HIV transmission among Seattle adolescents

Joshua Herbeck,[1] Elizabeth Wolf,[2,3] Stephen van Rompaey,[4] Katherine Thomas,[1] Mari Kitahata,[4,5] and Lisa Frenkel[2,3,6]

University of Washington [1]Department of Global Health, [2]Department of Pediatrics, [4]Center for AIDS Research, [5]Department of Medicine, [6]Department of Laboratory Medicine, and [3]Seattle Children's Research Institute

BACKGROUND

- Adolescents (youth 13 to 24 years old) represent a significant proportion of new infections in the United States.(*e.g.* 1, 2)
- Phylogenetic analyses of HIV gene sequences can be used to identify viral transmission clusters.(*e.g.* 3, 4)
- These clusters can be examined to infer risk factors for ongoing HIV transmission or increased relative infectiousness.(*e.g.* 5)

AIM: Describe factors associated with HIV transmission in Seattle adolescents

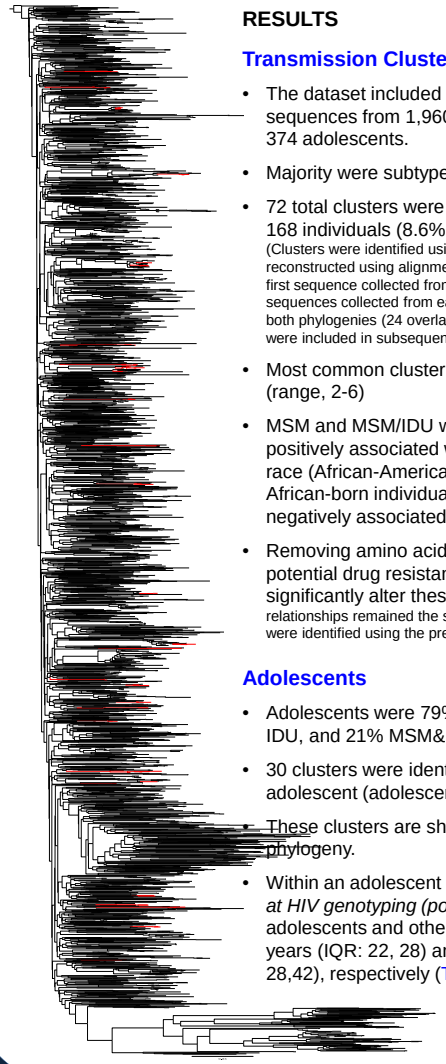
METHODS

- Partial HIV *pol* sequences (from 610 to 1080 bp in length) were obtained from the UW Clinical Virology Laboratory between 2/2000 and 3/2013.
- Clinical data linked to each *pol* sequence were abstracted from the UW HIV Information System and retrospective chart review.
- Demographics (age, sex, race), HIV transmission risk (self-reported), and housing status (including homelessness) recorded at the time of first HIV genotyping for drug resistance were abstracted from medical charts.
- Adolescents were classified as 13-24 years old at the time of first HIV care or earliest observed HIV-related data.
- We reconstructed maximum likelihood phylogenies using FastTree[6] within Geneious v. 8.0.5.[7] (with & w/out sites associated with drug resistance mutations)
- Clusters were identified using ClusterPicker[8] (sequences with a shared ancestral node, FastTree support value >95%, and maximum pairwise genetic distance <1.5%)
- Characteristics of individuals found in any cluster were compared to those of non-clustering individuals using logistic regression.

Table 1. Odds ratios for sequences *in* versus *not in* clusters

Characteristic	Total		In Cluster		Univariable			Multivariable[a]		
	N	%	N	%	OR	95% CI	*P*	OR	95% CI	*P*
Sex										
Total	1960	100	169	9						
Female	281	14	18	6	Ref.	--	--	Ref	--	--
Male	1665	85	151	9	1.46	0.88, 2.42	.15	0.70	0.33, 1.48	.35
Male to female[b]	14	1	0	0	--	--	--	--	--	--
Age Group										
Adult	1583	81	134	79	Ref.	--	--	Ref	--	--
Adolescent	374	19	35	21	1.11	0.75, 1.63	.61	1.09	0.73, 1.61	.68
Race										
White	1231	63	122	10	Ref.	--	--	Ref.	--	--
Black	375	19	18	5	**0.46**	0.28, 0.76	**.003**	**0.53**	**0.32, 0.89**	**.02**
Other[c]	180	9	12	7	0.65	0.35, 1.20	.17	0.76	0.40, 1.41	.38
Unknown	174	9	17	10	0.98	0.58, 1.68	.95	1.14	0.66, 1.96	.65
Risk Group										
Heterosexual[d]	373	19	17	5	Ref.	--	--	Ref.	--	--
IDU[e]	206	11	14	7	1.53	0.74, 3.16	.26	1.52	0.72, 3.18	.27
MSM[e]	987	50	102	10	**2.41**	1.42, 4.09	**.001**	**2.58**	1.28, 5.21	**.008**
MSM/IDU	394	20	36	9	**2.11**	1.16, 3.82	**.01**	**2.18**	1.02, 4.68	**.045**

[a] Multivariable model included sex, age group, race and risk group as covariates. [b] There were not enough patients categorized as male to female transgendered to include in either model. [c] "Other" race includes Asian, Black African, Hawaiian, Pacific Islander, Multiracial, and American Indian. [d] Heterosexual group includes those infected by transfusion and other (non-IDU, MSM or MSM/IDU) means. [e] IDU: Injection drug use; MSM: Men who have sex with men



RESULTS

Transmission Clusters

- The dataset included 3,118 total HIV-1 *pol* sequences from 1,960 individuals, including 374 adolescents.
- Majority were subtype B infections (96%).
- 72 total clusters were identified, representing 168 individuals (8.6% of all individuals) (Clusters were identified using 2 phylogenies, reconstructed using alignments composed of: 1. only the first sequence collected from each individual; and 2. all the sequences collected from each individual; all clusters from both phylogenies (24 overlapping, 48 non-overlapping) were included in subsequent analyses.)
- Most common cluster size was 2 individuals (range, 2-6)
- MSM and MSM/IDU were significantly positively associated with clustering. Black race (African-American race, rather than African-born individuals) was significantly negatively associated with clusters (Table 1).
- Removing amino acid sites associated with potential drug resistance mutations did not significantly alter these results (topological relationships remained the same, but slightly more clusters were identified using the previously defined thresholds).

Adolescents

- Adolescents were 79% male, 51% MSM, 8% IDU, and 21% MSM&IDU.
- 30 clusters were identified that included ≥1 adolescent (adolescent clusters).
- These clusters are shown in red in the phylogeny.
- Within an adolescent cluster, the median age *at HIV genotyping (pol sequencing)* for adolescents and other individuals was 24 years (IQR: 22, 28) and 35 years (IQR: 28,42), respectively (Table 2).

Table 2. Distribution and characteristics of HIV-infected individuals from Seattle that are placed within a phylogenetic cluster that contains at least one adolescent.

	Patients in clusters with ≥1 adolescent^			Patients in clusters with no adolescents	Patients not in clusters
	Adolescents^	Other*	All		
AGE, years (median, IQR)	**22.5** (21, 24)	**32** (27, 40)	26.5 (23, 35)	35 (29,42)	32 (26,38)
Sex[†]	34	52	72	97	1791
Male	29 (85)	50 (96)	66 (92)	85 (88)	1514 (85)
Race[†]	32	50	66	84	1634
White	27 (84)	42 (84)	57 (84)	65 (77)	1109 (68)
Black	4 (13)	4 (8)	7 (10)	11 (13)	357 (22)
Asian	1 (3)	3 (6)	2 (3)	3 (4)	43 (3)
HIV Risk Group[†]	34	52	72	97	1791
Heterosexual	3 (9)	4 (8)	7 (10)	10 (10)	356 (20)
IDU	3 (9)	3 (6)	5 (7)	9 (9)	192 (11)
MSM	24 (71)	37 (71)	48 (67)	54 (56)	885 (49)
MSM/IDU	4 (12)	8 (15)	12 (17)	24 (25)	358 (20)
Homeless[†]	3 (14)	11 (21)	7 (14)	3 (5)	77 (8)

[†] number of patients, (%), unless otherwise specified
^ Adolescents included patients without perinatally acquired HIV who were 13-24 years of age at time of first HIV care
* Characteristics for other individuals in adolescent clusters were counted once per adolescent, such that demographic characteristics for 8 individuals (4 adolescents and 4 adults) in "Other" column were counted twice.

CONCLUSIONS

- As described in previous work(*e.g.* 9, 10), the Seattle HIV epidemic is driven mainly by the MSM risk group. In this phylogenetic analysis, MSM and MSM/IDU individuals were significantly associated with clustering (ongoing HIV transmission).
- Adolescent individuals were not frequently found in phylogenetic clusters with other adolescents, but rather in clusters with adults.
- The Seattle MSM community may benefit from new prevention strategies aimed at age-discrepant pairs.
- Further work aimed at understanding the risks of HIV transmission among Seattle adolescents is needed.

REFERENCES

1. Centers for Disease Control and Prevention. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 U.S. dependent areas—2010. HIV Surveillance Supplemental Report 2012;17.
2. Saewyc, E, *et al.* Sexual Orientation, Sexual Abuse, and HIV-Risk Behaviors Among Adolescents in the Pacific Northwest. American Journal of Public Health, 2006; 96 (6).
3. Fisher M, *et al.* Determinants of HIV-1 transmission in men who have sex with men: a combined clinical, epidemiological and phylogenetic approach. AIDS, 2010; 24 (11).
4. Hue S, *et al.* HIV-1 pol gene variation is sufficient for reconstruction of transmissions in the era of antiretroviral therapy. AIDS, 2004, 18 (5).
5. Dennis, A. *et al.* Phylogenetic insights into regional HIV transmission. AIDS, 2012; 26 (14).
6. Price, M. *et al.* FastTree 2 -- Approximately Maximum-Likelihood Trees for Large Alignments. PLoS ONE, 2010; 5(3).
7. Kearse, M., *et al.* Geneious Basic: an integrated and extendable desktop software platform for the organization and analysis of sequence data. Bioinformatics, 2012; 28 (12).
8. Ragonnet-Cronin, *et al.* Automated analysis of phylogenetic clusters. BMC Bioinformatics, 2013, 14.
9. Public Health, Seattle/King County HIV Surveillance Report, through June 30, 2014.
10. Thiede, H. *et al.* Determinants of Recent HIV Infection Among Seattle-Area Men Who Have Sex with Men. American Journal of Public Health, 2009; 99 (No. 1S).

ACKNOWLEDGEMENTS We would like to thank James Mullins for assistance with this project.