Hepatitis A outbreak(s) in the U.S.
Do we care?

How life flows through our community

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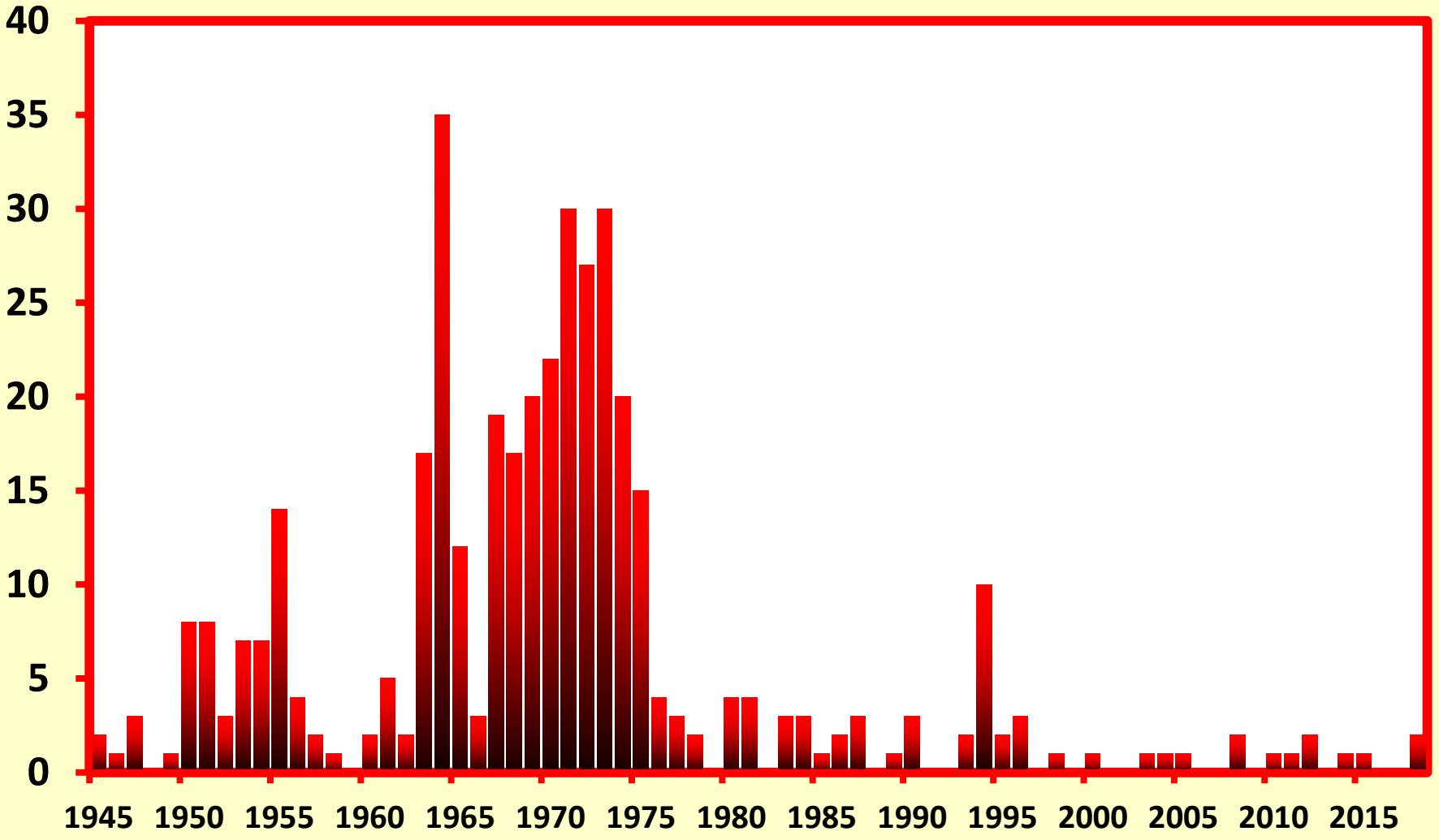
PubMed(MeSH) citations 1945-2018:
"[Hepatitis A or HAV] & Blood Transfusion"



Hepatitis A Virus (HAV)

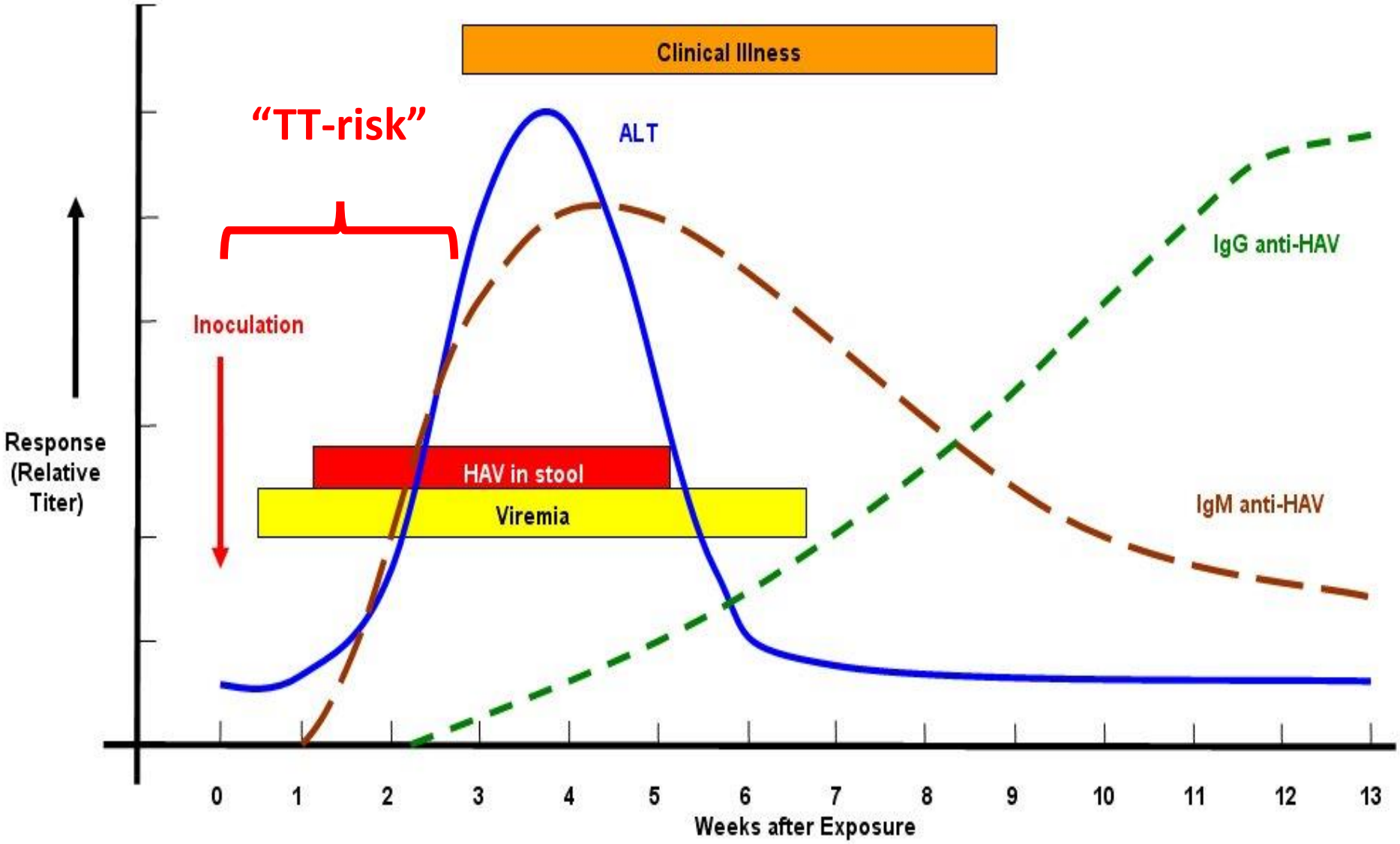
Family: *Picornaviridae*; Genus: *Hepatovirus*

- **Nonenveloped, icosahedral nucleocapsid symmetry, 27-32 nm**
- **Linear, positive-sense, ~7.5 kb ssRNA**
- **Persists days-months in fresh, sea & waste water, soils, marine sediment, live oysters, & cream-filled cookies**
- **Resists low pH, detergents & organic solvents**
- **Autoclaving effective & inactivated in minutes at 98-100°C.**
- **Inactivated by UV, formalin, β-propiolactone, iodine, chlorine/chlorine-containing compounds (sodium hypochlorite), pasteurization, & infectivity substantially decreased by 70% ethanol at 25°C.**
- ***Contemporary PDMPs are safe* (multiple orthogonal methods)**
- ***Amotosalen + UV, B_2 + UV & Solvent/Detergent not effective***

HAV:
clinical information

- Fecal-oral transmission predominates
- Incubation 10-50 days (average 1 month)
- Peak infectivity before appearance of IgM & symptoms
- Post-exposure prophylaxis with vaccine
- ISG still used in high-risk individuals
- Attack rate for clinical hepatitis 5-34%, highest >60 y/o
- Overall mortality <0.015%.
- Fulminant hepatitis in <1.5% of hospitalized patients who account for bulk of mortality
- Rx: supportive & transplant for fulminant

HAV: clinical & lab time course



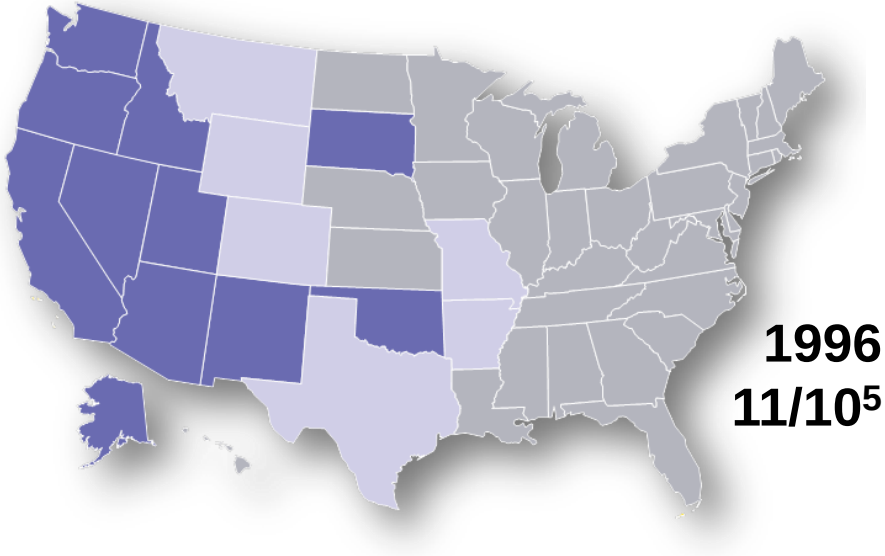
ACIP HAV Vaccine Recommendations
Groups at increased risk of HAV infection or severe HAV disease

1. International travelers
2. Men who have sex with men
3. Users of injection & non-injection drugs
4. Persons with clotting-factor disorders
5. Persons who work with nonhuman primates
6. Persons who anticipate close personal contact with an international adoptee
7. Persons with chronic liver disease
8. Persons experiencing homelessness

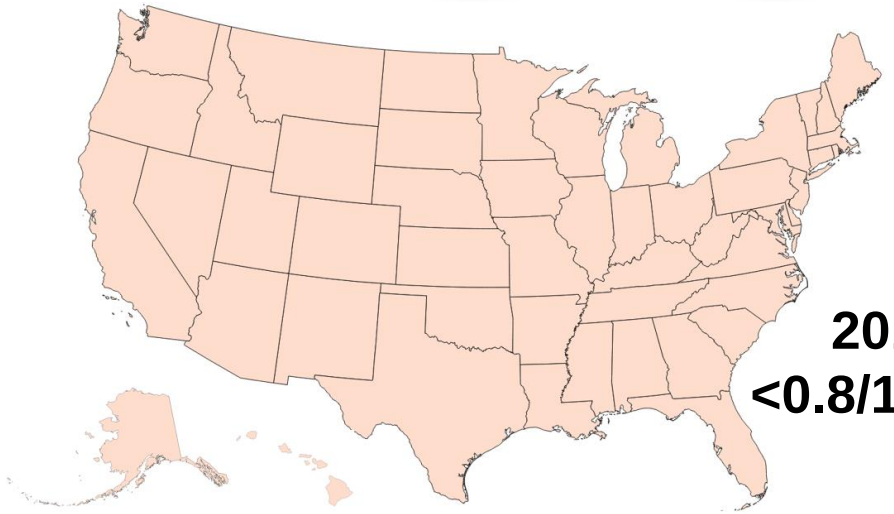
MMWR 1996;45(RR-15); MMWR 1999;48(RR-12); MMWR 2006;55(RR-7)

ACIP's incremental HAV vaccine history

- **1996: At 2 y/o in high-risk communities & through teens during outbreaks**
- **1999: Children in states with twice U.S. average incidence, & consider with rates greater than national average**
- **2006: Universal immunization**
  - **>1 y/o all states**
  - **Continue extant programs for 2-18 y/o**
  - **Catch up for outbreaks & areas with increasing rates**
  - **Anyone wanting immunity**



1996
11/10^5

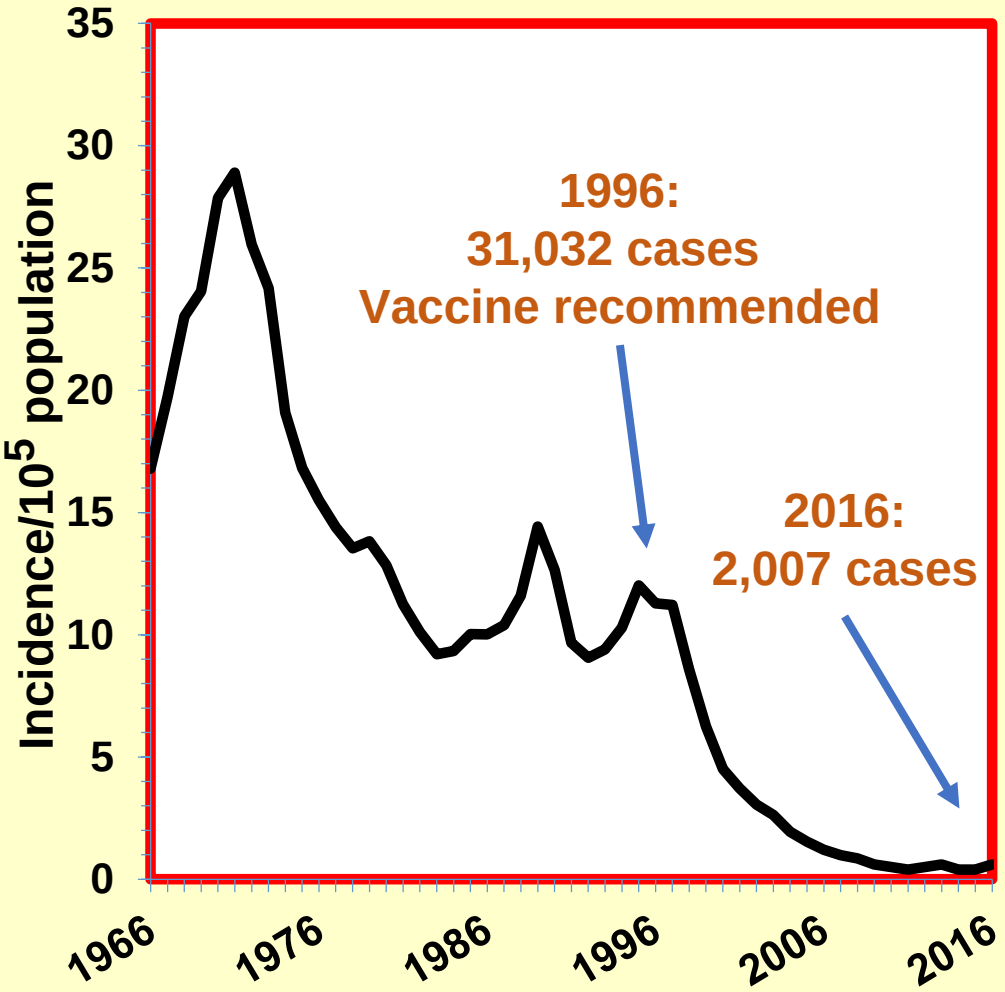


2015
<0.8/10^5

MMWR. 1996. 45(RR-15)
MMWR. 1999. 48(RR-12)
MMWR. 2006. 55(RR-7)

HAV epidemiology:
U.S. 1966-2016

- **U.S. is considered low *endemicity***
- **In pre-vaccine era there were ≥21,000 cases/year**
- **Cyclic increases every 10-15 years prior to introduction of vaccine**

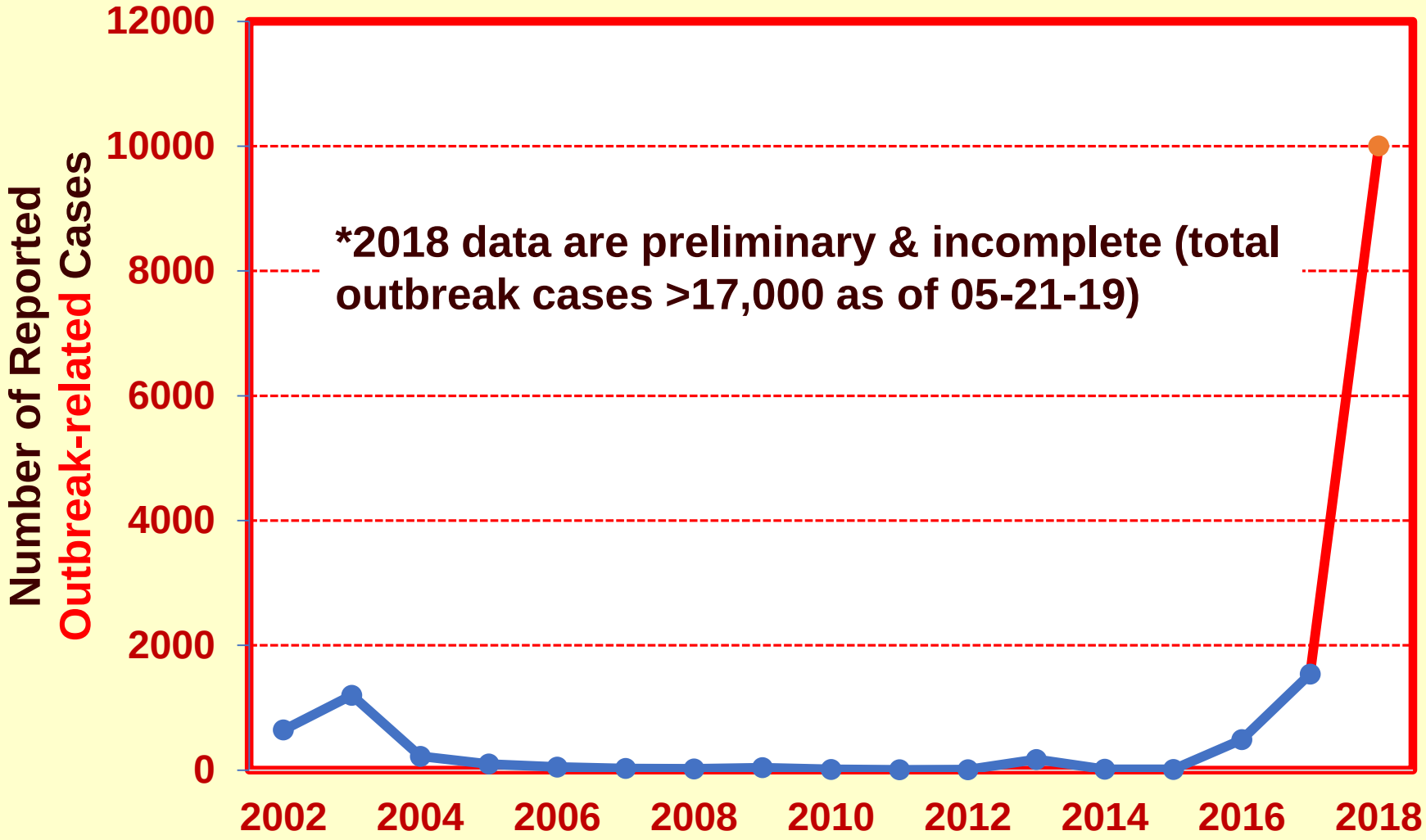


Fiore AE, et al. ACIP. 2006.

CDC. Surveillance for Viral Hepatitis-- United States, 2016.

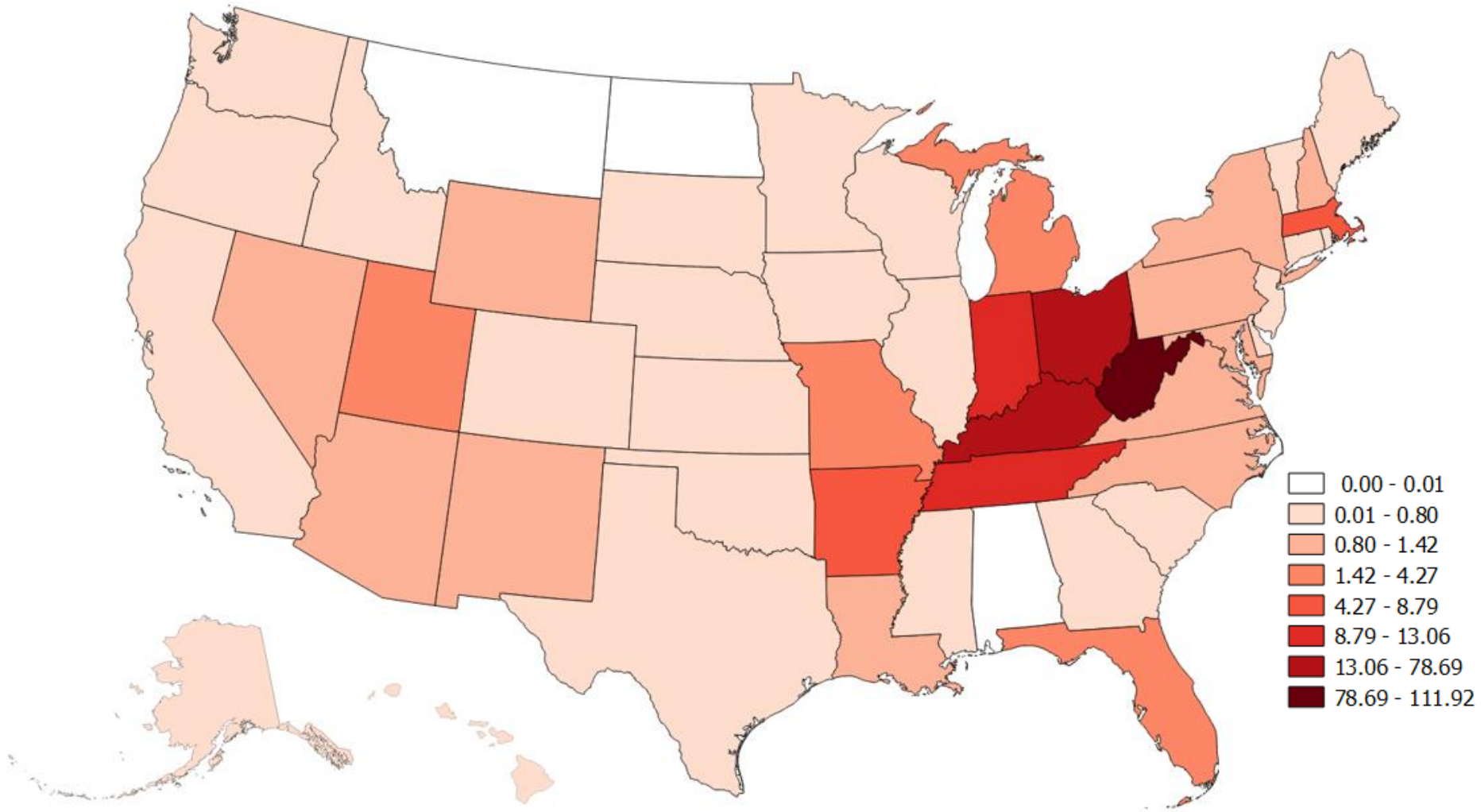
Murphy TV, et al. *MMWR Suppl* 2016.

Outbreak-related HAV case reports: U.S. 2002-18*



Source: Jones J. CDC. ProMED.

HAV incidence /10^5 population: 2018 (preliminary)



More than 15,000 cases, 8,500 (57%) hospitalizations, & 140 deaths since outbreaks began in 2016. Health Alert Network (HAN) update, March 2019.

HAV outbreaks: U.S. 2016

The following groups are at highest risk for acquiring HAV infection or developing serious complications from HAV infection in these outbreaks…

- **People using drugs (injection or non-injection)**
- **People with unstable housing & homelessness**
- **Men who have sex with men (MSM)**
- **People who are/were recently, incarcerated**
- **People with chronic liver disease, including cirrhosis, hepatitis B, or hepatitis C**

Deferred donors (mostly)

Source: CDC

Recommendations of the Advisory Committee on Immunization Practices for Use of Hepatitis A Vaccine for Persons Experiencing Homelessness

Summary

What is already known about this topic?

Hepatitis A (HepA) vaccine is highly safe and effective, and a complete HepA vaccine series provides long-term protection against hepatitis A virus (HAV) infection. Person-to-person HAV outbreaks among persons using drugs or experiencing homelessness are widespread and ongoing.

What is added by this report?

All persons aged ≥1 year experiencing homelessness should be routinely immunized against HAV. Vaccination of homeless persons facilitates integration of HepA vaccine into routine preventive services.

What are the implications for public health practice?

HepA vaccination of homeless persons would improve protection of persons at increased risk of exposure to HAV and complications of hepatitis A disease and reduce the risk for large-scale outbreaks by increasing immunity to HAV among homeless persons living in congregate settings where HAV can spread readily.

***MMWR*. 2019. 68(6):153-6**

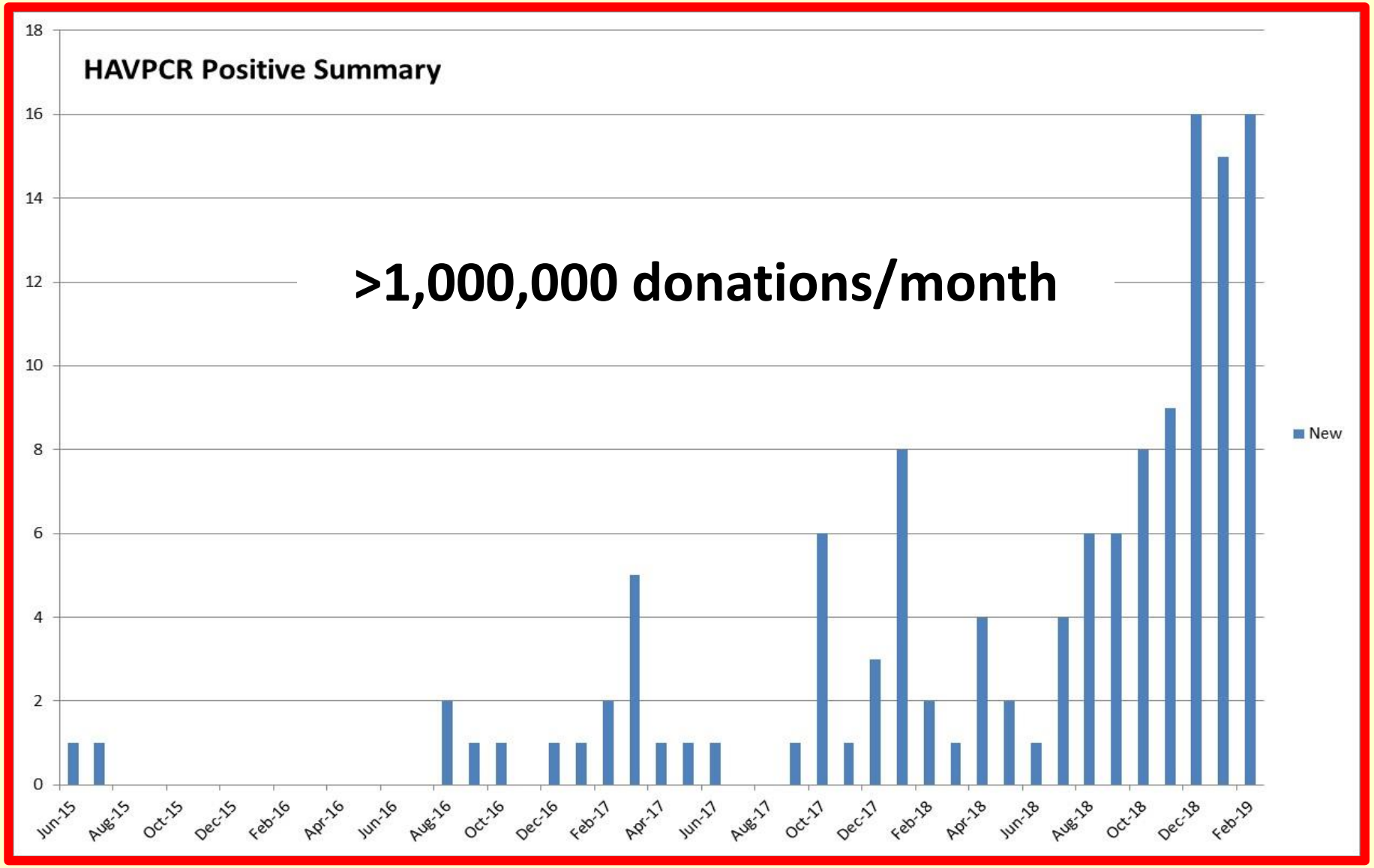
A homeless person is

- **"an individual whose primary residence during the night is a supervised public or private facility…that provides temporary living accommodations…**
- **a resident in transitional housing; without permanent housing who may live on the streets; stay in a shelter, mission, single-room occupancy facility, abandoned building or vehicle; or in any other unstable or nonpermanent situation;**
- **"doubled up," a term that refers to a situation where individuals are unable to maintain their housing situation & are forced to stay with a series of friends &/or extended family…."**

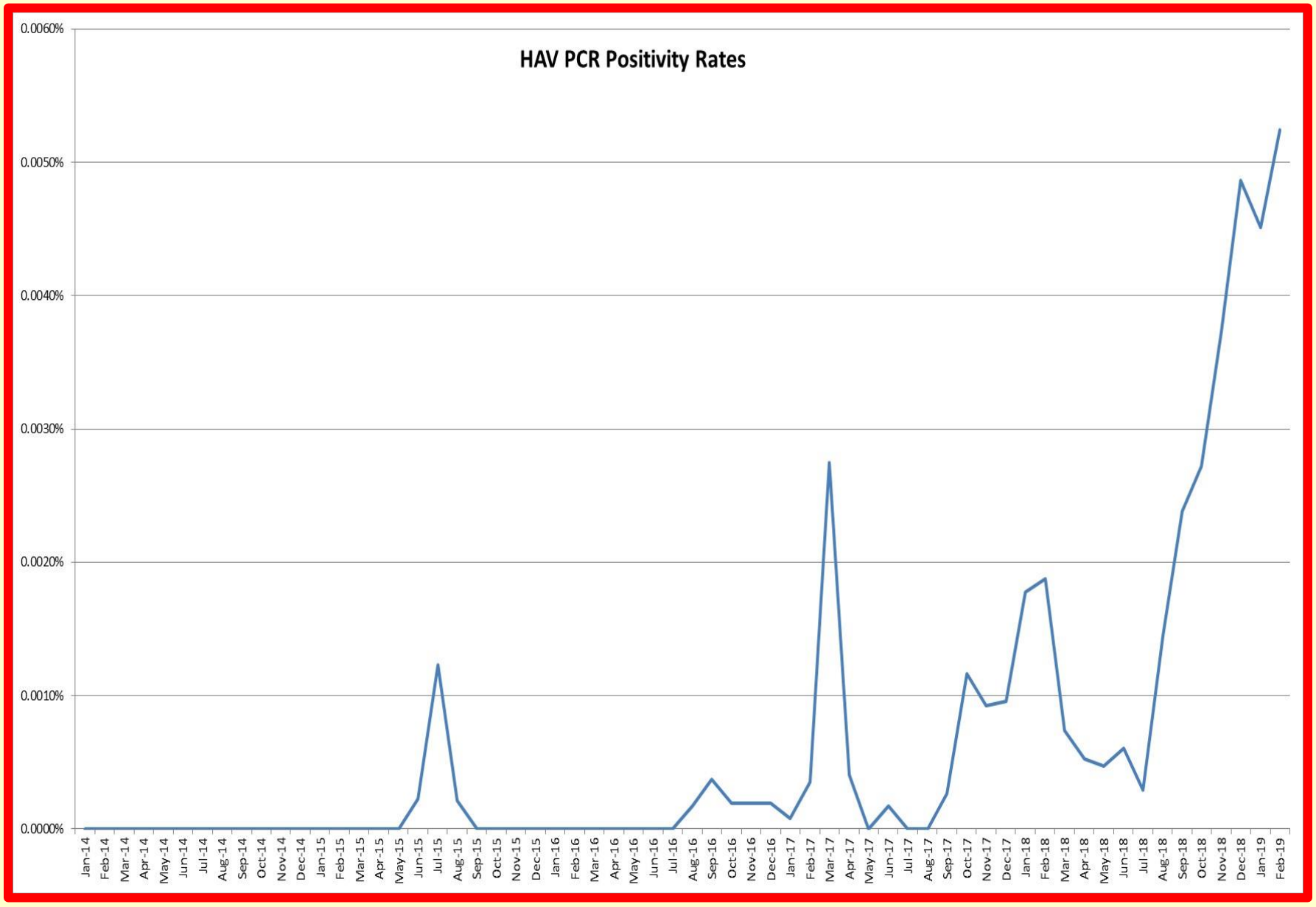
TT-HAV
(40 cases since I started medical school)

	Recipients	Component(s)
Meyers. *Ann. Int. Med*. 1974.	9 (all BMT)	Platelets, plasma
Seeburg. *Lancet*. 1981.	1	Whole blood
Barbara. *Lancet*. 1982.	1	Whole blood
Skidmore. *J. Med. Virol*. 1982.	1	Whole blood
Hollinger. *JAMA*. 1983.	1	RBC
Noble. *JAMA*. 1984.	11 (+2º spread total 55)	RBC
Sherertz. *Arch. Int. Med*. 1984.	1	FFP
Ishikawa. *Gastroenterol Jap.* 1984.	1	FFP, RBC
Azimi. *Am. J. Dis. Child*. 1986	2	RBC
Giacoia. *South. Med. J*. 1989.	4/6 +IgM	1 RBC, 1 Platelet
Nigro. *J. Infect.* 1990.	1	NA
Lee. *Ped. Inf. Dis.* 1992.	3	NA
Diwan. *Transfusion*. 2003.	2	RBC
Hughes. *Transfusion*. 2014.	1	FFP
Vestergard. *J. Inf. Chemo*. 2018	1	Platelet

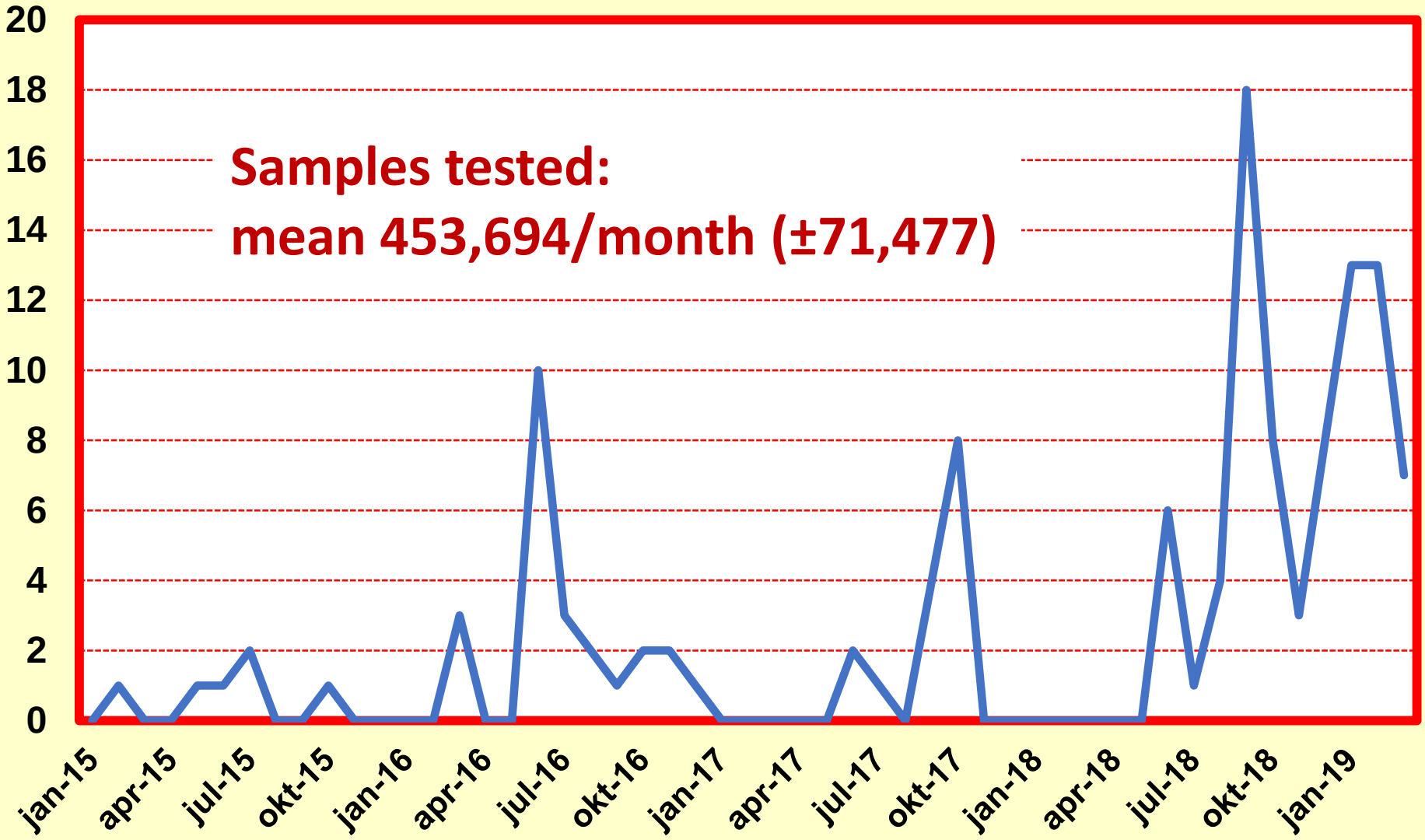
HAV positive source donations: US (lab 1)



HAV positive RATES source donations: US (lab 1)



HAV positive source plasma donations (lab 2)



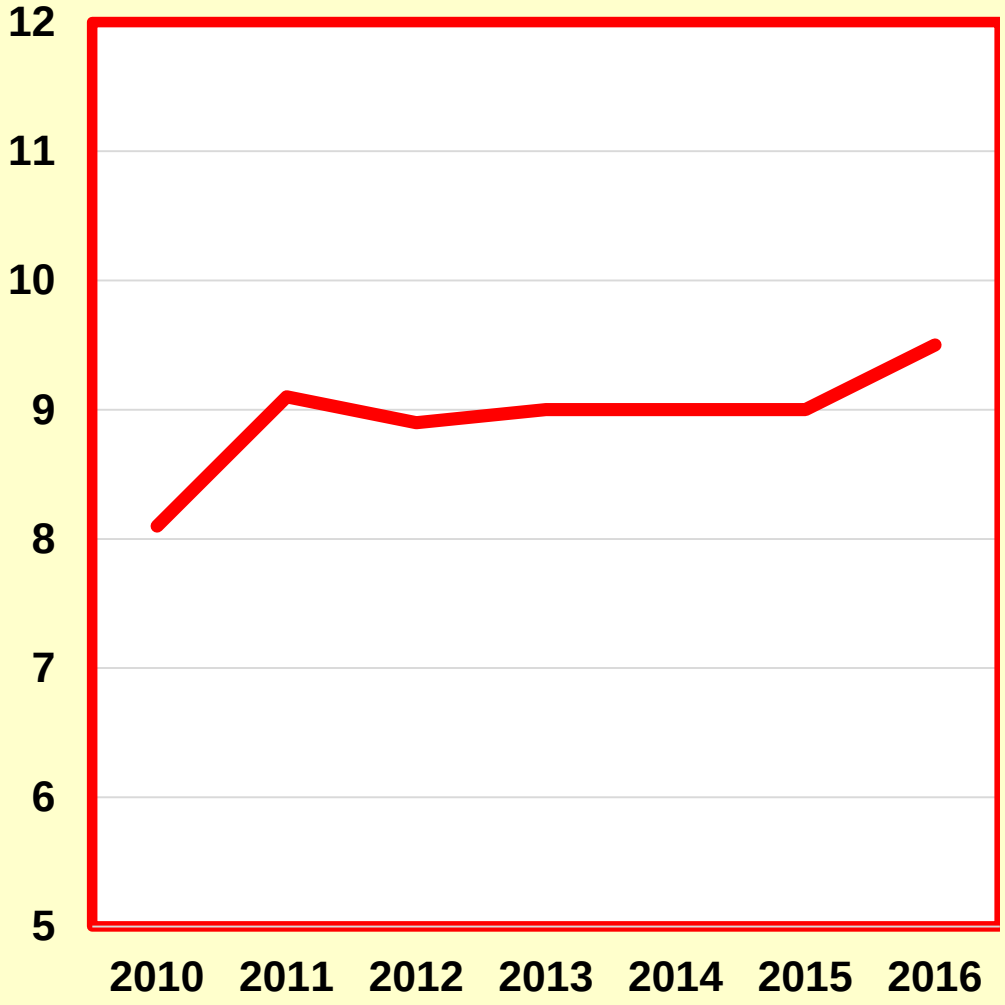
Lab 3: recovered plasma donations from ABC blood centers

Donations tested Dec. 2017 through Nov. 2018		Positives	Percent
HAV NAT	593,474	0	0.0
B19 NAT	2,587,160	91	.004

HAV blood donor “survey”

- **Online ABC survey re: HAV testing of recovered plasma donations**
  - **28 centers responded**
    - **1,184,838 units subjected to pooled nucleic acid testing**
    - **476,973 units from centers that would be notified of positive results**
    - **0 notifications**
  - **ARC (Pers. comm. Stramer S.)**
    - **Jan 2017-Nov. 2018**
    - **2 positive donors (5-6,000,000 donations)**

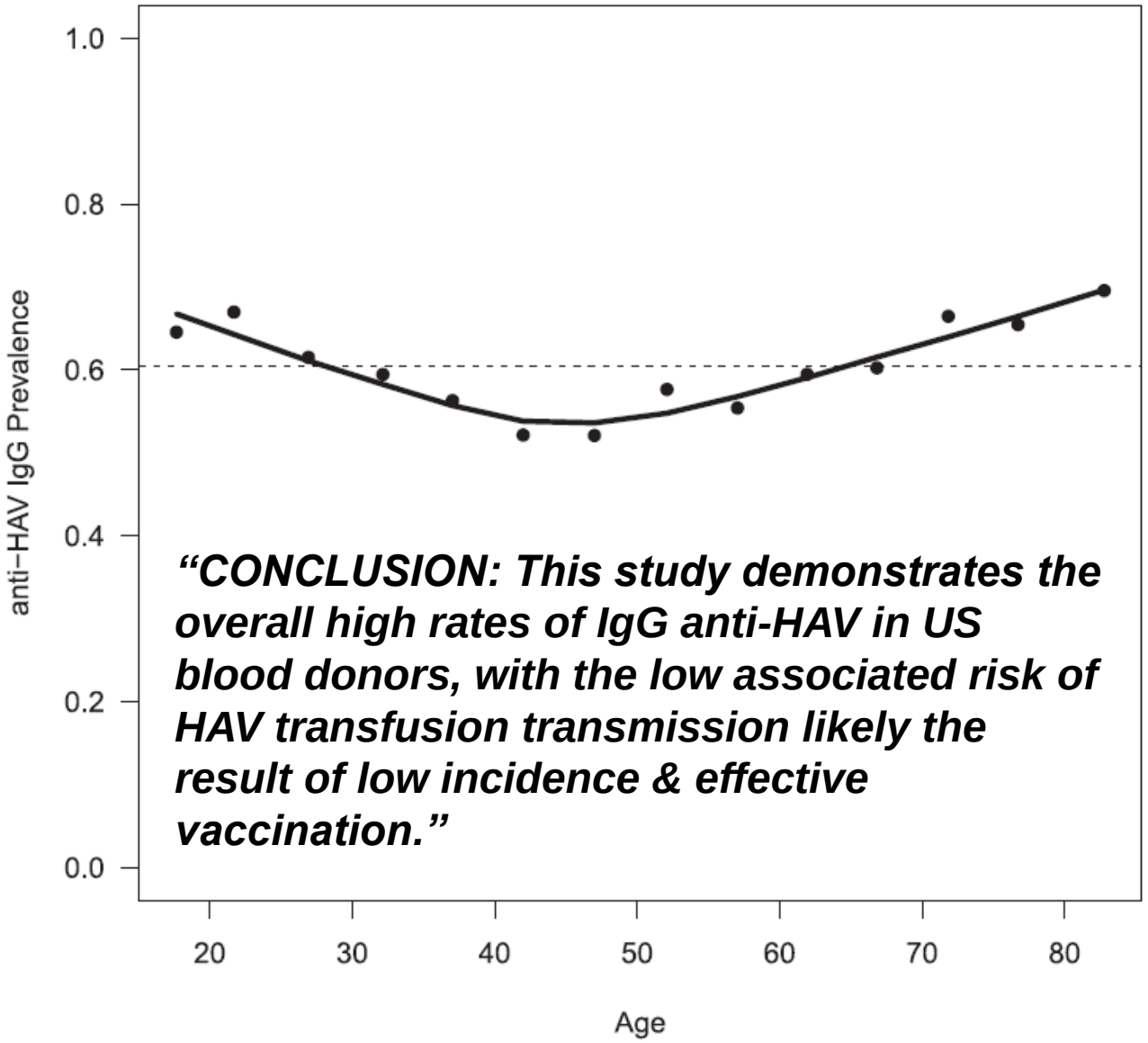
HAV immunization:
Percent of U.S. adults ≥19 years



- **1996: immunization of children in communities with high rates of infection.**
- **1999: immunization of children in 11 western states with rates >20/10^5 population, consideration in 6 more states with rates of 10-20/10^5.**
- **2006: routine immunization in all states**

Source: CDC

HAV IgG prevalence: 5001 ARC donors 2015



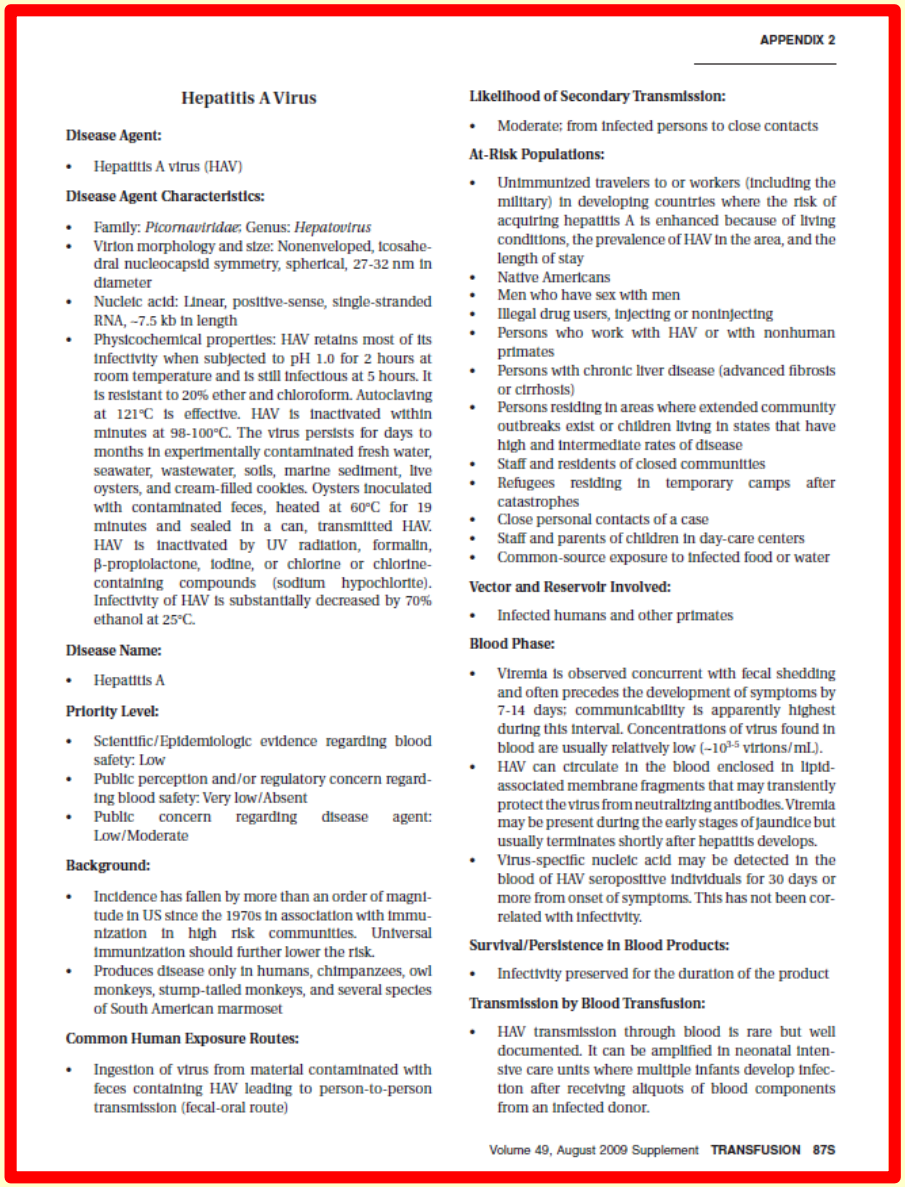
"CONCLUSION: This study demonstrates the overall high rates of IgG anti-HAV in US blood donors, with the low associated risk of HAV transfusion transmission likely the result of low incidence & effective vaccination."

≈60% of donors are immune.

Single IgM + gives estimate of .02% recent infection

Tejada-Strop *et al.* *Transfusion. 2019*

HAV fact sheet:
TTD EID workgroup 2009



APPENDIX 2

Hepatitis A Virus

Disease Agent:

- Hepatitis A virus (HAV)

Disease Agent Characteristics:

- Family: *Picornaviridae*; Genus: *Hepatovirus*
- Virion morphology and size: Nonenveloped, icosahedral nucleocapsid symmetry, spherical, 27-32 nm in diameter
- Nucleic acid: Linear, positive-sense, single-stranded RNA, ~7.5 kb in length
- Physicochemical properties: HAV retains most of its infectivity when subjected to pH 1.0 for 2 hours at room temperature and is still infectious at 5 hours. It is resistant to 20% ether and chloroform. Autoclaving at 121°C is effective. HAV is inactivated within minutes at 98-100°C. The virus persists for days to months in experimentally contaminated fresh water, seawater, wastewater, soils, marine sediment, live oysters, and cream-filled cookies. Oysters inoculated with contaminated feces, heated at 60°C for 19 minutes and sealed in a can, transmitted HAV. HAV is inactivated by UV radiation, formalin, β-propiolactone, iodine, or chlorine or chlorine-containing compounds (sodium hypochlorite). Infectivity of HAV is substantially decreased by 70% ethanol at 25°C.

Disease Name:

- Hepatitis A

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Low
- Public perception and/or regulatory concern regarding blood safety: Very low/Absent
- Public concern regarding disease agent: Low/Moderate

Background:

- Incidence has fallen by more than an order of magnitude in US since the 1970s in association with immunization in high risk communities. Universal immunization should further lower the risk.
- Produces disease only in humans, chimpanzees, owl monkeys, stump-tailed monkeys, and several species of South American marmoset

Common Human Exposure Routes:

- Ingestion of virus from material contaminated with feces containing HAV leading to person-to-person transmission (fecal-oral route)

Likelihood of Secondary Transmission:

- Moderate; from infected persons to close contacts

At-Risk Populations:

- Unimmunized travelers to or workers (including the military) in developing countries where the risk of acquiring hepatitis A is enhanced because of living conditions, the prevalence of HAV in the area, and the length of stay
- Native Americans
- Men who have sex with men
- Illegal drug users, injecting or noninjecting
- Persons who work with HAV or with nonhuman primates
- Persons with chronic liver disease (advanced fibrosis or cirrhosis)
- Persons residing in areas where extended community outbreaks exist or children living in states that have high and intermediate rates of disease
- Staff and residents of closed communities
- Refugees residing in temporary camps after catastrophes
- Close personal contacts of a case
- Staff and parents of children in day-care centers
- Common-source exposure to infected food or water

Vector and Reservoir Involved:

- Infected humans and other primates

Blood Phase:

- Viremia is observed concurrent with fecal shedding and often precedes the development of symptoms by 7-14 days; communicability is apparently highest during this interval. Concentrations of virus found in blood are usually relatively low (~10^{3-5} virions/mL).
- HAV can circulate in the blood enclosed in lipid-associated membrane fragments that may transiently protect the virus from neutralizing antibodies. Viremia may be present during the early stages of jaundice but usually terminates shortly after hepatitis develops.
- Virus-specific nucleic acid may be detected in the blood of HAV seropositive individuals for 30 days or more from onset of symptoms. This has not been correlated with infectivity.

Survival/Persistence in Blood Products:

- Infectivity preserved for the duration of the product

Transmission by Blood Transfusion:

- HAV transmission through blood is rare but well documented. It can be amplified in neonatal intensive care units where multiple infants develop infection after receiving aliquots of blood components from an infected donor.

Currently Recommended Donor Deferral Period:

- ~~FDA requires an indefinite deferral for a clinical history of viral hepatitis (regardless of the specific viral agent) after age 11.~~
- In the US, most viral hepatitis before the age of 11 is a result of HAV; consequently, individuals with a history of hepatitis prior to the age of 11 are allowed to donate.
- AABB recommends deferral of 120 days following appropriately documented exposure to a community HAV outbreak; this is a result of potential for transmission from secondary HAV cases.

AABB Association Bulletin
July 2013

- **Centers should have SOPs to manage *collections during outbreaks***
- **Cooperation with local public health to determine risks of exposure during outbreaks**
  - **Activate process when public health announces**
    - ***Point source* outbreak requiring PEP**
    - **Potential for *point source* due to food worker or other common source & evaluation for PEP is recommended**
- **No action if public health does not advise that specific individuals or groups need evaluation for PEP**

Conclusions:

- **Epidemic HAV in specific populations is occurring in the U.S**
  - **Drug users**
  - **Homeless**

  } **≈70%**
- **Universal immunization, recommended in 2006, has not yet penetrated the affected cohorts**
- **Risk from PDMP should be *de minimis*—except perhaps SD plasma**
- **VNRBD populations are, as yet, spared**

The AABB TTD committee is monitoring events & considering revisions to prior statements

Thanks

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