External Research – sponsored by HOPE Cape Town

1) Neurodevelopmental outcomes of HIV exposed uninfected children (2018)
2) Flow cytometric quantification of follicular helper T cells in relation to other lymphocytes in HIV infection (2017)
3) A prospective evaluation of feeding disorders in HIV infected children (2012)
4) The Sangoma 'Muti' Project (2012, 2014)

1) Neurodevelopmental outcomes of HIV exposed uninfected children

This is a neurodevelopmental study nested in the Mother and Infant Health study; a longitudinal study researching the innate immune abnormalities of HIV-exposed but uninfected (HEU) infants. Successful Prevention of Mother to Child transmission programmes have led to a significant reduction in the number of HIV-infected new-borns. Consequently an increasing proportion of South African infants (estimated at 30%) although HIV negative, have an HIV-infected mother. There are biological and environmental risk factors associated with having an HIV-infected mother which have the potential to affect infant cognition and behaviour. A pilot study was done in 2012 that laid the foundation for this study. *(http://www.sajch.org.za/index.php/SAJCH/article/view/409/295)*

The purpose of this research is to determine whether there is a difference in the neurodevelopmental outcome of HEU infants compared with a well-matched control group of HIV-unexposed infants (HUU). Ninety six children have been tested in infancy (11-14 months) and are now being reassessed as toddlers (30-42 months) using the Bayley scales of infant mental development.

A secondary objective of the study is to improve early detection of developmental delay. Finding suitable screening tools which are culture neutral and applicable in a low resource environment will allow early detection and prompt referral. In this way appropriate intervention could be instituted early to prevent or limit neurodevelopmental delay.

By: Dr Priscilla Springer (Paediatric Neurodevelopment specialist at Tygerberg Hospital)
https://www.ncbi.nlm.nih.gov/pubmed/29131457
Published in January 2018 in Tropical medicine and International health 2018 Jan; 23(1):69-78

2) Flow cytometric quantification of follicular helper T cells in relation to other lymphocytes in HIV infection

P Olifant, Dr R Glashoff

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

In the study Ms Oliphant and Dr Glashoff examined the 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 were investigated. The outcome of the study was 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.

This research was part of Paulina Oliphant's BSc Honours degree through Stellenbosch University's Medical Microbiology department. 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.

3) A prospective evaluation of feeding disorders in HIV infected children

Although swallowing disorders occur in almost 80% of HIV-infected adults, the prevalence in children is unknown. These disorders are associated with loss in quality of life, decreased drug adherence, aspiration pneumonia, and malnutrition. The purpose of this study is to describe the prevalence, aetiology, nature and morbidity of feeding and swallowing disorders in a sample of HIV-infected infants and children in the era of anti-retroviral treatment (ART). A secondary outcome was to assess the prevalence of functional gastrointestinal disorders in HIV-infected children.

Two-hundred-and nineteen children were enrolled in the study. The prevalence of swallowing disorders was 15%. This is lower than the 45% prevalence reported prior to the introduction of ART. Severity of feeding difficulties was associated with the developmental delay. Infections and structural abnormalities of the pharynx and oesophagus were rare. Functional gastrointestinal complaints were rare, an unexpected finding in a group of children with chronic disease.

By: Prof Etienne Nel (paediatric gastroenterologist at Tygerberg Hospital) and Alida Ellis
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3441289/
Published June 2012 in BMC Paediatrics 2012; 12: 68

4) The Sangoma 'Muti' Project

Traditional medicines used by Sangomas in South Africa: Assessment of the potential for pharmacokinetic drug interactions.

A research project was done to address the potential effect of traditional medicines used by traditional health practitioners (sangomas) on the blood concentrations (pharmacokinetics) of conventional drugs, including drugs used for treatment of HIV/AIDS. This information is important for the management of HIV patients, because traditional health practitioners will often give these patients herbal medicines for various conditions.

Two of the sangomas who cooperate with HOPE Cape Town supplied 15 traditional medicines and provided advice on how they are used by patients in their communities.

By Pius Fasinu (Doctoral [PhD] student in Pharmacology at Stellenbosch University)
Initial results of this project were presented at the 6th International Conference on Pharmaceutical and Pharmacological Sciences, Durban, South Africa (25.-27 September 2011)

His PhD dissertation entitled "In vitro assessment of some traditional medications used in South Africa for pharmacokinetic drug interaction potential" is available online at: *scholar.sun.ac.za/bitstream/handle/10019.1/85850/fasinu_invitro_2013*

Further papers arising from his research include:

"The Inhibitory Activity of the Extracts of Popular Medicinal Herbs on CYP1A2, 2C9, 2C19 and 3A4 and the Implications for Herb-Drug Interaction"

Studies have suggested an increasing practice of concurrent herb-drug consumption. One of the major clinical risks of such concomitant herb-drug use is pharmacokinetic herb-drug interaction (HDI). This is brought about by the ability of phytochemicals to inhibit or induce the activity of metabolic enzymes.

The aim of this study was to investigate the potential of the crude aqueous extracts of three popular medicinal herbs used in South Africa to inhibit major cytochrome P450 (CYP) enzymes.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4202397/
In African Journal of Traditional, Complementary and Alternative Medicine 2014; 11(4): 54–61.
By: Pius Fasinu, Patrick J Bouic and Bernd Rosenkranz

"Drug-drug interactions in ageing HIV-infected individuals"

The proportion of ageing HIV-infected individuals continues to increase. HIV-associated and age-related comorbidity necessitates polypharmacy in ageing individuals living with HIV/AIDS. The risk of drug-drug interaction increases with the number of administered drugs. Age-related changes in the body physiology are known to influence pharmacokinetic and pharmacodynamic profile of administered drugs. This paper reviews the reported incidence of drug-drug interactions in ageing HIV-infected individuals, providing relative mechanisms and possible factors responsible in comparison to younger population.

http://www.academicjournals.org/AJPP
Published October 2012 in African Journal of Pharmacy and Pharmacology Vol. 6(38). pp. 2710-2723, 15 October, 2012
By: Pius S. Fasinu and Bernd Rosenkranz

“An overview of the evidence and mechanisms of herb-drug interactions”

Given the globally increasing popularity of herbal medication use, the risk of herb-drug interactions is increasing despite the lack of knowledge about such interactions. This paper provides a general overview of the significance of pharmacokinetic and pharmacodynamic Herb-Drug interactions, detailing basic mechanism, and nature of evidence available.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3339338/
Published April 2012 in Frontiers in Pharmacology 2012: 3: 69
By: Pius Fasinu, Patrick J Bouic and Bernd Rosenkranz

“Liver-Based In Vitro Technologies for Drug Biotransformation Studies -A Review”

This paper reviews various in vitro technologies. It highlights the general principles of in vitro enzyme kinetics and the factors that determine the choice of each in vitro technology for biotransformation studies.

https://www.ncbi.nlm.nih.gov/pubmed/22300020
Published February 2012 in Current Drug Metabolism, 2012 Feb; 13(2):215-24.
By: Pius Fasinu, Patrick J Bouic and Bernd Rosenkranz

“When garlic makes you pregnant”

In this brief article for the Stellenbosch University journal, Pius describes the risk of interactions between herbal medication and western medication through their effect on liver enzymes. New voices in Science, Stellenbosch University journal 2013.