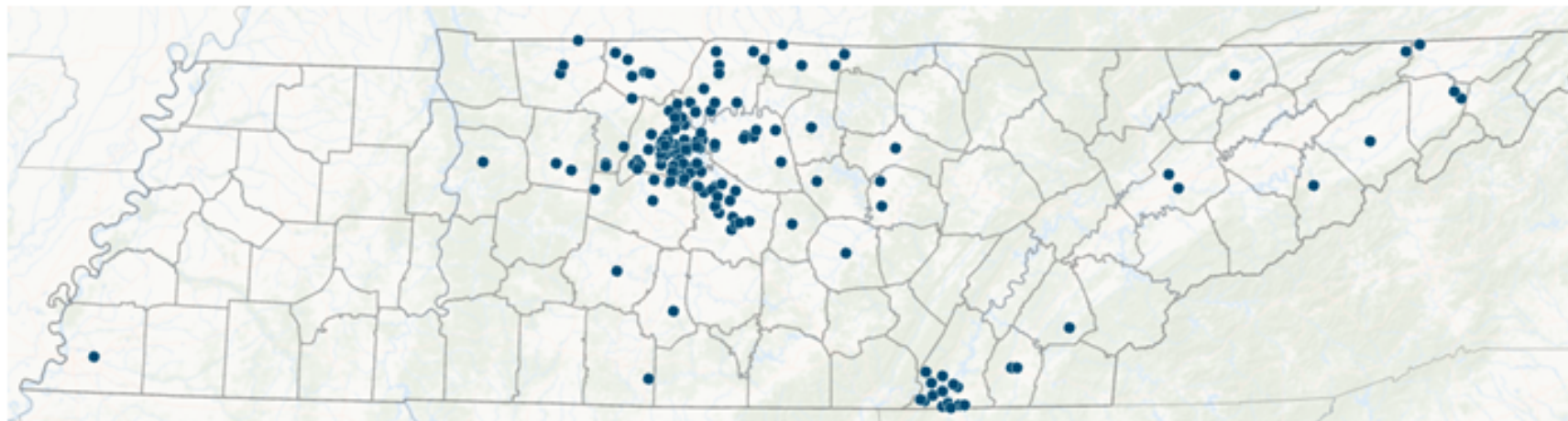
NDR	107
MCR	87
CHR	22
UCR	15
SCR	7
ETR	4
NER	4
KKR	3
SER	3
MSR	1
SUL	1

Hospitalizations: 147/254 (58%)

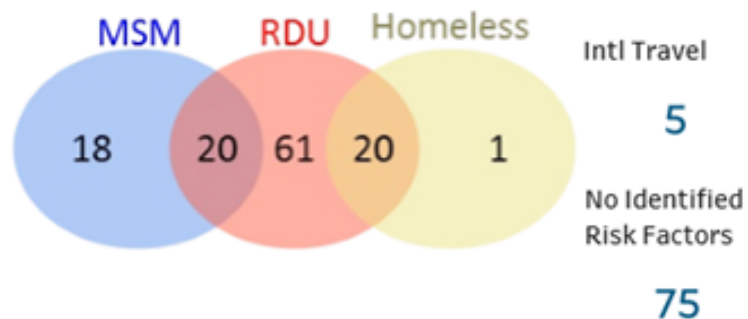
Deaths: 0

Hepatitis A Outbreak in TN: Distribution & Risk Factors

Confirmed Cases of Hepatitis A
Tennessee, December 01, 2017– August 31, 2018



Confirmed Cases of Hepatitis A in Tennessee by Risk Factor
December 01, 2017 – August 31, 2018



MSM: men who have sex with men
RDU: persons who use drugs
recreationally

Hepatitis A Outbreak in TN: Collaborations

- **Immunizations**
 - Overall leadership engagement with multiple partners
- **Emergency Preparedness**
 - Coordination, logistics, procurement
- **HIV/STD/VH**
 - Implementation (jails, prison intake facilities, STD clinics)
 - Education (MSM task force, social media)
 - Co-infection reports (HAV, HBV, HCV, HIV)
- **CDC**
 - SME
 - Multi-state calls
 - Genotyping

What Can You Do?

- Be aware!
- Assess for HAV risk.
- Immunize!

Questions?

THANK YOU