Increase of the prevalence of HIV-1 non-B subtypes in Germany Results from the HIV-1 seroconverter study

Somogyi S[1], Meixenberger K[1], Bartmeyer B[2], Jansen K[2], Scheufele R[2], Bieniek B[3], Dupke S[4], Jessen H[5], Schürmann D[6], Hamouda O[2] and Kücherer C[1] on behalf of the German HIV-1-Seroconverter Study Group

1 Robert Koch-Institute, Centre of HIV and Retrovirology, Nordufer 20, 13353 Berlin 2 Robert Koch-Institute, HIV/AIDS, STI and Blood-borne Infections, DGZ-Ring 1, 13086 Berlin
3 Medical Practice City Ost, Gubener Str. 37, 10243 Berlin 4 Medical Practice Driesener Sraße, Driesener Str. 11, 10439 Berlin 5 Medical Practice Jessen2 + Kollegen, Motzstr. 19, 10777 Berlin
6 Charité-University Medicine Berlin, Augustenburger Platz 1, 13353 Berlin

ROBERT KOCH INSTITUT

Background

The HIV-1 pandemic is caused by genetically divergent subtypes and circulating recombinant forms (CRFs). Currently HIV-1 is classified into four groups: group M, O, N and P. The epidemically relevant M group of HIV-1 is subdivided into nine genetically distinct subtypes A, B, C, D, F, G, H, J, K and presently 51 CRFs. Some studies revealed an impact of HIV-1 subtypes and CRFs on disease progression and potential preferential transmission routes are discussed. Although subtype B is the most common subtype in Europe, predominating HIV infections in men who have sex with men (MSM), an increase of non-B subtypes was observed in several European countries. We aimed to evaluate the dynamics of HIV-1 subtype spread in patients with a known date of infection (HIV-1 seroconverter cohort).

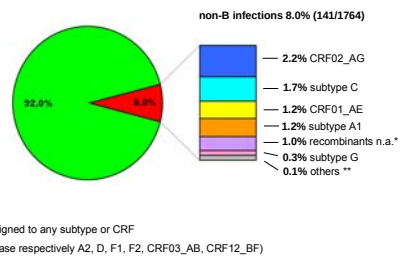
Material & Methods

The HIV-1 *pol* subtype was determined in 1764 drug-naïve HIV-1 patients in Germany with a documented seroconversion (1996 – 2010). The study is representative for MSM, the major transmission group of the study cohort (87.5%). *Pol*-sequences (99 amino acids of protease and 296 amino acids of reverse transcriptase) were PCR-amplified from viral RNA (ViroSeqTM genotyping system, Abbott). Subtype was determined using the REGA-tool (version 2.0) and if required by additional phylogenetic analysis with an extended panel of reference sequences (Neighbor joining and Maximum Likelihood; PHYLIP package version 6.5, Felsenstein J). Bootstrap analysis was performed with 1000 pseudo data sets. The $\chi 2$ test or the Fisher exact test was used as appropriate to compare categorical variables. Logistic regression was used to calculate time trends.

Results

Characteristics of the study population		Total	%
Genotyped *(pol)*		**1764**	**100**
Median age [years] ($CI_{95\%}$)		33 (27-39)	
Gender	male	1674	94.9
	female	88	5.0
Transmission group	MSM	1548	87.8
	HET	143	8.1
	IDU	23	1.3
	HPL	14	0.8
	Occupational risk (OR)	4	0.2
	unknown	32	1.8
Origin of the patients	Germany	1505	85.3
	Other countries	259	14.7

Figure 1. Drug naïve study population with established timeframe of seroconversion (1996-2010)



*not assigned to any subtype or CRF
**(one case respectively A2, D, F1, F2, CRF03_AB, CRF12_BF)

Figure 2. Prevalence of non-B subtypes and CRFs in the german seroconverter cohorte (1996-2010)
8.0% (141/1764) of the patients are infected with non-B subtypes and CRFs.

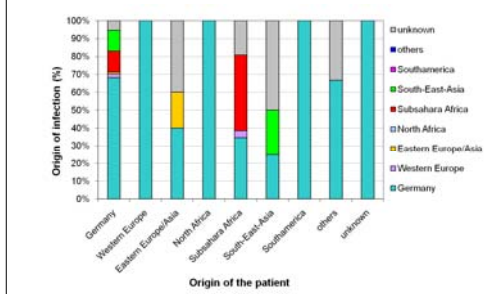


Figure 3. Origin of non-B infections in the study cohort
68.1 % (64/141) of the patients originate from germany and where infected in germany. Patients from high prevalence countries (Subsahara Africa and South-East-Asia) where mainly infected in the country, they originate from.

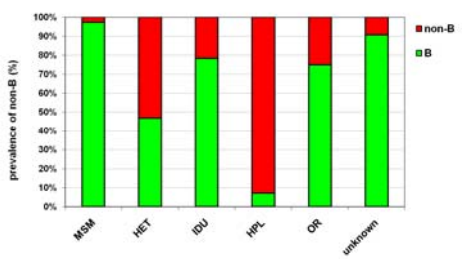


Figure 4. Prevalence of non-B infections in each of the transmission groups.
In MSM only 2.8% (43/1548) of the patients are infected with non-B viruses , in IDU non-B infections occure in 21.7% (5/23). In Heterosexuals non-B infections predominate with 53.1% (76/143).

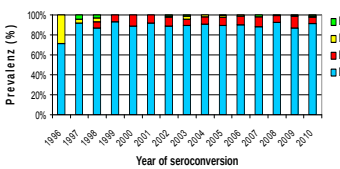


Figure 5a. Prevalence of transmission groups

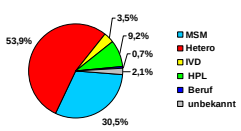


Figure 5b. Distribution of non-B infections in transmission groups

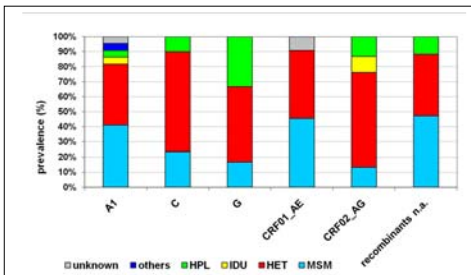


Figure 6. Prevalence of non-B subtypes and CRFs in different transmission groups
In MSM all relevant non-B subtypes and CRFs, identified in the study, are observed. There is no preferential transmission route for particular non-B viruses.

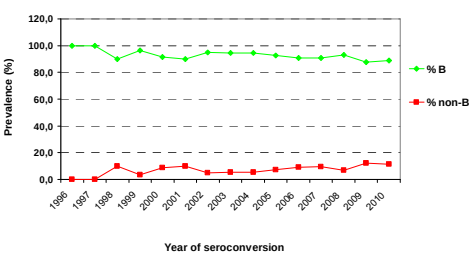


Figure 7. Prevalence of non-B infections over time (1996-2010)
There is a significant increase (p_{trend} = 0.009273) of non-B infections since 1998, which is not due to a specific subtype (data not shown).

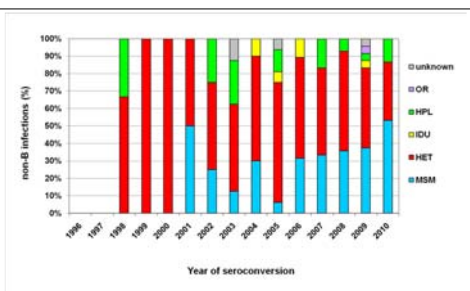


Figure 8. Distribution of non-B infections in transmission groups per year of seroconversion
Non-B infections are observed since 1998 in the german seroconverter cohorte.
They occure in all transmission groups, in MSM with a trend of increase since 2001.

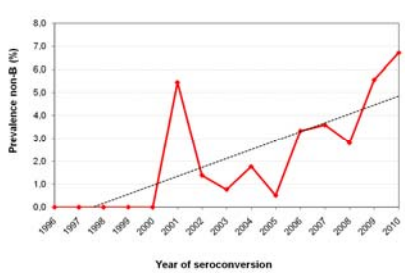


Fig. 9. Trend of non-B infections in MSM
There is significant increase for non-B infections in MSM over time (p_{trend} = 0.000552).

Conclusions

Despite the fact, that HIV-1 non-B strains are linked to heterosexually transmitted infections, no preferential transmission route for specific non-B viruses or CRFs was identified. Since non-B infections first occured in the german serovonverter study they are identified in all transmission groups with a trend of increase in MSM. These findings are consistant with studies in other European countries. The prevalence of non-B subtypes and CRFs in MSM should be further monitored to follow the spread of HIV-1 various subtypes and its potential impact on disease progression.

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contact: somogyis@rki.de

Participating institutions of the German Seroconverter Study