Eliminating Vertically-transmitted HIV/AIDS while Improving Access to Treatment and Care for Women, Children and Adolescents in Jamaica

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ABSTRACT

Background and Methods: To celebrate Jamaica’s 50th birthday after receiving independence from Great Britain, we summarize our collaborative published research in the prevention, treatment and care of paediatric, perinatal and adolescent HIV/AIDS in Jamaica.

Results: Public access to antiretroviral therapy (ART) in Jamaica has shown that a “test and treat” strategy associated with “treatment for prevention” works for HIV-infected pregnant women by reducing their HIV-attributable morbidity and mortality and reducing mother-to-child transmission (MTCT) rates to < 2%, islandwide. These women experience significant psychosocial stress and targeted interventions are assisting them to improve their quality of life. HIV-exposed and infected children come from large families with high rates of teen pregnancies and significant financial challenges needing sustained interventions. HIV-exposed but uninfected Jamaican infants have higher rates of community-acquired infections, including lower respiratory tract infections, sepsis and gastroenteritis compared to community controls, although their growth rates are normal. In evaluation of replication capacity, viral control and clinical outcomes after vertical transmission in Jamaican mother-infant pairs, HLA-B57 was found to confer the advantage of restricted HIV replication primarily by driving and maintaining a fitness-attenuating mutation in p-24 Gag. Viral sequences from 52 MTCT Jamaican pairs were compared and 1475 sites of mother-infant amino acid divergence within Nef, Gag and Pol were identified, suggesting modest fitness cost with many CD8 mutations. HIV-infected Jamaican children are surviving into adolescence and adulthood, as a result of increased public access to ART and improved collaborative capacity in ART management. Successful transition of HIV-infected children through adolescence into adulthood requires a strong multidisciplinary team approach, including long-term ART management addressing non-adherence, drug resistance and toxicity, treatment failure and limited options for second line and salvage therapy, while attending to their sexual and reproductive health, psychosocial, educational and vocational issues and palliative care.

Conclusion: Over the past nine years, Jamaica has made excellent strides to eliminate vertically transmitted HIV/AIDS, while reducing the HIV-attributable morbidity and mortality in pregnant women and in HIV-infected children. Continued successful transition of HIV-infected children through adolescence into adulthood will require a strong multidisciplinary team approach.

Keywords: AIDS, children, HIV, Jamaica, pMTCT, Youth

Eliminando la Transmisión Vertical del VIH/SIDA Mejorando a la par el Acceso al Tratamiento y el Cuidado de las Mujeres, los Niños y los Adolescentes en Jamaica

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RESUMEN

Antecedentes y Métodos: A fin de celebrar el 50 aniversario de Jamaica tras recibir la independencia de Gran Bretaña, resumimos nuestra investigación colaborativa publicada sobre la prevención, tratamiento y cuidado del VIH/SIDA pediátrico, perinatal y juvenil en Jamaica.

Keywords: AIDS, children, HIV, Jamaica, pMTCT, Youth

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Footnotes: Funded in part by the Global Fund for AIDS, Tuberculosis and Malaria, Clinton Health Access Initiative, Elizabeth Glaser Paediatric AIDS Foundation, Pfizer Foundation, United States National Institutes of Health, United States National Institutes of Child Health and Human Development, Embassy of Jamaica in Washington, DC, University of the West Indies and the Jamaican Ministry of Health.
BACKGROUND
Jamaica is a middle income developing island nation in the Caribbean, with a population of 2.8 million and an adult HIV seroprevalence of 1.7% in 2011, where an estimated 32 000 persons are currently living with HIV (1). The first case of AIDS was diagnosed in 1982 in Jamaica; since then reported cases have gradually increased so that the epidemic is now characterized as mixed, with features of a generalized epidemic in the population, but concentrated in those who are most at risk. The Jamaican HIV epidemic has had strong leadership from the National AIDS Programme over the years mainly through the efforts of Professor J Peter Figueroa with financial support from international partners (1−3). Children in Jamaica with HIV infection are now surviving into adolescence and young adulthood, as a result of increased public access to antiretroviral therapy (ART) and improved capacity in ART management.

Purpose
To celebrate Jamaica’s 50th birthday after receiving political independence from the British, we summarize herein our collaborative research in paediatric, perinatal and adolescent HIV/AIDS in Jamaica. We report our collaborative research efforts to virtually eliminate mother-to-child transmission of HIV/AIDS and the outcomes of interventions to improve treatment and care to children and youth living in Jamaica.

Leadership and Training
In 1986, the first case of paediatric HIV/AIDS was diagnosed by Celia Christie, then a Paediatric Infectious Diseases Fellow, visiting Jamaica from Yale University (4). Patricia Burke and Russell Pierre later established the Family Centre at the University Hospital of the West Indies (UHWI) where some children with HIV were being treated before ART became available. Reports of paediatric cases gradually increased islandwide and a hospital-based description by Tracy Evans-Gilbert et al reported HIV/AIDS as a leading cause of death in young children (5). In 2002, a team of government and academic healthcare personnel from The University of the West Indies (UWI) began collaborating together to address the Jamaican paediatric and perinatal epidemic through an International Leadership Award to
A five-point strategy was utilized comprising leadership and train-ing, preventing mother-to-child transmission, paediatric and maternal treatment and care, outcomes-based research activities, as well as collaboration locally, regionally and internationally (6–12).

The intervention began in the Greater Kingston Metropolitan Region with “The Kingston Paediatric and Perinatal HIV/AIDS – KP P AID S Programme,” and then extended islandwide to the “Jamaica Paediatric and Perinatal HIV/AIDS – JaPPAID S Programme”. It was coordinated from each hub by nurse-managers working through the antenatal clinics, paediatric sites, obstetric hospitals, laboratories and the National AIDS Programme collaborating with the patient-families and the entire healthcare team (8). Training was ongoing to the multidisciplinary healthcare team and students through didactic lectures, conferences, small group discussions and also clinical preceptorships, including training of five clinical postdoctoral paediatric fellows and nine cohorts of graduating paediatricians from the UWI. A collaborative database was developed and a memorandum of understanding was implemented to guide our collaborations and the process for research publications. Data were collected prospectively, analysed, reported nationally and utilized to inform peer-reviewed publications of several outcomes-based and other research activities (2−69).

Preventing Mother-to-child Transmission of HIV and Perinatal HIV/AIDS

Harvey et al implemented the first efforts to prevent mother-to-child transmission of HIV through the offering of nevirapine prophylaxis in a pilot study to HIV+ pregnant women and their babies, but reported limited follow-up and testing of the babies (13). In the first year of the KPPAID S Programme, Johnson et al reported HIV testing of 53% of 7383 pregnant women to identify 107 HIV+ women in Greater Kingston, 75% of whom received zidovudine, or nevirapine; with repeat pregnancies and poor partner notification observed in over 30% (14). Whyte et al also noted that there was no significant difference in mother-to-child transmission rates between women presenting early (7.7%) and late presenters (10%, p = 0.897), although the overall MTCT rates were 8.2% (15). During the first three years, Christie et al reported that while modified short course zidovudine or nevirapine significantly decreased MTCT rates from 29% to 6%, highly active antiretroviral therapy (HAART) later decreased MTCT to < 2% in Greater Kingston and < 5% islandwide (7).

The Table shows the uptake of the pMTCT cascade from 2005 to 2011 in the Jamaican public sector, with > 95% of pregnant women now being tested for HIV, > 85% of women are receiving ARTs and 100% of babies are getting ART chemoprophylaxis and being offered full replacement formula feeds; the 2011 national pMTCT rates are reported as 1.19%, which is synonymous with the established targets for the virtual elimination of paediatric AIDS [ie ≤ 2%] (16).

The significant downward trend in recent years of reported new cases of paediatric HIV/AIDS and attributable deaths in Jamaica is shown (Figure). Johnson et al reported further that the use of HAART when given to women in pregnancy along with the implementation of a comprehensive system of care including assessments of viral load and CD4 counts had greatly decreased HIV/AIDS-attributable maternal morbidity and mortality (17). Palmer et al noted that evaluation of the 15% noncompliance with ART in pregnancy revealed gaps in antenatal clinic attendance, prescribing and administering ART, hospital record documentation and follow-up of HIV exposed infants (18).

Psychosocial factors among HIV-infected and non-infected women in the peripartum period were evaluated by Weller et al who noted that significantly more HIV-infected women reported negative emotions, (eg guilt and tension), prayed, slept, or changed their eating habits, in addition to seeking the advice of a traditional faith healer (19).

Rodriguez et al noting a repeat pregnancy rate of 30–40% in over 800 HIV+ pregnant Jamaican women, reported the driving factors for repeat pregnancies included
issues relating to economics, fear of disclosure, rejection of contraceptives, reluctance to change lifestyle practices and the fact that having children was important in affirming the well-being and definition of womanhood, as a parent and as a partner (20). Rodríguez et al. further revealed in the same cohort that 70% of the women reported some kind of contraceptive use, with condoms accounting for 66%, although only half admitted consistent condom use and 16% had a tubal ligation. Their perceived inefficiencies of the healthcare system included delays in performing tubal ligations, inadequate access to contraceptive choices and advice, need for ongoing psychosocial support groups for stigma and discrimination (21). McCarthy also reported that psychotherapeutic interventions to mothers helped to identify, manage and treat their psychological and psychosocial issues and the resultant healing resulted in their accepting their HIV+ status, increased adherence to treatment, with gradual stabilization and self-efficacy to address the challenges of caring for themselves and their HIV-exposed infants, while enhancing the multidisciplinary approach to care (22).

Moore et al reported that the challenges of a HIV voluntary counselling and testing (VCT) programme in the antenatal clinics included lack of quality control and lost opportunities for late presenters, while the successes included increased uptake of VCT and reduction of stigma (23). Hylton-Kong et al emphasized the role of the “contact investigator” as an essential member of the pMTCT team (24). Billings noted the increased prevalence of tattoos and body piercing in young women who are also sexually active and recognized the possible threat of transmission of blood-borne pathogens due to the unethical and unsterile practices of persons who are involved in this unregulated trade in Jamaica (25). Notwithstanding, Christie et al have reported that Jamaica along with several other Caribbean islands are well on their way to achieve their stated targets for the virtual elimination of vertical, or mother-to-child transmission of HIV/AIDS (26).

HIV-exposed Infants
Rodríguez et al in examining psychosocial dynamics and family structure noted that HIV-exposed and infected children come from large families, with a high prevalence of teen pregnancies and institutional care, creating a significant financial burden for Jamaica which needs sustained interventions to successfully address this (27). Steel-Duncan et al in following HIV-exposed infants early on in the Greater Kingston Metropolitan regional epidemic, reported that 97% received prophylaxis, 90% were not breastfed and 88% received cotrimoxazole prophylaxis, but challenges with stigma, non-compliance, breast milk substitution and follow-up care were noted and later addressed (28). Evans-Gilbert et al reported HIV-exposed infants were at risk of defaulting paediatric care if their mothers defaulted antenatal and post delivery care, therefore emphasizing the need for closer follow-up of these “at risk” mothers after delivery to identify and define the HIV-status of their exposed infants (29).

Mussi-Pinhasa et al, in collaboration with the NISDI Perinatal Study Group, examined a cohort of HIV-exposed infants in Latin America and the Caribbean and reported the high risk of lower respiratory tract infections in HIV-exposed, uninfected infants (30). Fulford et al, in studying a similar cohort of HIV-exposed uninfected infants here in Jamaica, recognized 83% with at least one infection, comprising lower respiratory tract infections, sepsis, or acute gastroenteritis compared to normal HIV-negative and unexposed community controls, and although 30% of these HIV-exposed uninfected infants required hospitalizations, their growth trends were normal (31). Other collaborations with the NISDI Perinatal Study Group showed that Caesarean section before labour and membrane rupture was relatively safe for newborns of HIV-infected women (32). Similar NISDI collaborations reported the prevalence of congenital anomalies after the first trimester exposure to maternal ARTs was similar to that after the second and third trimester (33).

Immunology of Perinatal HIV in Mothers and Infants
International collaboration with Maggie Feeney et al to evaluate the immunology of perinatal HIV in Jamaican mother-infant pairs defined the HIV epitopes targeted by HIV-infected and non-infected Jamaican infants and reported qualitative differences in the CD8 response and deficient HIV-specific CD4 cells which may contribute to inability of young infants to limit HIV replication (34). In assessing the HLA B57-associated mutations on replication capacity, viral control and clinical outcomes after vertical transmission in Jamaican mother-infant pairs, it was concluded that HLA-B57 conferred its advantage of restricted HIV replication primarily by driving and maintaining a fitness-attenuating mutation in p-24 Gag (35). Frequency, epitope specificity and functional attributes of HIV-specific T-cells and sequence variation within B57-restricted epitopes were compared between Jamaican “spontaneous controllers” who maintained their normal CD4% and viral loads less than 3000 copies/ml without HAART and “treatment progressors” on HAART and it was concluded that among HLA B57 positive long-term survivors, spontaneous control of viraemia is not associated with a qualitatively or quantitatively superior T-cell response, but with uncompensated fitness-attenuating mutations in the viral capsid (36). Finally, viral sequences from 52 MTCT Jamaican pairs were compared and 1475 sites of mother-infant amino acid divergence within Nef, Gag and Pol were identified and it was concluded that there was modest fitness cost with many CD8 mutations (37).

Paediatric HIV/AIDS
Pierre et al characterized the natural history of paediatric HIV in a primarily ARV-naive population in Jamaica using the CDC criteria to define the disorders, reporting 88% of the children developing HIV from MTCT, 37% being severely symptomatic with Pneumocystis jirovecii pneumonitis and
tuberculosis, the most frequent opportunistic infections and Streptococcus pneumoniae, the most frequent bacterial pathogen (38–40). Using modified WHO guidelines, Pierre and Evans-Gilbert et al further reported that HAART was effective in decreasing opportunistic infections, hospitalizations and deaths in the HIV-infected children in both major cities in Greater Kingston and Montego Bay (41, 42–44). About 20–30% of the children were being placed on second line HAART (41, 43, 44). Adherence to HAART was 100% in children in institutional care compared to 78% among those in family based care, correlating with CD4% and according to White et al, non-adherence was related to older age of child, missing clinic appointments and nausea (45). Antiretrovirals and cotrimoxazole were reported to be safe in Jamaican children by Pryce et al, except for the few children early in the epidemic who changed ARV therapy due to anaemia from zidovudine, rash from nevirapine and indinavir associated haematuria and a few others who had drug toxicity with some biochemical abnormalities (46, 47). Roye et al found multiple drug genotypic resistance in the subset of children failing first-line ARVs (48). Heslop et al has reported a high genetic diversity of HIV in children with clade B, the predominant genotype in these children (49, 50).

At the height of the paediatric HIV epidemic, reports of tuberculosis (TB) increased, with HIV-infected children being statistically more likely to be older, have failure to thrive, digital clubbing, hepatosplenomegaly, adenopathy and negative Mantoux skin tests, to die, or have longer hospital stays when compared to the HIV-noninfected cohorts with TB (51). Geoghagen et al also reported concurrent outbreaks of infectious diseases, including tuberculosis, scabies and varicella in HIV-infected children living in a residential institution and emphasized the importance of education and appropriate immunization in children and the employees (52). Drug-resistant disseminated tuberculosis was also being seen (53). Immune reconstitution syndrome with BCG-lymphadenitis presumably from the Bacillus Calmette Guerin vaccine administered in the first week of life, was reported among several children after they had commenced HAART (54). Nicholson et al has reported disseminated histoplasmosis as a serious opportunistic infection in our cohort (55). Steel-Duncan et al noted renal manifestations including HIV-associated nephropathy and urinary tract infections linked to the common enteric pathogens (56). This work was extended by Byam et al who reported on the drug resistance patterns of these pathogens, recommending cotrimoxazole as a poor choice for empiric treatment of sepsis and urinary tract infections in this clinical setting (57).

Lewis et al reported anaemia, leucopenia and thrombocytopenia as not infrequent associations in ARV-naive HIV-infected Jamaican children (58). Walker et al defined the prevalence of encephalopathy to be 23% in the Jamaican paediatric cohort associated with significant neurocognitive dysfunction (59). However, opportunistic enteric infections and infestations have not been reported in Jamaican children with HIV/AIDS who are on ARTs and cotrimoxazole (60). Partnerships with the private sector have enabled education of children in Jamaica’s primary and secondary schools through debating competitions around moths of critical thinking, child rights, anti-discrimination, healthy lifestyles, parental and community responsibilities (61).

**Adolescent HIV/AIDS**

There are about 512 children and adolescents living with HIV/AIDS who are currently enrolled in treatment and care in Jamaica, most having acquired HIV from MTCT; 88% (451) are currently receiving HAART using modified WHO guidelines and of these, 73% (332) are < 12 years old and 27% (119) are aged > 13 years. Among the 451 on HAART, 70% (327) are on first line HAART, 29% (121) are on second line HAART and 0.7% (3) are receiving salvage therapy. These children and youth are mostly healthy and ambulatory. As a result of the strong collaborative partnerships and interventions by the Ministry of Health and the UWI, the significant downward trend in recent years of reported new cases of HIV/AIDS and deaths in children in Jamaica is shown (Figure).

Walker, and Harrison et al, have reported that adolescents with HIV are increasingly being recognized from the now ageing population of children who acquired HIV by vertical transmission and those who acquired HIV horizontally, from consensual, or forced sexual intercourse (62, 63). Moore et al recently reported that among 115 adolescents aged 12–24 years being treated for HIV/AIDS at the UHWI, 98% received formal education, 46% of those > 18 years were employed, 71% acquired HIV by MTCT and 22% sexually, several had sexually transmitted infections and several became pregnant; it was concluded that this heterogeneous cohort of HIV-infected maturing youth had sexual/reproductive health, psychosocial, educational and vocational challenges that required a multidisciplinary team approach to address (64). Lewis-O’Connor et al have noted bone metabolic disease as a recognized cause of pathological fractures in HIV-infected adolescents on HAART; it is clear that screening with DEXA scan is desirable but financially constrained in resource-limited settings and so the management for maturing perinatally infected children should include supportive measures to include optimized ART regimes, calcium and vitamin D supplementation, improved diet and exercise (65). Dunkley-Thompson also emphasized the need for healthcare providers to recognize and report the long-term non-progressors among the missed population of perinatally acquired HIV-infected teens to link them to appropriate treatment, care and prevention programmes (66). Pilgrim et al have noted that the majority of HIV-infected adolescents lived with parents or guardians, suggesting support despite stigma and discrimination (67). Moore also reported that among the adolescents with horizontal acquisition of HIV/AIDS, about half had acquired HIV infection forcibly (64). In addition to the legal inter-
ventions, post-exposure prophylaxis and psychotherapy must be included in the treatment for youth who are the victims of sexual assault (68−69).

Adolescents and youth in Jamaica continue to be at risk of HIV infection due to early sexual debut, 13 years in males and 15 years in females (1). Despite the increased perception of HIV risk in this population, there is no significant change in youths reporting multiple sex partnerships or the age of first sex (1). Contributing factors include poor condom negotiating skills by females, early sexual initiation with older men, high prevalence of sexual abuse of adolescent females and increased detection through voluntary counselling and testing for all antenatal clinic attendees (1). Youth who are being infected from sexual transmission are also at risk for possible onward transmission of HIV to their partners. There is also the growing population of youth who themselves were saved from MTCT who are now growing up in the same environment that contributed to their parents’ infection and are now at risk for acquiring HIV from sexual transmission.

**Operational Challenges**

Although Jamaica has reached the virtual elimination target in that the rate for HIV+ infants born to HIV-infected mothers is now 2% or less, an incidence of MTCT of 0.3 cases per 1000 live births also has to be attained and both targets be maintained for three years, for the country to be officially certified. There are several concrete operational and other challenges that still need to be overcome to achieve these goals. These include closing the gap to improve ART uptake in the 15% of women who still elude the pMTCT programme by presenting late, or not at all, or who are not HIV+ tested, or do not reveal their HIV+ serostatus on the labour ward. HIV rapid testing, although available, needs to be routinely performed on the labour ward for women who do not have a HIV test result in their hospital chart. Partners need to be brought in for counselling and HIV testing. The repeat pregnancy rates of about 25−30% each year and related risky sexual behaviours need to be addressed. The 15% of HIV-exposed infants who are “lost to follow-up” need to be identified for definitive HIV polymerase chain reaction (PCR) testing; although we know they are probably HIV-negative because their mothers did participate in the pMTCT cascade and the infants benefitted from ART prophylaxis and replacement formula, further they would have presented to the health sector with AIDS-defining illnesses, if they were HIV-infected. Their linkage to and retention in care, needs a better integrated and decentralized service delivery to expand access to HIV diagnosis and treatment interventions and thereby reduce loss to follow-up. HIV testing data for the women from the private sector of about 30% need to be accounted for by improving public private partnerships, although it is known that these women are eventually accounted for among the HIV+ deliveries, as they deliver their babies in the public hospitals. Stigma and discrimina-

**CONCLUSION**

Over the past nine years, Jamaica has made excellent strides in the public sector to eliminate vertically transmitted HIV/AIDS, while reducing the HIV-attributable morbidity and mortality in pregnant women and in HIV-infected children.

Public access to ART in Jamaica has shown that a “test and treat” strategy associated with “treatment for prevention” works for HIV-infected pregnant women by reducing their HIV-attributable morbidity and mortality and reducing mother-to-child transmission rates to < 2% islandwide. These women experience significant psychosocial stress and targeted interventions are assisting them to improve their quality of life. HIV-exposed and infected children come from large families with high rates of teen pregnancies and significant financial challenges needing sustained interventions. HIV-exposed but uninfected Jamaican infants have higher rates of community-acquired infections, including lower res-
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