HEPATITIS A VIRUS IN BLOOD DONORS : RECENT FRENCH EXPERIENCE

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BACKGROUND
AIM OF THE STUDY

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Hepatitis A: an epidemiological survey in blood donors, France 2015 to 2017

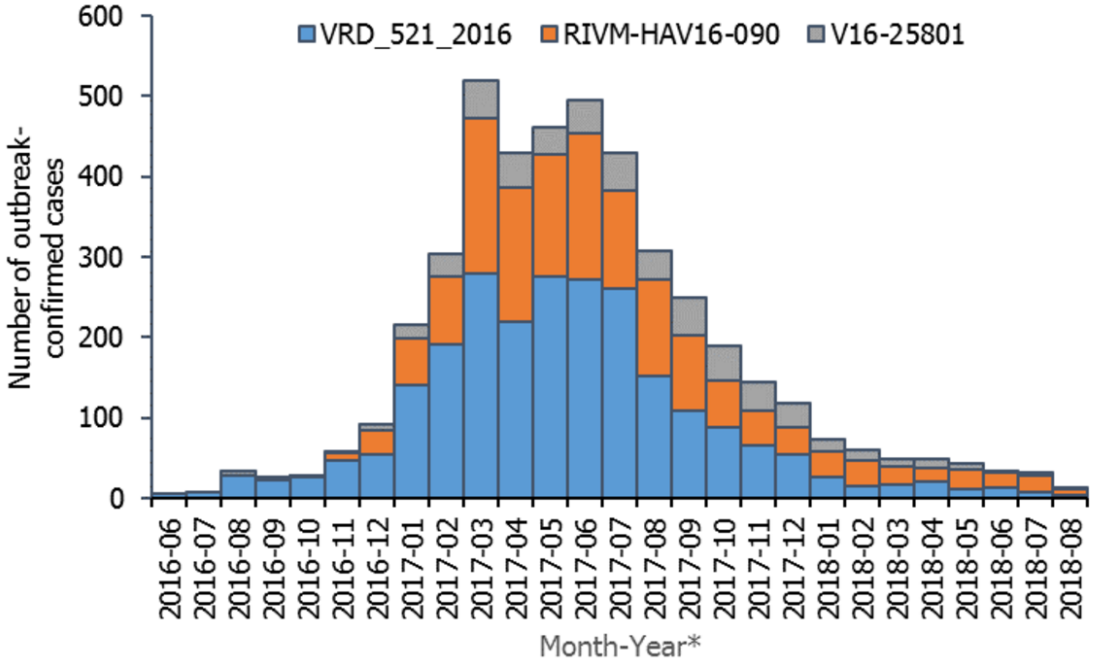
- Since mid-2016, hepatitis A virus (HAV) outbreaks, involving at the beginning predominantly men having sex with men (MSM), have affected most European countries.

➥ 3 outbreak strains :

VDR_521_2016 (UK return from Spain)

RIVM_HAV16_090 (Europride Amsterdam)

V16_25801 (Berlin, 2017)



- 25032 laboratory-confirmed cases were reported in 24 EU countries between January 2017 to August 2018
- 4475 outbreak confirmed cases (June 2016 – sept 2018)
  - Male-to-female (M/F) sex ratio = 6,8
  - 2017 May (M/F) sex ratio = 11,8
  - 2018 May to August (M/F) sex ratio = 4,0

ECDC : Epidemiological update 12,sept 2018 : Hepatitis A outbreak in the EU/EEA mostly affecting men who have sex with men.

IN FRANCE

- In mainland France, the number of reported cases increased from 701 and 666 in 2015 and 2016, respectively, to 3351 in 2017 with a frequency peak in July 2017.
- In 2016/2017, a significant number of cases appeared associated with MSM activity as deduced from an 80% proportion of males among notified cases and the detection of MSM-associated outbreak strains in > 90% of analyzed cases.

- Hepatitis A virus NAT screening is a requirement for donations contributing to plasma-derived medicinal products.
- Plasma for fractionation collected by the French transfusion public service (EFS) is provided to LFB (French pharmaceutical company),
- HAV-RNA screening is performed by EFS on behalf of LFB on all blood donations for therapeutic use since 2015.

AIMS OF THE STUDY :

- To estimate the HAV-RNA prevalence in blood donors before and after the 2017 HAV outbreak in France,
- To quantify the risk to collect an asymptomatic blood donor infected by HAV,
- To investigate HAV infection risk factors,
- To describe viral loads, genotypes,
- To study transfused blood products and recipients outcome.

MATERIAL & METHODS

NAT screening (EFS labs) :

- HAV-RNA screening is carried out using :
  - the Procleix HAV/B19 assay (Grifols)
  - Tigris System automation (Grifols)
  - On pool of 96 donations (estimated LOD: 100 UI /ml).

Virological analysis (National Reference Center) :

- Viral load in individual samples is assessed with the RealStar® HAV RT-PCR Kit (Altona Diagnostics) using serial dilutions of the WHO International Standard for HAV-RNA NAT assays.
- Viral strain characterization by amplification and sequencing of a 508 base-pair fragment encompassing the VP1/2A junction.
- Phylogenetic analysis (donors and recipients strains)

Epidemiological investigations :

- questions about professional exposure, the presence of HAV infected persons in the circle of family and friends, the presence of children < 3 years-old, travel history, and seafood consumption.
- Sexual risk factors were not systematically investigated.

Gallian et al, Euro Surveill. 2018;23(21)

RESULTS (1): HAV-RNA PREVALENCE

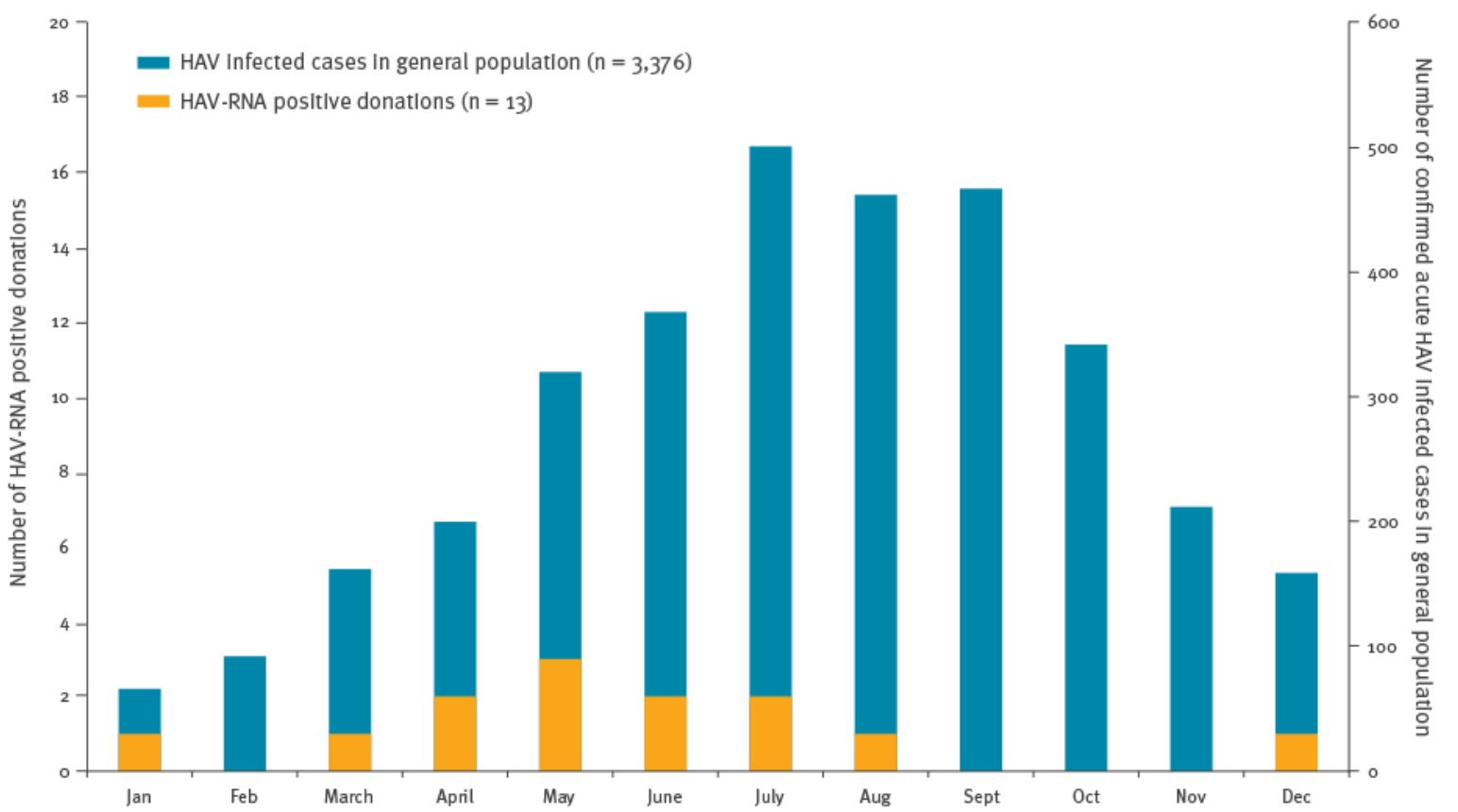
- Thirteen donors were found HAV-RNA positive in 2017 vs 2 donors in 2015 and 3 donors in 2016.

- Hepatitis A virus RNA prevalence of blood donations was ~5 fold higher in 2017 (4,4/10E^6 donations) than in 2015-2016 period (0,9/10E^6 donations) p=0.0005.

Gallian et al, Euro Surveill. 2018;23(21)

RESULTS (2): HAV-RNA PREVALENCE

Monthly number of laboratory-confirmed hepatitis A cases stratified by cases in the general population (Data obtained through the national mandatory reporting system) and hepatitis A virus-RNA positive blood donations, France, 2017 (n = 3,389)



- Frequency peaked at 9.4 /10E^6 donations in April-July 2017, at a time when the number of cases in general population was still increasing.

Gallian et al, Euro Surveill. 2018;23(21)

RESULTS (3): CLINICAL AND VIROLOGICAL FINDINGS

- All involved donors were confirmed asymptomatic at time of blood donation.

- Sixteen donors reported clinical symptoms compatible with acute HAV infection : 11 had symptoms 2 to 12 days after donation, one 31 days post-donation. Two had had symptoms 2 and 8 weeks before donation.
- Two remain asymptomatic after donation,

- Genotype IA MSM outbreak-associated strains were identified in 12 of the 13 cases detected in 2017 (VDR_521_2016 in 6 and RIVM-HAV16-090 in 6). Genotype IIIA : 1 case.

- Viral loads (2015 to 2017) ranged from 1.2 to 8.59 log10 IU/mL and did not differ significantly between 2015-2016 and 2017.

Gallian et al, Euro Surveill. 2018;23(21)

RESULTS (4): RISK FACTORS, BLOOD PRODUCTS OUTCOME

- Despite a higher male to female ratio (5,5 vs 0,7 before 2017) and the identification of MSM-associated outbreak strains, only 1/11 infected male donors in 2017 self-reported as MSM.

- Other HAV risk factors (food or professional exposure mainly) were identified in 6 (5 males, 1 female) of the 12 evaluable donors in 2017 while no risk factors were identified for the remaining 5 donors (4 males, 1 female). Similar food or professional exposure risk factors were identified in 4 of the 5 blood donors identified in 2015 and 2016.

- Involved red blood cell concentrates were destroyed (n=9) if not already transfused (n=3). Nine platelet concentrates were transfused before results were made available. All collected plasma were discarded (n=17).

- In 2017, haemovigilance enquiry of HAV-RNA positive blood transfusions (n=12) revealed one case of transfusion-transmitted hepatitis A (confirmed by molecular comparison of donor and recipient viral strains) involving an apheresis platelet concentrate.

Gallian et al, Euro Surveill. 2018;23(21)

2018 and 2019 (up to mid-May) update (1) :

- Thirteen donors were found HAV RNA positive in 2018 and none from January to mid-May 2019

In 2018 :

- Decrease of sex ratio, 10 males / 3 females , sex ratio (M/F) = 3,33 *vs* 5,5 in 2017 and 0,7 in 2015-2016 (Europe : May to August 2018 (M/F) sex ratio = 4,0)

- HAV genotypes : molecular characterization available for 9/13 donations
  - Decrease of genotype IA : in 6 cases in 2018 vs 12 in 2017,
  - Genotype IB detected in 3 cases

2018 and 2019 (up to mid-May) update (2) :

In 2018 :

- HAV risk factors were identified in 8 donors (6 males, 2 female) :
  - Food exposure : n=3
  - Professional risk exposure : n=1
  - Affected areas : n=4
- Nine donors reported clinical symptoms compatible with acute HAV infection : 6 had had symptoms 1 to 21 days after donation, 3 had had symptoms 2 to 15 days before donation.
- Two remain asymptomatic after donation.

2018 and 2019 (up to mid-May) update (3) :

In 2018 :

- All involved red blood cell concentrates were destroyed (n=11). All collected plasma were discarded (n=13). Seven platelet concentrates were transfused before results were made available, only one was discarded.

- Haemovigilance enquiries identified 2 additional transfusion-transmitted hepatitis A, involving 2 Intercept-treated pooled (n=5) whole blood platelet concentrates.

CONCLUSION

- During the 2017 HAV outbreak in France, the risk of collecting asymptomatic blood donors was increased 5 fold (while remaining a rare event). This risk persist at the same level during ~1 year after the peak observed in general population, despite a decrease in cases in general population.

- Genotype IA MSM outbreak-associated strains were identified in most cases detected in 2017, but to a lesser extent in 2018. In 2018, others strains (genotype IB) were detected, probably in relation with the outbreaks at that time.

- At least 3 transfusion-transmitted hepatitis A documented in 2017-2018 (all non severe).

- Resistance of HAV to the pathogen reduction technologies.

- Risk mitigation may be improved by increasing the frequency of NAT testing runs but require impacting modifications.

Thank you for your attention !

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