

HCV SPREADS AMONG HIV-POSITIVE MEN WHO HAVE SEX WITH MEN: Separate transmission networks in Europe and Australia

T van de Laar (1), M Danta (2,3), A Baumgarten (4), S Bhagani (2), S Bruisten (1,5), M-L Chaix (6), G Dore (3), G Dusheiko (2), M Fisher (7), H Götz (8), S Neifer (4), M Nelson (9), M Prins (1,5), S Pol (6), O Pybus (10), W Rawlingson (3,11), J Rockstroh (12), M Vogel (12), P White (3,11) and R Coutinho (1,5,13)

(1) Health Service, Amsterdam, The Netherlands; (2) Royal Free and University College, London, UK; (3) University of New South Wales, Sydney, Australia; (4) Practice DCB, Berlin, Germany; (5) CINIMA AMC, Amsterdam, the Netherlands; (6) Necker Hospital, Paris, France; (7) Brighton and Sussex University Hospital Trust, Brighton, UK; (8) Health Service, Rotterdam, the Netherlands; (9) Chelsea and Westminster Hospitals, London, UK; (10) Oxford University, Oxford, UK; (11) Prince of Wales Hospital, Sydney, Australia; (12) University of Bonn, Bonn, Germany; (13) RIVM, Bilthoven, the Netherlands

Objective

Is sexual transmission of HCV among HIV-positive men who have sex with men (MSM) restricted to small city-bound outbreaks or do large scale international transmission networks exist?

Introduction

- Increased sexual risk behavior after the introduction of HAART has resulted in the emergence of high-risk sexual networks susceptible to new STI.
- Since 2000 HCV incidence among HIV-positive MSM in Europe and Australia is rising and linked to high-risk sexual behavior.
- HIV/HCV coinfection has been associated with lower rates of spontaneous HCV clearance, accelerated HCV related liver disease, less favorable HCV treatment outcomes, restrictions in HAART and enhanced clinical progression of HIV.

Methods

- Study participants were 226 HIV-positive MSM diagnosed with acute HCV infection after 2000 at HIV or STI clinics in England (n=107), the Netherlands (n=58), Germany (n=24), France (n=12) and Australia (n=25).
- HCV RNA amplification (436 bp) using a nested RT-PCR based on the NS5B region of the HCV genome.
- Phylogenetic trees were constructed by the maximum likelihood method using HKY substitution model with gamma distribution (PAUP* 4.0).
- Date of origin for each cluster was calculated using the molecular clock approach based on a Bayesian MCMC Method and Beast v.1.3.
- Percentage of divergence events that took place after the introduction of HAART in 1995 were calculated.

Results

- HCV NS5B Amplification succeeded in 200/226 (88%) of MSM cases; 175/200 (88%) were infected with difficult-to-treat HCV strains of genotypes 1 and 4.
- Phylogenetic analysis revealed 11 distinct monophyletic clusters containing 4-37 sequences each, covering 79% of all MSM sequences (Table 1). Figure 1 shows a phylogenetic tree of the predominant HCV subtype 1a.
- Five out of six larger cluster (>10 sequences) contained sequences of more than one European country (Table 1); country-specific clusters tend to be smaller (< 10 sequences) or are Australian (Table 1).
- In Europe, 88% of MSM clustered with at least one other MSM; 74% of MSM were infected with a HCV strain circulating in more than one European country.
- The year of origin of specific MSM clusters goes back to 1975, but the majority (85%) of HCV spread, measured in divergence events, occurred after 1995 (Table 1).

Table 1: Identified HCV clusters in HIV-positive MSM from England (UK), the Netherlands (NL), Germany (GE), France (FR) and Australia (AU), the year of cluster origin and the percentage of cluster divergence since 1996

Cluster	Geno	Size (n)	Countries in cluster	Year of origin (95%CI)	Divergence since 1996
Cluster 1	1a	37	UK, NL	1984 (1974-1992)	86 %
Cluster 2	4d	34	NL, FR, GE, UK	1975 (1961-1988)	85 %
Cluster 3	1a	19	NL, UK, GE	1993 (1985-1999)	95 %
Cluster 4	1a	17	UK, GE	1988 (1977-1997)	94 %
Cluster 5	1a	12	GE, NL, UK, AU	1996 (1989-2001)	100 %
Cluster 6	4d	12	UK	1995 (1989-1999)	91 %
Cluster 7	1a	6	NL, GE	1998 (1990-2003)	100 %
Cluster 8	1a	6	AU	1983 (1970-1993)	20 %
Cluster 9	3a	6	UK, FR	1984 (1974-1993)	0 %
Cluster 10	1a	4	AU	2001 (1996-2004)	100 %
Cluster 11	1b	4	UK	-	-

Conclusion

- Phylogenetic analysis reveals two separate networks in Europe and Australia of high-risk HIV-positive MSM in which HCV rapidly and persistently spreads.
- Increasing evolutionary distances and degree of international mixing with cluster size are consistent with model of regional spread.
- Routine HCV screening in HIV-positive MSM is a must!
- Sexual network targeted prevention is needed to mitigate further spread of HCV and to prevent spillover to MSM currently outside this network.

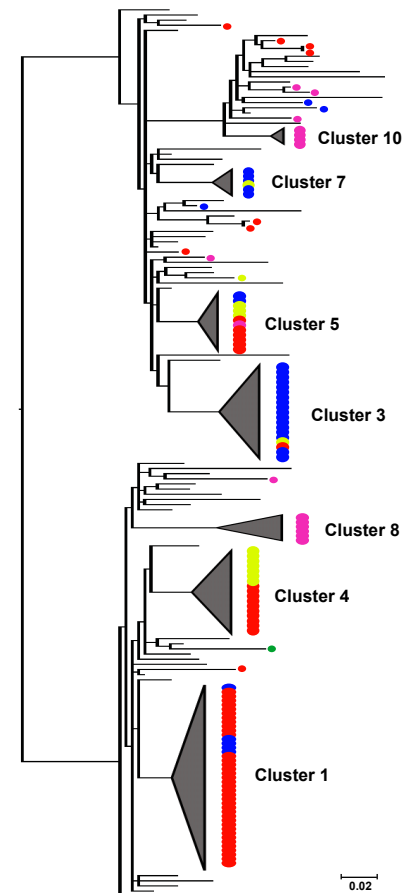


Figure 1: NS5B phylogenetic tree of HCV subtype 1a. Monophyletic clusters are shaded, country of origin: (●) England, (●) Netherlands, (●) Germany, (●) France, (●) Australia