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Background. HIV-associated neurocognitive disorders cause significant morbidity and mortality despite the advent of antiretroviral therapy. An understanding of fundamental mechanisms underlying HIV infection and transmission events in the central nervous system (CNS) is needed. Microglia are resident myeloid cells that are readily infected by HIV and may constitute a CNS reservoir. We evaluated and compared existing microglial cell lines and primary cell-derived microglia as potential model systems for studying HIV-microglia interactions.

Methods. We cultured two immortalized human microglial lines (HMC3, C20) and developed two primary microglial models: induced microglia (iMG) derived from primary human monocytes; and microglial-like cells (iMGL) differentiated from induced pluripotent stem cells (iPSCs). We compared these four microglial cell types to commercially available fetal microglia (PM) for a microglial comparator, and monocyte-derived macrophages as a non-microglial comparator cell. Each cell type was evaluated for the presence of typical myeloid and microglia-specific markers by flow cytometry and immunofluorescence microscopy. HIV infection was performed using macrophage-tropic HIV or VSV-G-pseudotyped HIV.

Results. After differentiation, the iMG and iMGL displayed characteristic microglial morphology: a spindle shape and a reduction in the central body, along with ramified cell processes. Flow cytometry revealed significant differences in surface markers among the cell types. iMG and iMGL displayed CD11b, CD45, CXCR4, CCR5 and lack of expression of CD4 and CX3CR1. In contrast, HMC3, C20, and PM were negative for CD11b, CD45, CX3CR1, CD4, CXCR4. Immunostaining showed that iMG and iMGL were positive for microglial markers TMEM119 and P2RY12. RNA Seq analysis is currently underway to determine gene expression differences between the microglial cell lines and our microglia models. In preliminary results, iMG and iMGL were both readily infected with HIV, and comparison with other lines is ongoing.

Conclusion. There is no standard model available for defining the molecular and cellular events involved in HIV infection of microglia. Significant differences in microglial markers and in HIV receptor and coreceptor levels were noted in this study. iMG and iMGL appear to be viable microglial models susceptible to HIV infection.

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2519. Urban vs Rural HIV-infected Persons Have Differential Gene Expression for Estrogen Signaling, Inflammation, and Cytokine Production Pathways

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Background. People aging with HIV (PAWH) are living longer with effective antiretroviral therapy and new HIV diagnoses are rising in older populations. Concurrent with trends in age, the epidemiology of HIV infection in the United States has shifted geographically and racially; the Southeast and African Americans now have the highest HIV incidence and prevalence. Although there are marked health disparities for rural and African American PAWH, limited data exist comparing aging phenotypes between rural and urban PAWH, and no data exist comparing mechanistic pathways between these populations. Among African American PAWH, we hypothesize that rural PAWH will be more likely than urban PAWH to have a molecular profile of advanced aging associated with chronic disease burden and shorter health span.

Methods. Demographics, clinical data, and RNA were collected from 14 matched pairs from rural (Wake Forest University, Winston-Salem, NC) and urban cohorts (ALiVE cohort, Johns Hopkins University, Baltimore, MD) matched on age, sex, Short Physical Performance Battery score, smoking status, and sample collection date. Raw sequences were examined for quality, aligned using STAR, and normalized using DESeq2. DESeq2 tested matched pair differential gene expression. Genes with an average read count threshold > 5, a genomic control adjusted P-value < 0.01 and a fold change > 1.3 were retained for further analysis using STRING, MCODE, and IPA to find functional and biological patterns.

Results. Of the 399 genes meeting significance criteria, 212 showed higher expression in the rural group; the remaining 187 genes showed lower expression in the rural group. Top enriched canonical pathways in the IPA analysis identified differential estrogen signaling ($P < 0.0001$), inflammation ($P < 0.001$), and cytokine production ($p = 0.005$). Protein–protein interactions involved in cell–cell signaling and intracellular trafficking were also differentially identified between the 2 populations.

Conclusion. Urban and rural PAWH have differential gene expression, particularly centered around estrogen signaling and inflammatory cytokine production. These findings merit further investigation to determine clinical significance, including correlation with phenotypes and healthspan between rural and urban PAWH.

Disclosures. **All authors:** No reported disclosures.

2520. Resource utilization in adolescents and young adults with HIV in the HIV Research Network

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Background. Adolescents and young adults (AYA) with HIV experience worse health outcomes than adults with HIV in the United States. Little is known about AYA patterns of utilization of costly healthcare resources.

Methods. We estimated utilization of outpatient, emergency department (ED), and inpatient care among 13–30 year-olds from 2006–2015. We stratified outpatient visits, ED visits and inpatient days per person-year (PY) by transmission mode (perinatal (PHIVY), non-perinatal (NPHIVY), age (13–17, 18–23, 24–30 years), CD4 strata (< 200, 200–499, ≥ 500 cells/μL) and presence or absence of viral load (VL) suppression (<, ≥ 400 copies/mL[c/mL]) combined with antiretroviral (ARV) use. We also quantified outpatient, ED, and inpatient care associated with specific AIDS-defining conditions.

Results. Among 4,450 AYA (PHIVY: 15%; NPHIVY: 85%), mean (SD) follow-up was 2.8 years (2.5) [PHIVY: 4.2 years (3.1); NPHIVY: 2.5 years (2.3)]. Mean age was 21.4 years (PHIVY: 16.9 years; NPHIVY: 22.3 years) and female sex was 28% (PHIVY: 52%; NPHIVY: 23%). Among PHIVY, most person-time (PT) was spent between ages 13–23 years (13–17 years: 43%; 18–23 years: 45%), CD4 ≥ 500/μL (61%), and VL < 400 c/mL (69%). Among NPHIVY, most PT was spent between ages 24 and 30 years (56%), CD4 ≥ 500/μL (54%), and VL < 400 c/mL (66%). PT spent while prescribed ARVs and VL ≥ 400 c/mL was 30% (PHIVY) and 24% (NPHIVY). For both PHIVY and NPHIVY, outpatient visit rates were higher at younger ages (13–17 years and 18–23 years), lower CD4 (< 200, 200–499/μL), and among those prescribed ARVs (Figure 1). Rates of ED visits and inpatient days were higher during PT spent at older ages (18–23 years, 24–30 years), lower CD4 (< 200, 200–499/μL), and VL ≥ 400 c/mL (Figures 2 and 3). Overall, utilization was higher among PHIVY than NPHIVY (outpatient: 12.1 vs. 6.0/PY; ED: 0.4 vs. 0.3/PY; inpatient: 1.5 vs. 0.8/PY). The overall rate of AIDS-defining conditions was 4.5/100 PY (Figure 4).

Conclusion. Among AYA with HIV, more ED visits and inpatient days were observed during time spent at older ages, lower CD4 counts, and VL ≥ 400 c/mL. While AIDS-defining conditions were rare, associated resource utilization was substantial. Interventions to improve retention in care, virologic suppression, and immune response may improve outcomes, and thus decrease costly resource utilization, for AYA with HIV as they transition to adulthood.

Figure 1. Outpatient visits per person-year

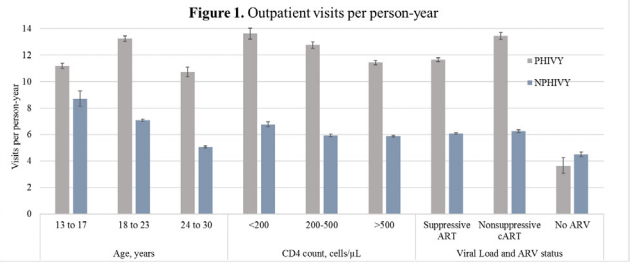


Figure 2. Emergency department visits per person-year

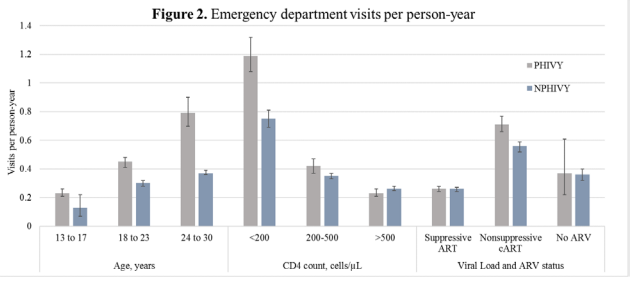


Figure 3. Inpatient days per person-year

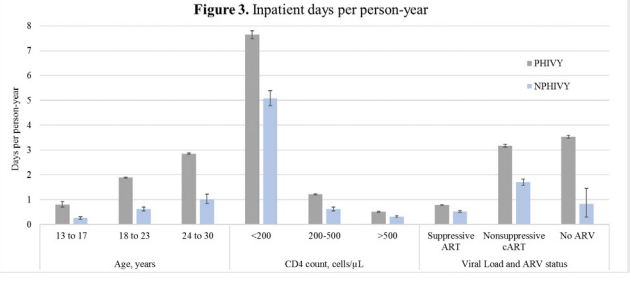
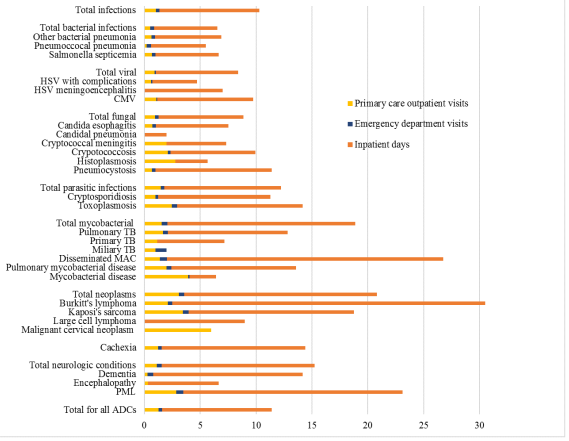


Figure 4. Inpatient days, primary care outpatient visits, and emergency department visits per AIDS-defining condition



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2521. Prevalence and Associated Factors of Protective Antibody Responses against Diphtheria, Tetanus, and Pertussis among HIV-Infected Thai Adolescents Stable on Combination Antiretroviral Treatment

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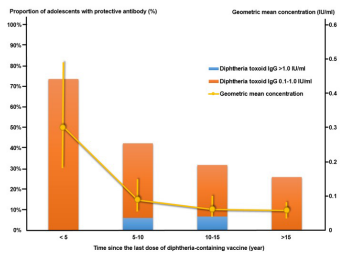
Background. To assess the prevalence and associated factors of protective antibodies against diphtheria, tetanus, and pertussis among HIV-infected adolescents stable on combination antiretroviral treatment (cART).

Methods. A multicenter seroprevalence study was conducted. Perinatally HIV-infected Thai adolescents (11–25 years) who had previous evidence of severely immune suppression (CD4 < 15% or < 200 cells/mm^3), were currently stable on cART (CD4 > 350 cells/mm^3 for > 6 months or CD4 > 200 cells/mm^3 with viral suppression [VS; HIV RNA < 50 copies/mL] for > 12 months) and had completed a 5-dose series of diphtheria, tetanus, whole cell pertussis (DTwP) vaccine during childhood were enrolled. Adolescents who received immunosuppressive agents or blood components within 6 months were excluded. Protective antibodies for diphtheria, tetanus, and pertussis were defined as diphtheria toxoid IgG ≥ 0.1 IU/mL, tetanus toxoid IgG ≥ 0.1 IU/mL, and anti-pertussis toxin IgG ≥ 5 IU/mL, respectively. Logistic regression analysis was performed to identify factors associated with protective antibody response to each antigen.

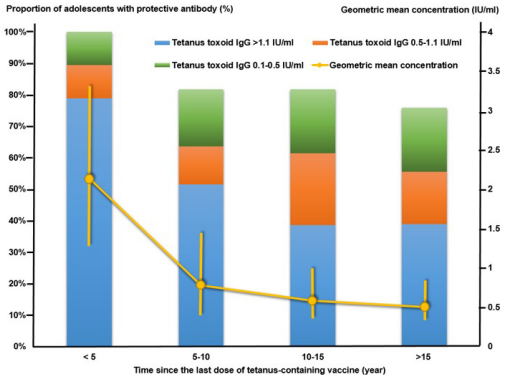
Results. Of 150 adolescents, 47% were male, a median age was 19 years. Forty (27%) and 0 (0%) adolescents had ever received tetanus, diphtheria (Td) or tetanus, diphtheria, acellular pertussis (Tdap) vaccine during adolescence, respectively. A median duration since the last dose of DTwP/Td vaccine was 12 years. At enrollment, 67% of adolescents were on NNRTI-based cART regimens, a median cART duration was 13 years. A median CD4 was 29%, and 90% had VS. Prevalence of protective antibodies against diphtheria, tetanus, and pertussis were 37%, 82%, and 52%, respectively. Proportion of adolescents with protective antibodies and geometric mean concentrations of antibodies to all antigens declined over time after the last immunization (Figures 1–3). Associated factors of protective antibodies to diphtheria, tetanus and pertussis are shown in Table 1.

Conclusion. Although having completed a 5-dose series of DTwP during childhood, significant proportion of our perinatally HIV-infected adolescents had no protective antibodies to those antigens, particularly diphtheria and pertussis, when entering adolescence. Tdap vaccination is a crucial strategy to prevent such diseases in the future.



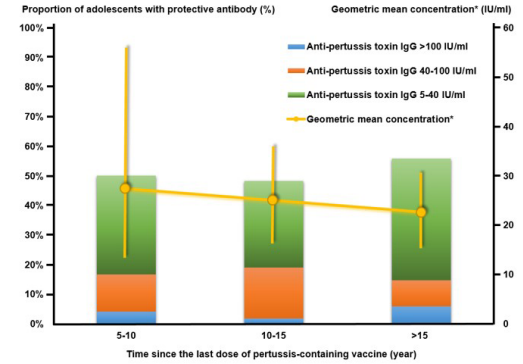
Total number of adolescents (*n*=150)	19	33	44	54
Number of adolescents with protective antibody (n, %)	14 (73.7%)	14 (42.4%)	14 (31.8%)	14 (25.9%)
Geometric mean concentration (IU/ml, 95% CI)	0.30 (0.19-0.49)	0.09 (0.05-0.15)	0.06 (0.04-0.10)	0.06 (0.04-0.08)

Figure 1. Proportion of perinatally HIV-infected Thai adolescents with protective antibody against diphtheria and geometric mean concentration of antibody by the time since the last dose of diphtheria-containing vaccine. Scale on the left represented the proportion of adolescents with different protective antibody levels against diphtheria. Scale on the right represented the geometric mean concentration (GMC) of antibody to diphtheria with the means indicated as yellow dots (yellow vertical lines denote 95% CI). Antibody levels were 0.1-1.0 IU/ml (orange) and >1.0 IU/ml (blue).



Total number of adolescents (*n*=150)	19	33	44	54
Number of adolescents with protective antibody (n, %)	19 (100%)	27 (81.8%)	36 (81.8%)	41 (75.9%)
Geometric mean concentration (IU/ml, 95% CI)	2.13 (1.35-3.37)	0.78 (0.41-1.48)	0.58 (0.34-1.00)	0.50 (0.30-0.84)

Figure 2. Proportion of perinatally HIV-infected Thai adolescents with protective antibody against tetanus and geometric mean concentration of antibody by the time since the last dose of tetanus-containing vaccine. Scale on the left represented the proportion of adolescents with different protective antibody levels against tetanus. Scale on the right represented the geometric mean concentration (GMC) of antibody to tetanus with the means indicated as yellow dots (yellow vertical lines denote 95% CI). Antibody levels were 0.1-0.5 IU/ml (green), 0.5-1.1 IU/ml (orange) and >1.1 IU/ml (blue).



Total number of adolescents (*n*=150)	24	58	68
Number of adolescents with protective antibody (n, %)	12 (50.0%)	28 (48.3%)	38 (55.9%)
Geometric mean concentration* (IU/ml, 95% CI)	27.42 (13.57-55.42)	25.05 (17.37-36.12)	22.70 (16.39-31.44)

*NOTE: *Calculated among only adolescents with protective antibody against pertussis (anti-pertussis toxin IgG ≥5 IU/ml).*

Figure 3. Proportion of perinatally HIV-infected Thai adolescents with protective antibody against pertussis and geometric mean concentration of antibody by the time since the last dose of pertussis-containing vaccine. Scale on the left represented the proportion of adolescents with different protective antibody levels against pertussis. Scale on the right represented the geometric mean concentration (GMC) of antibody to pertussis with the means indicated as yellow dots (yellow vertical lines denote 95% CI). Antibody levels were 5-40 IU/ml (green), 40-100 IU/ml (orange) and >100 IU/ml (blue).

Table 1. Associated factors of protective antibody responses to diphtheria, tetanus and pertussis among perinatally HIV-infected Thai adolescents stable of combination antiretroviral treatment.

Parameters*	Univariable analysis		Multivariable analysis	
	Crude odds ratio	95% confidence interval	Adjusted odds ratio	95% confidence interval
Associated factors of protective antibody responses to diphtheria				
Age 11-15 years (vs. >15 years)	3.93	1.35-8.35	**4.46**	**1.97-10.13**
Nadir CD4 ≥5% prior to cART initiation (vs. <5%)	2.21	1.13-4.34	**2.60**	**1.22-5.54**
Receiving PI-based regimen (vs. NNRTI-based regimen)	2.06	1.01-4.12	**2.24**	**1.02-4.96**
Ever received Td vaccine during adolescence	2.37	1.13-4.96	**2.41**	**1.06-5.48**
Associated factors of protective antibody responses to tetanus				
Nadir CD4 ≥5% prior to cART initiation (vs. <5%)	3.00	1.18-7.61	**2.93**	**1.09-7.93**
cART duration, year	1.15	1.04-1.28	**1.14**	**1.02-1.26**
Plasma HIV RNA, $\log_{10}$ copies/ml	0.43	0.20-0.91	**0.41**	**0.19-0.88**
Ever received Td vaccine during adolescence	5.56	1.25-24.80	**5.41**	**1.08-24.45**
Associated factors of protective antibody responses to pertussis				
WHO clinical stage prior to cART initiation (vs. Stage 1)				
Stage 2	9.45	1.08-83.06	7.71	0.85-69.92
Stage 3	6.53	0.76-56.62	4.54	0.50-40.52
Stage 4	7.50	0.82-68.94	4.78	0.48-47.24
Duration of viral suppression, year	1.10	1.02-1.20	**1.11**	**1.02-1.21**

Abbreviations: cART, combination antiretroviral treatment; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; Td, tetanus, diphtheria vaccine; WHO, World Health Organization.
*Logistic regression analysis was performed to identify associated factors with protective antibody responses to each antigen. Parameters demonstrating *P* <0.10 in the univariable logistic regression model were included in the multivariable analysis. All parameters listed in the table were included in the multivariable logistic regression model for each antigen indicated above.

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2522. Prescription Drug Use Among Women with HIV Who Are of Childbearing Potential

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