

854. Impact of Antimicrobial Stewardship and Rapid Diagnostics in Children with *Staphylococcus aureus* Bacteremia

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Background. Rapid diagnostic testing (RDT) in combination with antimicrobial stewardship programs (ASPs) has been associated with improved outcomes in adults with *Staphylococcus aureus* bacteremia (SAB). Data in children are lacking. In January 2017, Atrium Health implemented a pediatric ASP with blood culture RDT. The objective of this study was to determine the impact of those interventions.

Methods. This was a retrospective, multicenter, quasi-experimental study of children ≤ 18 years with monomicrobial SAB from March 2015 to August 2016 (pre-intervention; PRE) and March 2017 to August 2018 (post-intervention; POST). The primary outcome was time to an optimal antibiotic. Secondary outcomes included time to effective antibiotic, total antibiotic exposure in the first 5 days, duration of bacteremia, infectious diseases (ID) consultation, time to central line removal, hospital and pediatric ICU length of stay (LOS), need for vasopressors or intubation, recurrence of SAB within 90 days, and inpatient mortality.

Results. Of 101 patients with SAB, 32 and 36 met inclusion criteria for the PRE and POST groups, respectively. The median time to optimal antimicrobial therapy decreased by 23 hours (PRE 44.3 hours vs. POST 21.3 hours; $P = 0.008$). Duration of bacteremia (65h vs. 40.9 hours; $P = 0.028$) and mortality (12.5% vs. 0%; $P = 0.044$) was also significantly reduced. Differences in median time to effective therapy (7 hours vs. 5.1 hours; $P = 0.74$), total antibiotic exposure in the first 5 days (160.4 hours vs. 152 hours; $P = 0.4$), hospital LOS (9.9 vs. 8.5 days; $P = 0.25$), and pediatric ICU LOS (7 vs. 4 days; $P = 0.11$) did not meet statistical significance, but trended downward. The POST group had more patients with ID consultation (78% vs. 89%, $P = 0.024$) and shorter time to central line removal (68 hours vs. 20 hours; $P = 0.037$). There was no difference in the need for vasopressors (3 vs. 3 patients; $P = 0.99$) or intubation (2 vs. 4 patients; $P = 0.68$). Throughout the study period, recurrence of SAB only occurred in one patient (PRE).

Conclusion. Concurrent implementation of RDT and an ASP in pediatric patients with SAB decreased time to optimal antimicrobial therapy, duration of bacteremia, and mortality. RDT coupled with timely feedback from an ASP contributed to improved SAB management and clinical outcomes in children.

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855. Evolution of Group B Streptococcal Capsular Type V Invasive Infections in Neonates and Young Infants: A Whole Genome Sequencing Study

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Background. Since 1970 group B *Streptococcus* (GBS) has been a frequent cause of sepsis or meningitis in young infants. Capsular polysaccharide type V was first recognized in 1990 and has increased to the point where it now causes ~15% of GBS infections. GBS type V strains are almost entirely sequence type 1 (ST1) in adult infections. To understand the emergence of type V GBS, we compared infant strains before 1990 to more contemporary isolates from young infants and adults.

Methods. Thirty-five strains isolated from blood or CSF of infants <90 days of age (Houston, 1979–1996) were compared with the following previously sequenced type V, ST1 strains: (1) 14 from infant blood or CSF from Center for Disease Control and Prevention (CDC) (2015–2017), (2) 193 blood ST1 isolates from adults (Houston, 1992–2013), and (3) 516 invasive isolates from the CDC (2015–2017). Isolates were sequenced using an Illumina MiSeq instrument followed by molecular typing, antimicrobial resistance gene determination, and phylogenetic analysis. Antimicrobial susceptibility testing (AST) was performed using disk diffusion and E-test.

Results. The majority (29/35) of Houston young infant strains were ST1. Type V GBS strains isolated prior to 1990 were more likely to be of ST-2 or ST-26 (5/10) compared with those from 1990 or later (24/25 and 14/14 CDC infant invasive type V). Tetracycline resistance was identified in 83% (29/35) while macrolide resistance (MR) occurred in only 23% (8/35) of the strains. Compared with early neonatal isolates, MR was significantly more frequent among contemporary neonatal (12/14, 86%, $P < 0.0001$) and adult (502/710, 71%, $P < 0.0001$) ST1 GBS. Phylogenetic analysis showed two distinct clades defined, in part, by MR. A high-frequency MR (340/360, 94%) clade was defined by the presence of *erm(B)* on Tn3872 while the low-frequency MR clade (159/350, 45%) was more diverse in mobile elements contributing to MR. The majority (27/29) of early neonatal ST1 GBS strains were observed in the low-frequency MR clade.

Conclusion. Infant invasive disease due to type V GBS before 1990 consisted of more diverse STs but is now almost exclusively ST1. Differences in the frequency of MR between early neonatal and contemporary type V ST1 GBS suggest MR may, at least in part, have driven the expansion of type V ST1 GBS.

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856. Invasive *Haemophilus influenzae* Disease in Children: A Canadian Multicenter Study on Emerging Serotypes

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Background. Our objective was to describe the serotype distribution and clinical spectrum of invasive *Haemophilus influenzae* (Hi) disease in children admitted to participating centers within the Paediatric Investigator's Collaborative Network on Infections in Canada (PICNIC).

Methods. All cases of Hi bacteremia were identified from the PICNIC Database of Gram-negative bacteremia (2013–2017). Disease was defined as complicated if the following occurred: (a) >2 sites were affected, (b) surgical intervention was required, (c) organ failure, (d) ICU admission, (e) seizures, (f) sensory or motor deficits, (g) treatment-related complications, or (h) death.

Results. There were 98 cases of Hi bacteremia. Male to female ratio was 64:34 and median age was 12 (IQR: 7–48; range 0–216) months. Hi serotypes included: a ($N = 31$; 32%), b ($N = 9$; 9%), f ($N = 15$; 13%), c ($N = 1$; 1%), e ($N = 1$), nontypeable ($N = 34$; 35%) and unknown ($N = 7$; 7%). Clinical foci included: bacteremia without a focus ($N = 19$; 19%), meningitis ($N = 29$; 30%), cellulitis ($N = 8$; 8%), septic arthritis ($N = 6$; 6%), pneumonia ($N = 33$; 34%), epiglottitis ($N = 1$; 1%), and endovascular infection ($n = 3$; 3%). Complicated disease occurred in 29 (30%) cases; there was one (1%) death. Where serotyping was available, complication rates were: 42%, 22%, 100%, 0%, 33%, and 21% for Hia, Hib, Hic, Hie, Hif and nontypeable Hi, respectively. Factors associated with complicated disease were: age <5 years ($P = 0.009$), bacteremia without a focus ($P = 0.006$) and a CNS focus ($P < 0.001$). Hia was the leading serotype in meningitis (55%; $P = 0.022$). Nontypeable Hi was most frequent in pneumonia cases (56%; $P = 0.003$) and never caused cellulitis (0% vs. 14%; $P = 0.023$). Neonatal disease ($N = 5$) was predominantly caused by nontypeable Hi (80%; $P = 0.040$). Of note, 26 (27%) of our Hi isolates were ampicillin resistant.

Conclusion. In the era of efficacious conjugate Hib vaccines, serotype has emerged as the leading cause of typeable Hi disease in Canada and is highly associated with meningitis, especially in young children. Strategies for preventing Hi disease need to target this emerging serotype and efforts should be focused toward developing an effective vaccine for serotype a disease.

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883. Evidence from a Multistate Cohort: Enrollment in Affordable Care Act Qualified Health Plans Results in Viral Suppression

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Background. In individual states, the Patient Protection and Affordable Care Act has been associated with improved viral suppression (VS) rates for AIDS Drug Assistance Program (ADAP) clients or low-income people living with HIV (PLWH). This study aims to assess whether this association is consistent in multiple states (Nebraska, South Carolina, Virginia).

Methods. The multistate cohort included ADAP clients who were eligible for ADAP-funded Qualified Health Plans (QHPs). Data were collected from 2014 through 2015. A log-binomial model was used to estimate the association of demographics (age, race/ethnicity, sex, AIDS, rurality, HIV risk factor, previous VS) and healthcare delivery factors (income, previous ADAP plan, previous HIV care engagement) with QHP enrollment prevalence and 1-year risk of VS.

Results. For the cohort ($n = 7,800$; 5% NE, 36% SC, 59% VA), 52% enrolled in ADAP-funded QHPs with enrollment ranging from 35% to 63% by state. Enrollment in ADAP-funded QHPs in 2015 was higher for those who had ADAP-funded QHPs in 2014 (adjusted prevalence ratio [aPR] 3.28; 95% confidence interval [CI] 3.21–3.35) and those who were engaged in care in 2014 (aPR 1.16; 95% CI 1.05–1.27), and it was lower for those with a rural residence (aPR 0.91; 95% CI 0.81–1.00). Of those who were consistently engaged in care ($n = 4,597$), as defined by one viral load in 2014 and one viral load in 2015 separated by at least 180 days, those who received medications from

Direct ADAP had a VS rate of 80.2% and those with ADAP-funded QHPs had a VS rate of 86.0%. The number needed to enroll in ADAP-funded QHPs for an additional PLWH to achieve VS is 18. Those who achieved VS in 2014 (adjusted risk ratio [aRR] 1.39, 95% CI 1.30–1.48) and those who enrolled in QHPs in 2015 (aRR 1.06, 95% CI 0.99–1.13) were more likely to achieve/maintain VS.

Conclusion. Additional efforts should be made to reach rural PLWH for QHP enrollment. State ADAPs, especially those in the South and those in states without Medicaid expansion, should consider investing in purchasing QHPs for PLWH because increased enrollment could improve VS rates. This evidence-based intervention could be a part of “Ending the HIV Epidemic.” Once ADAP clients are enrolled in ADAP-funded QHPs, they stay enrolled, and QHP enrollment is associated with VS across states and demographic groups.

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884. Patient Adherence to Long-Acting Injectable Cabotegravir + Rilpivirine Through 48 Weeks of Maintenance Therapy in the Phase 3 ATLAS and FLAIR Studies

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Background. Cabotegravir (CAB) and rilpivirine (RPV) are under development as a novel long-acting (LA) regimen for maintenance of HIV virologic suppression. Pooled Week 48 data from pivotal Phase 3 trials demonstrated noninferiority of CAB LA + RPV LA vs. current antiretroviral regimen (CAR) on the primary endpoint, proportion of subjects with HIV-1 RNA ≥ 50 c/mL (1.9% and 1.7%, respectively). Adherence to dosing visits, use of oral dosing (bridging) to cover planned missed injections and injection tolerability were examined for subjects in the ATLAS and FLAIR studies.

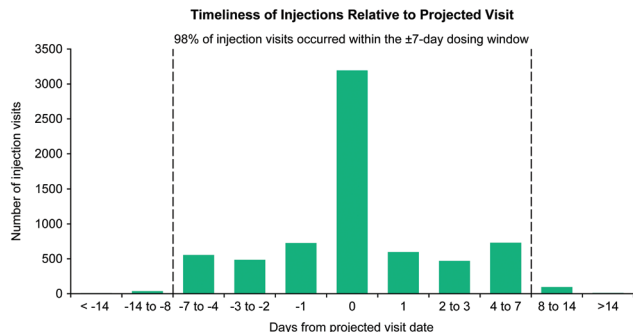
Methods. Virologically suppressed subjects (HIV-1 RNA < 50 c/mL) were randomized to switch to CAB LA + RPV LA or to continue CAR. On-time injections occurred Q4 weeks within a +7-day dosing window of the projected dosing date. Adherence to LA therapy was calculated as the number of on-time injection visits divided by the number of expected dosing visits through Week 48. Injection visits outside the pre-specified window and missed injection visits with/without the use of oral dosing were quantified. Injection tolerability was assessed via adverse event reporting.

Results. A total of 14,682 injections of CAB and RPV were administered to 581 subjects during 6,920 injection visits. 98% of injection visits took place within the allowed ± 7 -day dosing window with 3,194 (46%) on the projected dosing date. Forty-six (<1%) injection visits were early and 106 (2%) were late. Oral bridging was used in 16 subjects overall; 8 planned missed injection visits were successfully covered, with no change to virologic suppression status. No subject with HIV-1 RNA ≥ 50 c/mL at Week 48 had missed/late injection visits. 25% (3,663/14,682) of injections were associated with local injection site reactions (ISRs). The most common ISR was pain (3,087/3,663 = 84%). Most ISRs were grade 1–2 (99%), short duration (median 3 days), with few associated discontinuations (<1%).

Conclusion. Subjects receiving CAB LA + RPV LA demonstrated high rates of adherence to injection visits through week 48, with 98% of injections occurring within the ± 7 -day dosing window. Oral bridging with CAB and RPV was an effective strategy for maintaining viral load suppression to cover missed injection visits. Injections were well-tolerated with few associated discontinuations.

Timeliness of Injections Relative to Date of Projected Dosing Visits	ATLAS	FLAIR	Pooled (IM)
Total Number of Expected Visits	3343	3577	6920
Within Window Injection Visit (+/- 7 days relative to projected visit date)	3252/3343 (97%)	3507/3577 (98%)	6759/6920 (98%)
Injection Visit on Projected Visit Date	1567/3343 (47%)	1627/3577 (45%)	3194/6920 (46%)
Early Out of Window Injection Visit (more than 7 days early relative to target visit date)	28/3343 (<1%)	18/3577 (<1%)	46/6920 (<1%)
Late Out of Window Injection Visit (more than 7 days late relative to target visit date)	59/3343 (2%)	47/3577 (1%)	106/6920 (2%)
Missed Injection Visit*	4/3343 (<1%)	5/3577 (<1%)	9/6920 (<1%)

*Of the 9 missed injection visits, 8 were covered by oral bridging with no change to virologic suppression status



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885. HIV-1 Treatment Failure and Extensive Drug Resistance in Perinatally Infected Children Failing First-Line Antiretroviral Therapy in Western Kenya

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Background. Understanding drug resistance in perinatally HIV-infected children (PHIC) when viral load (VL) monitoring is limited is critical for life-long antiretroviral use. Resistance data in PHIC in sub-Saharan Africa are limited. Though guidelines recommend PI-based first-line regimens in PHIC, many worldwide remain on NNRTI-based regimens. We examined treatment failure, resistance, and outcomes in Kenyan PHIC on first-line NNRTI-based therapy.

Methods. PHIC were enrolled in 2010–2013 at the Academic Model Providing Access to Healthcare in Eldoret, Kenya, a large program caring for >160,000 HIV patients; >15,000 PHIC. VL testing, not routinely available then, was done for all, and resistance testing was done in viremic PHIC. Clinical data were derived from medical records. Subtype and resistance interpretation were with Stanford Database tools. Associations between failure (>1,000 copies/mL) or resistance, and demographic, clinical or lab variables were evaluated with Fisher exact and Wilcoxon rank-sum tests.

Results. Of 482 PHIC enrolled, 52% were female, median age 8.4 years (range 1–15), median CD4% 28 (range 0–53), 79% on zidovudine (AZT)/abacavir (ABC)+lamivudine(3TC)+efavirenz (EFV)/nevirapine (NVP) for median 2.3 years. Treatment failure was seen in 31%, associated with low CD4% and count. Genotypes were available in 124, 47% female, median age 8.3 years (range 2–15), median CD4% 22 (range 0–45), 81% on AZT/ABC+3TC+EFV/NVP for median 2.5 years, median VL 7,515 copies/mL. Subtypes were A 76%, C 3%, D 15%, recombinants 6%. Reverse transcriptase mutations were in 93%; 93%-NNRTIs, median 2/patient, most common Y181C (44%); 89%-NRTIs, median 3/patient, most common M184V (85%); 89%-dual class, median 5/patient. Intermediate-high resistance to potential second-line drugs included 62% etravirine, 66% rilpivirine, and 19% tenofovir. Of 92/124 (74%) PHIC with follow-up data, 27% remained on NNRTI-based first-line (median CD4 count 461), of whom 24% had suppressed VL and 48% died; and 73% switched to PI-based second-line (median CD4 count 591), of whom 72% had suppressed VL and 6% died ($P < 0.05$ for both).

Conclusion. PHIC in western Kenya on NNRTI-based first-line regimens had high treatment failure rates and extensive drug resistance with poor clinical outcomes, demanding urgent interventions.

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886. Pregnancy Outcomes Following Raltegravir Exposure

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Background. Safety data are needed regarding HIV treatment in women of reproductive potential and during pregnancy. This review is to evaluate pregnancy outcomes following prospective exposures (exposure report prior to knowledge of pregnancy outcome) to raltegravir during pregnancy.

Methods. Exposures to raltegravir during pregnancy reported cumulatively through March 26, 2019 to the internal safety database at Merck & Co., Inc. were reviewed. This database includes all reports of pregnancy from clinical trials sponsored by the company, spontaneous post-marketing reports, and noninterventional data sources. Prospective pregnancy reports were evaluated to determine rates of spontaneous abortion, stillbirth, and congenital anomalies, including neural tube defects. Data from two ongoing cohorts of pregnant women with HIV-1 infection, not included in the internal safety database, were also reviewed.

Results. A total of 2,508 prospective pregnancy reports with reported outcomes were identified among women exposed to raltegravir: 919 from the internal safety database (Table 1) and 1,589 from the UK/Ireland and French pregnancy cohorts. Among the 2,508 prospective pregnancy exposures, 945 were in the first trimester, of which 757 were within the periconception period (within 28 days of conception). Of the 471 documented first trimester exposures identified in the internal safety database, the rates of spontaneous abortion (6.9%), stillbirth (1%), and congenital anomalies (1.5% per live births) were similar to the rates observed in the background populations of the United States. Among outcomes following any exposure, the rate of congenital anomalies was 3.4% per live births. There were no reports of neural tube defects identified within the internal safety database or among the cohort data.

Conclusion. Prospectively collected pregnancy outcome data do not suggest an association between raltegravir exposure and spontaneous abortion, stillbirth, or