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Ongoing Studies

1) NGO case histories of the early paediatric ART experience at Tygerberg Hospital - what have we learnt?
2) Vaccine immunity in adolescent perinatally infected HIV+ patients
3) Immune Activation study

1) NGO case histories of the early paediatric ART experience at Tygerberg Hospital - what have we learnt?

Dr A Houston, [Dr S Purchase, Dr M Esser, Prof M Cotton]
-in progress

In South Africa there are very few studies documenting long term outcomes in HIV+ children, partly because there are very few South African children who have been on treatment for longer than 10 years. The children funded by HOPE Cape Town were some of the initial children to start ARV's in the public sector in South Africa. They now represent a unique and pioneering group of South African young adults and adolescents, and can help clinicians identify some of the challenges and benefits of long-term ART for children. This study aims to document the success and struggles of this cohort of patients.

2) Vaccine immunity in adolescent perinatally infected HIV+ patients

Dr L Frigatti
-in progress

In the coming decades, the aging cohort of perinatally HIV-infected children entering adolescence will dominate the future of paediatric HIV in South Africa (SA). Adolescents aged 9 to 14 years will comprise the largest group of HIV-infected children in SA by 2020. Similar trends are likely to occur across Africa, and thus understanding the long-term health issues in this population is of vital importance.

HIV-infected children and adults often have an increased risk of infection or experience more severe morbidity following exposure to vaccine-preventable diseases, and therefore a lower threshold for extending indications and offering vaccination may be appropriate relative to the general population. Protection from vaccination may be sub-optimal in HIV-positive children, and while protection derived from vaccination improves with antiretroviral therapy, it often not as effective and declines more rapidly than in HIV-negative children. However, many of these vaccines still afford protection and for some vaccines it is possible to improve protection by offering modified vaccine schedules, with higher or more frequent doses, without compromising safety.

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Adolescence is a unique period for vaccination opportunities. There are new and important vaccines specifically designed for the adolescent period and vaccines that are currently being developed will target adolescents and young adults. In addition to this, pertussis, influenza and rubella vaccine can be given to adolescents to protect their children. Adolescents particularly those with HIV often lose contact with medical services and default treatment and medical care. HIV- Adolescent immunization may keep young people in care, the same way that childhood immunization at regular intervals allows an opportunity for general health care in young infants. It may also be a bridging strategy to adult care.

South African HIV-infected adolescents have received the country's standard Expanded Program for Immunization (EPI) childhood schedule. Human papilloma virus (HPV) vaccine is recommended at 9 years and tetanus and reduced dose diptheria at 12 years. There are no specific recommendations for the growing population of South African HIV-infected adolescents. International recommendations provide more frequent and broader cover of vaccine preventable diseases.

The overall aim of this project therefore is to offer an improved vaccination schedule for HIV-infected adolescents. We will check immune response to EPI vaccines and vaccinate adolescents according to responses. Response to revaccination will be checked to ensure optimal protection is afforded.

Dr Lisa Frigati is a paediatric infectious disease specialist at Tygerberg Hospital. She is currently doing her PhD.

3) Immune Activation study

Dr R Glashoff

-in progress

Hope Cape Town has helped to sponsor research by Dr Richard Glashoff into laboratory markers for immune activation in HIV+ patients.

Monitoring of HIV infection has traditionally relied on the CD4 T cell count and viral load measures. These markers are very useful in monitoring overall disease progression and also assessing patient response to ARV therapy. There are, however, some major limitations to use of these 2 tests alone. HIV infection is characterized by systemic inflammation and immune activation. Markers of inflammation and immune activation have been shown to be better predictors of disease outcome than either CD4 count or viral load. Unresolved immune activation can be problem in patients on therapy – in that promotes immune exhaustion and is also associated with more rapid development of certain chronic conditions such as cardiovascular disease (heart problems). The usefulness of monitoring laboratory parameters associated with immune activation is that it can flag patients that have unresolved immune activation – and who should be monitored for complications associated with this. In addition, the immune activation status at start of ARV therapy can predict development of IRIS

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(immune reconstitution inflammatory syndrome). The most useful measure of immune activation is the expression of CD38 on CD8 T cells.

In the study Dr Glashoff will be examining CD38 expression in relation to CD4 count and viral load in treated and untreated patients. Some additional markers around a unique subset of CD4 T cells will be investigated. The outcome of the study will be an appreciation of usefulness of monitoring immune activation in patients, how it relates to classical markers (CD4 count and viral load) and to some novel, recently described markers. Ultimately the study hopes to promote the monitoring of immune activation in patients initiating therapy and also in those with complications despite a controlled viral load.

Dr Richard Glashoff is a Senior Specialist Scientist in the Immunology Unit within the National Health Laboratory Service (NHLS); is a joint position including research with Stellenbosch University. He is primarily mandated with developing research capacity in immunology, but also in diagnostic laboratory support and teaching/training.