Control of HIV viraemia is not enough in perinatal HIV

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Approximately 2.5 million children under 15 live with HIV, and with access to antiretroviral therapy (ART), large numbers will survive and transition to adult care. With effective ART as simple as a single-tablet regimen, HIV treatment is considerably less burdensome than many other chronic diseases of childhood and it has been argued that global funding streams directed towards HIV eradication lack equity in terms of global health needs. With WHO guidance to commence ART in all children diagnosed with HIV prior to their 5th birthday, children born with HIV currently face a lifetime on treatment, with drug exposure throughout postnatal growth and development [1]. The future for children with perinatal HIV infection (PaHIV) in adult life is unknown and cannot necessarily be extrapolated from horizontally acquired HIV in adult cohorts where HIV is acquired on a mature immune system. The effects of treatment on post-pubertal growth and neurocognitive development are underdetermined. Concerns are growing regarding life-long adherence to ART, malignancies, fertility, cardiovascular risk, neurocognitive and mental health. From a single-centre perinatal cohort of 104 young people, median age 22.5 years (interquartile range 21.2–25.1) in adult care, we describe three cases of severe HIV/ART-associated morbidity despite more than a decade of viral suppression, highlighting the need for ART-free viral remission.

Case 1
A Black African male aged 24, diagnosed with PaHIV at age 13, commenced Atripla with a nadir CD4 cell count of 130 cells/μL and was virologically suppressed (VL<50 copies/mL) on first-line therapy for 10 years. In 2013, his CD4 cell count was 660 cells/μL and CD4:CD8 ratio 0.7. He presented with cervical lymphadenopathy, and Hodgkin lymphoma stage IVA was diagnosed. He relapsed 1 month after completing six cycles of standard ABVD (adriamycin, bleomycin, vinblastine and dacarbazine) chemotherapy with subsequent disease progression during three cycles of salvage DHAP (dexamethasone, cytarabine, bleomycin, vindesine and dacarbazine) chemotherapy with subsequent disease progression. Tcillobinavir/ritonavir, zidovudine and lamivudine simplified to once-daily boosted darunavir and Truvada with sustained virological suppression for 10 years. In 2012, during investigation for asymptomatic thrombocytopenia (platelets 78–111 ×10^9/L), CT imaging confirmed non-cirrhotic portal hypertension with a history of 8 years of didanosine exposure in earlier childhood. Endoscopy revealed Grade 2 oesophageal varices and despite B blockade, she has had two subsequent admissions for gastrointestinal haemorrhage to date.

Case 2
A Black African male aged 20, was diagnosed in 2002, aged 6, with perinatal HIV/HBV co-infection, with a pre-treatment liver biopsy inflammatory score 6/18, fibrosis 4/6 and HBV PCR of 58,000,000 copies/mL. His nadir CD4 cell count was 260 cells/μL and HIV viral load 69,000 copies/mL. He commenced efavirenz, lamivudine, abacavir and tenofovir (TDF), the latter under

case 3
A Black African female aged 25 was diagnosed with PaHIV aged 4, and commenced first-line therapy with didanosine, nevirapine and stavudine aged 8 with a nadir CD4 cell count 420 cells/μL. Virological failure in 2005 precipitated a switch to lopinavir/ritonavir, zidovudine and lamivudine simplified to once-daily boosted darunavir and Truvada with sustained virological suppression for 10 years. In 2012, during investigation for asymptomatic thrombocytopenia (platelets 78–111 ×10^9/L), CT imaging confirmed non-cirrhotic portal hypertension with a history of 8 years of didanosine exposure in earlier childhood. Endoscopy revealed Grade 2 oesophageal varices and despite B blockade, she has had two subsequent admissions for gastrointestinal haemorrhage to date.

Conclusion
Despite marked improvements in ART, the unknown future faced by adults living with perinatal HIV infection, despite long-term viral suppression, adds weight to the prioritisation of HIV reservoir eradication strategies.

References
1. World Health Organization. March 2014 supplement to the 2013 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach. http://www.who.int/hiv/pub/guidelines/arv2013/arvs2013supplement_march2014/en/ (accessed June 2015).