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Acute hepatitis A among HIV-infected Thai MSM is linked to MSM outbreaks In Europe and Taiwan

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Background

- In 2016-17 outbreaks of acute Hepatitis A virus (HAV) infection were reported among men who have sex with men (MSM) in Taiwan, the Netherlands, Germany, and the United Kingdom [1,2,3,4].
- Phylogenetic analysis linked the outbreaks in Asia and Europe with transmission presumably through oral-anal sexual contact.
- HAV is becoming less common in Thailand; the age at which 50% of the population is seropositive for anti-HAV antibodies increased from 4.48 years in 1972 to 42 years in 2014 Figure 1).
- No outbreak of HAV had been reported in the Bangkok metropolitan area since 2002 (Figure 2).

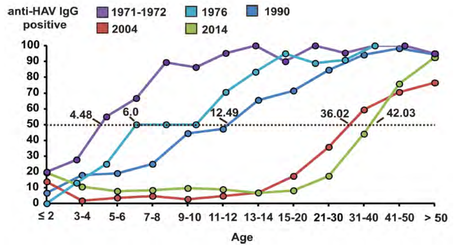

Figure 1: Comparison of anti-HAV IgG positivity from 1971 to 2014. Intersection of the seroprevalence curve with the dotted line indicates the mean age at which 50% of the individuals in the population possessed anti-HAV IgG. (source: Sa-nguanmoo, PLoS One, 2016 [5]).

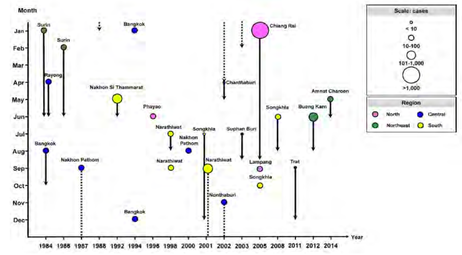

Figure 2: Documented hepatitis A outbreaks in Thailand from 1984 to 2014. The most recent outbreak in the Bangkok metropolitan area was in Nonthaburi in 2002. (source: Sa-nguanmoo, PLoS One, 2016 [5]).

Methods

- The SEARCH010/RV254 cohort has recruited participants with acute HIV infection (AHI) in Bangkok and Pattaya, Thailand since 2009 [6].
- 478 individuals enrolled through June 2017.
- No cases of acute HAV (defined as anti-HAV IgM positive with symptoms of acute hepatitis) were diagnosed until 2017, when 5 cases were identified.
- Phylogenetic analysis used a 378 bp sequence of *vp1* compared to reference sequences from GenBank.
- The phylogenetic tree was produced in MEGA V6.0.

Results

- Five cases of acute HAV were identified in the cohort in March-May 2017.
- All were symptomatic, with abdominal pain (n=5), fatigue (5), jaundice (3), fever (3), and nausea/vomiting (2) most frequently reported (Table 1).
- All were male, median age 37 years (range 20-43).
- None had traveled outside of Thailand. All reported male sexual partners within the preceding 3 months.
- Laboratory abnormalities are reported in Table 2.
- Four cases were on antiretroviral therapy a median 19.5 (range 7-53) months with HIV RNA <20 copies/ml and median (range) CD4 804 (602-1008) cells/mm^3.
- One case was diagnosed with acute HAV simultaneously with AHI and had HIV RNA of 7.2 log$_{10}$ copies/ml and CD4 132 cells/mm^3.
- Pre-existing hepatitis B infection was present in one case, another case had pre-existing hepatitis C infection.
- HAV was sequenced from stool and/or plasma in 3 cases; phylogenetic analysis showed 100% concurrence between the Bangkok MSM cases and with HAV in the recent Taiwan and Netherlands outbreaks (Figure 3).
- An additional female case in Bangkok not in the cohort and not known to have HIV (ChulaCU22-HAV17) was diagnosed in June 2017 with 99.7% similarity to the MSM cases on the 378 bp sequence and 99.9% similarity to the first identified MSM case on a longer 1110 bp sequence.

Symptom	n	%
Abdominal pain	5	100%
Fatigue	5	100%
Jaundice	3	60%
Fever	3	60%
Nausea/Vomiting	2	40%

Table 1: Symptoms of acute hepatitis A infection reported among HIV-infected Thai MSM, 2017 (n=5)

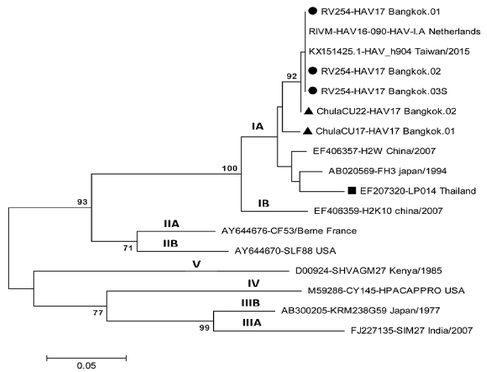

Figure 3. Phylogenetic analysis of *vp1* in selected hepatitis A strains of among HIV-infected MSM in Bangkok, Thailand, 2017. Roman numerals indicate genotype; numbers at nodes are bootstrap values. Produced in MEGA V6.0. ● = MSM case Bangkok 2017; ▲ = non-MSM case Bangkok 2017; ■ = Thailand case outbreak prior to 2015.

Laboratory	units	median	range
ALT (maximum)	IU/L	760	572 – 2,611
AST (maximum)	IU/L	272	110 – 1,253
Total bilirubin (max.)	mg/dL	5.7	3.4 – 7.8
Direct bilirubin (max.)	mg/dL	5.4	2.5 – 5.9
CD4 (n=4 on ART)	cells/mm^3	804	602 – 1,008
Anti-HAV IgM S/CO ratio (n=3)		9.36	7.94 – 11.02
Anti-HBs positive (n,%)		3	60%
HBsAg positive (n,%)		1	20%
Anti-HCV positive (n,%)		1	20%
Anti-HEV IgM positive (n,%)		0	0%

Table 2: Laboratory abnormalities among HIV-infected Thai MSM with acute hepatitis A infection, 2017 (n=5)

Conclusions

- This is the first outbreak of acute HAV reported among HIV-infected MSM in SE Asia, and the first HAV outbreak locally transmitted in Bangkok since 2002.
- Phylogenetics shows that the Bangkok HAV cases are linked to outbreaks among MSM in Europe and Taiwan, most likely imported to Thailand by one or more MSM and transmitted locally via sexual networks.
- Next Steps:
  - Screen all participants in the HIV cohort for anti-HAV IgG
  - Offer HAV vaccine to non-immune participants
  - Test for immune response in all vaccine recipients
- Recommendations:
  - Reporting systems for HAV infection in Thailand should be strengthened
  - HAV vaccine should be promoted for MSM and for people with HIV infection In Thailand
  - MSM who engage in sex while traveling should be aware of the risk for HAV infection and should be screened and vaccinated

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