Failure of risk-behavior based donor selection: what can the virus tell us.

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Introduction

Transfusion-transmissible infections (TTI) remain a major concern for blood safety. To minimize the number of potentially infectious donations, the Netherlands have implemented risk-behaviour based donor selection. Nevertheless, routine TTI donor screening identified 235 new donors and 61 repeat donors positive for Human Immunodeficiency virus (HIV), hepatitis B virus (HBV) or hepatitis C virus (HCV) during the last decade (2005-2014).

HIV, HBV and HCV are characterized by high genetic variability. Different genotypes have spread via distinct transmission networks; therefore the molecular typing of individual viral genomes can be linked to geographic origin, route of transmission and time of infection. To estimate the characteristics and magnitude of undisclosed risk factors among donors with HIV, HBV and HCV, viral typing results were combined with the self-reported risk behaviour at reported at posttest counseling. At post-test counseling 12% of donors disclosed risk factors which, if revealed during the donor selection procedure, would have caused permanent donor deferral.

Materials and Methods

- *Participants:* Dutch new and repeat donors with HIV RNA (n=31) or HCV RNA (n=47) in the period 2005-2014, or HBV DNA (n=125) in the period 2009-2014.
- *Viral typing:* Amplification and sequencing of the HIV *pol* gene (1200 bp), HBV Core, Polymerase and Surface gene (± 1980 bp), and HCV NS5B gene (707 bp).
- *Phylogenetic analysis:* Phylogenetic trees were built per HIV-subtype with a GTR model in Fasttree (Subtype B) or a maximum-likelihood (ML) approach in MEGA (non-subtype B), and contained all donor sequences plus 8673 HIV-sequences from the Dutch ATHENA cohort. Clusters within subtype B were identified using Phylopart with a local support value 0.9 and median pairwise patristic distance below the 5th percentile of distances in the whole tree. For HBV and HCV, ML phylogenetic trees were built using GTR+G model in MEGA. Phylogenetic clusters were linked to specific routes of transmission, geographic location or time of infection based on the self-reported risk behaviour at posttest counselling.

Results

HIV:

- The majority (67%) of HIV-strains were of subtype B (Western-Europe), 13% CRF02_AG (Western Africa), 13% subtype C and 8% others (Sub Saharan Africa).
- Phylogenetic analysis male donors: 10/12 (83%) of subtype B and 1/2 (50%) of non-subtype B infected male donors were part of robust MSM clusters (Figure 1).
- Phylogenetic analysis female donors: 1/4 (25%) of subtype B infected female donors were part of MSM clusters (she reported sex with a bisexual man); 5/6 (83%) of non-subtype B infected female donors had a male African sexual partner.

HBV:

- HBV genotype is strongly associated with donor ethnicity: A1 (Latin America), A2 (Western Europe), B and C (South-East Asia), B3 (Surinam), D1 (Turkey + Central Asia), D2 and D3 (Eastern Europe + Indonesia), D7 (Morocco) (Figure 2).
- The genotype distributions of acute HBV (70% genotype A2) and chronic HBV (69% non-genotype A2) reflect different HBV epidemiologies (Figure 2).
- One single HBV genotype A2 strain accounts for 25/34 (74%) of HBV-positive repeat donors, 3/6 (50%) of new donors with acute HBV infection, and 4/63 (6%) of new donors with chronic HBV infection (Figure 2).

HCV:

- Only 2 Dutch repeat donors acquired HCV during the last 10 years.
- HCV genotype distribution in Dutch donors: 1a (37%), 1b (22%), 3a (17%), 2b (7%), 4d (5%), others (13%).
- There was no evident link between HCV genotype and self-reported risk-behavior, except for HCV subtypes acquired in non-western countries.

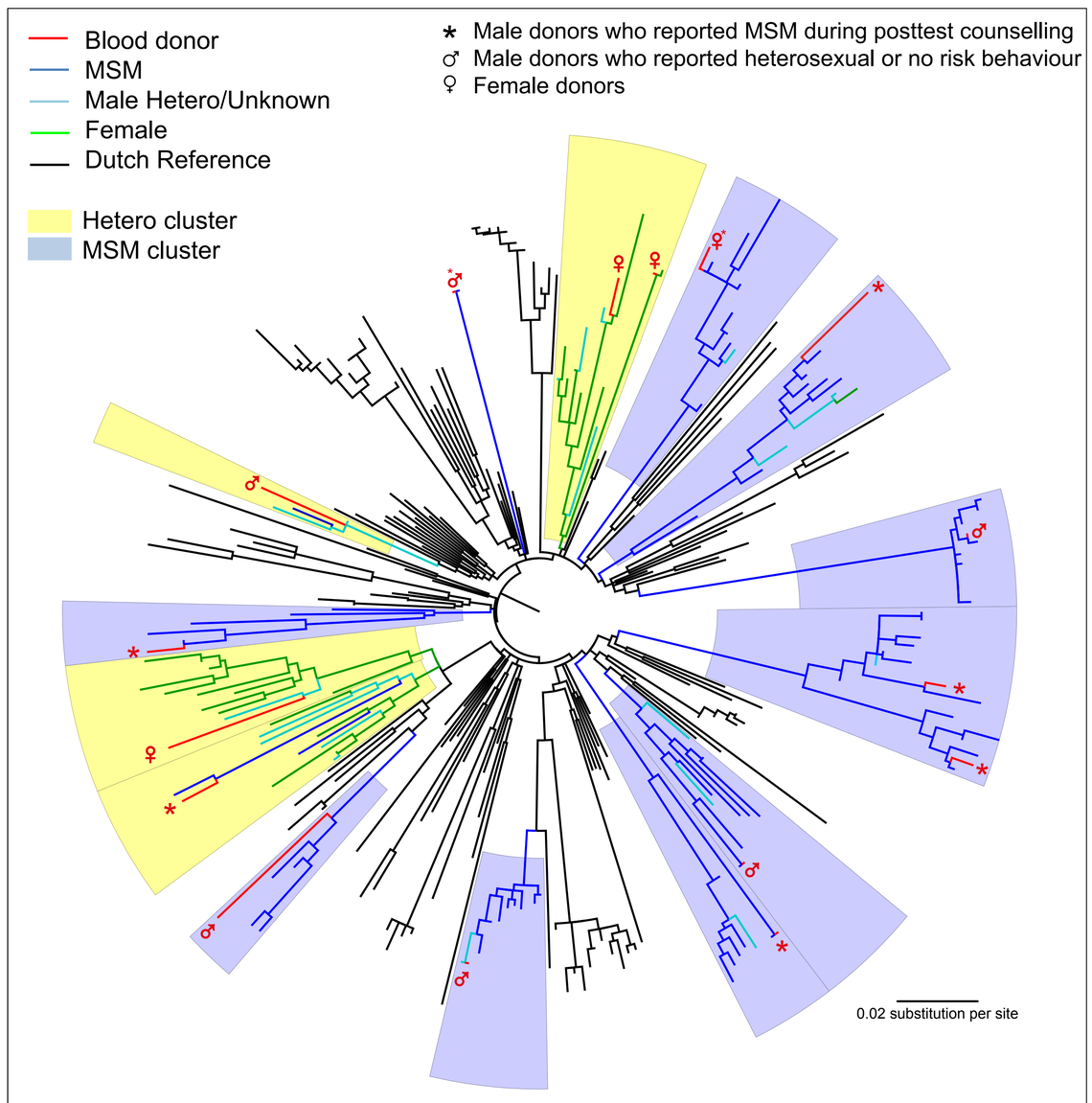

Figure 1: Phylogenetic tree of HIV-subtype B (16 donors + 6861 ATHENA sequences) Transmission clusters contained 14/16 Dutch donors with HIV subtype B, and varied in size from 4 to 103 individuals. Clusters containing donors were highlighted; if these clusters had >10 sequences, the 10 genetically most related to the donor were shown.

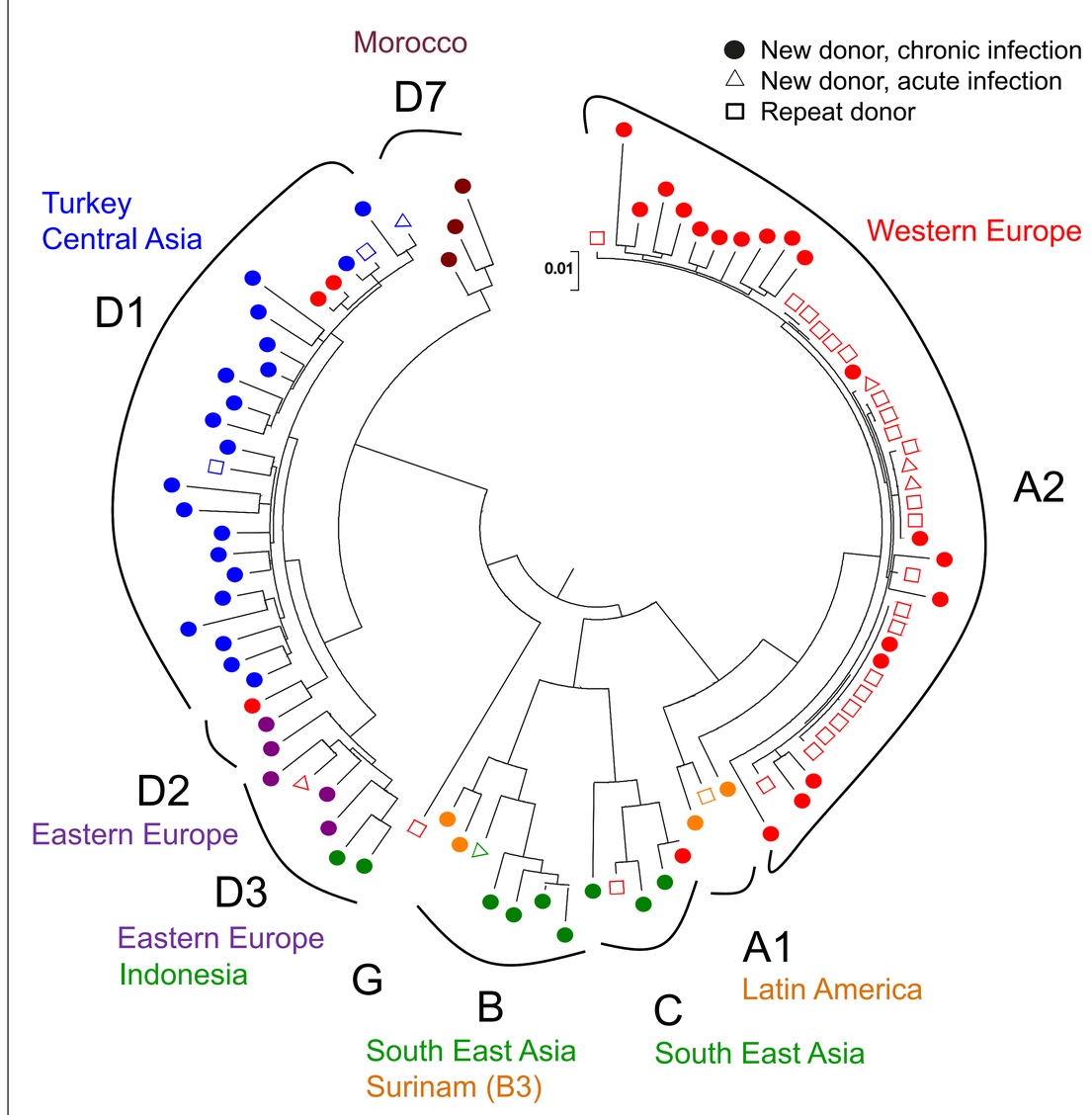

Figure 2: Phylogenetic tree of HBV donor sequences (97 donor sequences)

Conclusions

- **Our molecular epidemiological approach revealed that 86% of HIV-positive male donors in the Netherlands are part of MSM transmission networks; only 46% of the HIV-positive male donors disclosed male-to-male sex during posttest counselling.**
- **Viral typing confirmed heterosexual transmission in 90% of female donors with HIV, mostly by partners from high-endemic countries**
- **Longstanding HBV infections in Dutch donors show a wide diversity of HBV genotypes and are strongly linked to donor ethnicity, whereas 70% of acute HBV infections are of one single HBV A2-lineage that affects both MSM and heterosexuals.**
- **The HCV epidemic among the general Dutch population has been halted; no link was found between HCV genotype and risk behaviour in Dutch new donors.**