

Stellenbosch University

HIV Aids



a strategic research priority



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MESSAGE FROM THE RECTOR AND VICE-CHANCELLOR

As a research-driven institution focused on crucial themes of the international development agenda, Stellenbosch University plays an active role in shaping a future of hope for all the people of South Africa and the continent at large. With 22 million people in sub-Saharan Africa carrying the HI virus it is clear that HIV and infectious diseases present a huge challenge to South Africa and the rest of the world. Hence, our approach to focus on HIV and AIDS as a strategic research priority.

Strategic priorities require strategic partnerships. Collaborative research in the broadest sense of the word, is the best approach to address challenging issues such as HIV and AIDS. At Stellenbosch we are entering an era of Hope. We want to be role-players in creating a better world and delivering substantive and sustainable solutions to the daunting problems of our modern society. In the words of a dear friend and colleague, Dr Betty Siegel of Kennesaw State University: “We are all excellent in what we do independently ... but we are so much better together”. Let us join hands and forces in turning the tide on this pandemic.



Prof. H Russel Botman

Rector and Vice-Chancellor



“At Stellenbosch we are entering an era of Hope. We want to be role-players in creating a better world...”

MESSAGE FROM THE VICE-RECTOR: COMMUNITY INTERACTION AND PERSONNEL

Many high profile national and international projects concerning HIV/Aids had little impact, in spite of extensive resources being invested and lofty ideals being impressively communicated. One reason might be that this is an especially difficult terrain; another might be the absence of credible research. In addition, agencies and institutions may also be characterised by a lack of coherence, coordination and commitment.

Much of the Stellenbosch University (SU) academic brand relates to research excellence, with the university having defined itself explicitly as a research-oriented institution. Furthermore, the development, dissemination and application of knowledge have been emphasised as a strategic priority. And more recently the Millennium Development Goals and the Pedagogy of Hope have become points of reference with regards to the institutional objectives. As a result of the nature of the challenges facing HIV/Aids and the academic and research expertise which exists in the University, it is inevitable that the expectation would be that SU should make a major contribution to research in this field.

It is the aim of the broad EU funded HEAIDS Project to contribute to the creation of an institutional environment where researchers can increase the quality and relevance of HIV-related research through collaboration, networking and partnerships. This publication offers opportunities for HIV experts to collectively contribute to internal and external networking and knowledge sharing. It is no coincidence that SU has included research collaboration in its proposal to the HEAIDS Project. While we believe that our researchers can make a valuable national contribution (with the real possibility of international recognition), we are also sure that our institution should be a direct beneficiary of our research endeavours in the field of HIV/Aids. For this to happen, the establishment of a collaborative network of experts seems to be imperative. (HEAIDS, in its Gap-analysis, identifies the need for “quality research” to be developed and disseminated as a key objective.)



The Office for Institutional HIV Co-ordination, the Division of Research Development and the individual researchers and units which have responded to the objective of collaboration, need to be commended and challenged. SU has, within a short space of time, established itself as a significant roleplayer regionally, as well as nationally. In particular, we have been singled out by HEAIDS for the commitment and dedication to and delivery on the project. We expect our research community to confirm and even improve our stature and should not accept taking a back-seat to other universities.

We must ensure that a sustainable collaborative network is developed. This should not only be beneficial to the University and national agencies, but should also prove to be beneficial to our research community, especially to funding and research partnerships. “Somewhere, something incredible is waiting to be known,” in the words of the American astronomer, writer and scientist Carl Sagan.

Prof. Julian Smith

*Vice-Rector: Community Interaction and Personnel
Chairperson of the HIV Institutional Coordinating Committee
(HICC), Stellenbosch University*

MESSAGE FROM THE VICE-RECTOR: RESEARCH

The vision of Stellenbosch University, as a research-driven university includes promoting academic excellence and knowledge partnerships; building scientific and intellectual capacity in Africa; playing an active role in South Africa's development; and promoting institutional diversity.

Research is a strategic element of the “knowledge partnership” approach expressed in the powerful credo ‘Your Knowledge Partner’, namely the fostering of mutually beneficial knowledge-based relationships, both with civil society and our industrial partners.

With due cognisance of the challenges of relevance and significance, the core activities of teaching and learning, research and community interaction, are aligned with the following overarching themes:

1. Consolidating democracy and ensuring regional peace and security
2. Eradicating endemic poverty
3. Contributing to human dignity and health
4. Ensuring environmental and resource sustainability
5. Maintaining the competitiveness of the industry

HIV/Aids research plays an important role in the strategic area (3), although relevant to (2). In January 2008, Stellenbosch University (SU) became involved in a larger national Higher Education AIDS programme (HEAIDS) that is being funded by the European Union with a view to develop, facilitate and strengthen institutional structures that will promote collaboration and networking between researchers in the field of HIV/Aids. The aim of the specific project is to create a collaborative forum of research experts across disciplines that prioritise HIV research, which will in turn inform national and global strategies.

A memorandum of understanding was also signed between Stellenbosch University and the Human Sciences Research Council in September 2008 to establish a framework for collaboration in the areas of research, staff development,



development and administrative initiatives, student supervision and sharing of facilities and resources. One of the main transdisciplinary umbrella themes that were identified for the initial phase of collaboration is the social aspects of HIV/Aids.

In January 2009, we compiled a register of 270 SU projects linked to HIV/Aids research with active involvement from medical sciences, broad natural sciences as well as human and social sciences. It shows that the researchers at Stellenbosch University is committed to producing knowledge in this field that is both significant and relevant and that can be actively applied and translated into policy for the betterment of our society.

I hope that this selection of contributions to the field of HIV/Aids research will trigger the possibility of future collaboration and networking with us. In doing so, you will contribute to one of our major research themes “Contributing to human dignity and health” and join hands with us to leave a significant scientific footprint in Africa. In addition you will contribute towards making Africa a continent of hope.

Prof. Arnold van Zyl
Vice-Rector: Research

Understanding

HIV/Aids



SOUTH AFRICAN CENTRE FOR EPIDEMIOLOGICAL MODELLING AND ANALYSIS

In May 2006, the DST/NRF Centre of Excellence for Epidemiological Modelling and Analysis (SACEMA) was launched at Stellenbosch University campus. SACEMA uses mathematics to model the prevalence, incidence and dynamics of diseases such as HIV/Aids and tuberculosis. The aim is to develop evidence-based management strategies for the control of these diseases. In the first three years of its existence SACEMA has been involved in several research projects on HIV/Aids resulting in scientific publications, presentations, meetings and the acquisition of funding. Presented here are the results of some of the keynote research projects.

Male Circumcision: Number One medical breakthrough

The first male circumcision randomised controlled trial was carried out at Orange Farm in South Africa. It showed that male circumcision reduces sexual transmission of HIV from women to men by 60%. Recently the results of the trial were confirmed in two further randomised controlled trials carried out in Uganda and Kenya. Based on the results of the South African trial a theoretical study was conducted by SACEMA founder Brian Williams and co-authors, including several other SACEMA workers. The study explored the implications of the findings for the promotion of male circumcision as a public health intervention to control HIV in sub-Saharan Africa. It was estimated that male circumcision could avert 2.0 million new HIV infections and 0.3 million deaths over the next ten years in sub-Saharan Africa (assuming that full coverage of male circumcision is achieved over this period). In the ten years after that, it could avert a further 3.7 million new HIV infections and 2.7 million deaths, with about one quarter of all incident cases prevented and the deaths averted occurring in South Africa.

As other strategies have not yet exhibited comparable efficacy in reducing the risk of sexually transmitted HIV (the “ABC” approach, vaccine, microbicides, antiretroviral drugs for prevention), male circumcision has an important

role in preventing the transmission of HIV, especially in southern Africa where the prevalence of male circumcision is low and the prevalence of HIV is high. For this reason male circumcision was voted by *Time* magazine as the Number One medical breakthrough of 2007. SACEMA has published scientific articles on the topic and organised three meetings to discuss ways of promoting male circumcision as a public health intervention.

The aim is to develop evidence-based management strategies for the control of HIV/Aids and tuberculosis.

Holy Grail for incidence estimation

Interpretation of HIV data would be considerably simplified, and also made much more valuable, if it were possible to make simple estimates of HIV incidence. The Holy Grail in this regard is a test that could be used to identify clearly recent infections from a cross-sectional survey. SACEMA has made important contributions in this field.

A technique for estimating incidence from cross-sectional surveys, BED, initially resulted in overestimates. SACEMA workers have made several separate contributions to the development of methods by which the estimates could be improved through statistical adjustments. The ideal has not yet been realised, but research projects are still ongoing to improve the technique. Furthermore SACEMA has put the theoretical framework for the estimation of incidence by techniques such as BED on a much sounder mathematical and theoretical ground. As a result of these research activities, SACEMA is now seen internationally as an



Anton Jordaan, SSFD

important player in the field of incidence estimation from cross-sectional survey.

Two dependent problems: HIV and TB

SACEMA also focuses on research on the interaction of HIV and TB. Modelling the interaction between these two diseases is particularly important because there is a tendency to treat the two problems independently. SACEMA developed a microsimulation model for general use in simulating HIV/TB epidemics. Furthermore an impressive report

document was produced that has served as the basis for further work in this area. As a result of this earlier work new projects were started and significant funding from the Canadian International Development Agency was secured in support of work in various areas.

Project leader:

Prof. John Hargrove

SACEMA

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THE CENTRE FOR INFECTIOUS DISEASES

Acknowledging the urgent need for an interdisciplinary approach to generating new knowledge and expertise in the field of infectious diseases, the Faculty of Health Sciences at Stellenbosch University created the Centre for Infectious Diseases (CID) which was officially opened on 21 April 2008. The CID is a joint platform where experts from various disciplines within the Faculty can work together and share their expertise in research, training and service. Adult and paediatric infectious diseases, microbiology, virology, infection control, epidemiology, public health and basic biomedical sciences are all represented in the new centre.

Research of CID members is mainly focused on the HIV/Aids and tuberculosis epidemics in South Africa and beyond with special focus on sub-Saharan Africa, but other areas such as hospital infections, growing antibiotic resistance and revival of old diseases such as malaria, environmental health, tick-borne diseases, and prospective clinical trials on new drugs and drug strategies, are also significantly represented.

Professor Jean Nachega, an internationally acclaimed expert and researcher on infectious diseases, was appointed as the first director of the CID. His research, teaching, and professional activities include planning, design, monitoring, and evaluation of clinical trials, cohort studies and programmes for prevention and treatment of HIV/Aids and related opportunistic infections.

Selected HIV/Aids scientific contributions of CID members

Professor Nachega and colleagues shed light on the relationship between adherence to Non-Nucleoside Reverse Transcriptase Inhibitor-based HIV Therapy and virologic outcomes. The linear dose-response pattern is linked to various virologic outcomes in HIV-infected adults (Nachega *et. al. Ann Intern Med.* 2007 Apr 17;146(8): 564–73). In addition, Professor Nachega and colleagues provided robust evidences of the superiority of adherence over CD4+ T-cell count monitoring to predict virological failure in HIV-infected adults on highly

active antiretroviral therapy in southern Africa. Based on the results of this study and others, the World Health Organisation's recommendations related to monitoring of highly active antiretroviral therapy (HAART) in resource-limited settings are being revised (Bisson & Nachega: *PLoS Med.* 2008 May 20;5(5): e109). Professor Nachega and colleagues conducted the first study in southern Africa showing that in initial HAART regimens, efavirenz was associated with superior virologic and clinical outcomes to nevirapine, suggesting that efavirenz might be the preferred non-nucleoside reverse transcriptase inhibitor in resource-limited settings. However, its higher cost and potential teratogenicity are important barriers to implementation (*AIDS.* 2008 Oct 18;22 (16): 2117–25).

The CID is a joint platform where experts from various disciplines within the Faculty can work together and share their expertise in research, training and service.

In a recent groundbreaking trial, Professor Mark Cotton and colleagues, investigated antiretroviral-treatment strategies in the Children with HIV Early Antiretroviral Therapy. Indeed, in countries with a high seroprevalence of human immunodeficiency virus type 1 (HIV-1), HIV infection contributes significantly to infant mortality. In this study, Professor Cotton and colleagues found that early HIV diagnosis and early antiretroviral therapy reduced early infant mortality by 76% and HIV progression by 75%. Based on the results of this study, international pediatric guidelines have been changed (Violari, Cotton *et.al. N Engl J Med.* 2008 Nov 20;359 (21): 2233–44).

A study led by Dr Gert van Zyl and Professor Wolfgang Preiser investigated resistance to NVP in mothers who had received a dual-drug regimen for prevention of mother-to-child transmission. In specimens obtained within 60 days of delivery, NVP resistance mutations were detected in 13 of 76 patients (17.1%, 95% confidence interval: 8.7–25.6%), i.e. at a much lower rate than in studies on patients receiving sd NVP alone (37.5%, 95% confidence interval: 23.0–50.6%). This finding strongly supports the current provincial guidelines which have now been adopted for the whole country (*J Med Virol.* 2008).

Selected research capacity-building initiatives of CID members

An application for an African Institutions Initiative Grant entitled “Southern Africa Consortium for Research Excellence” (SACORE) was considered at a meeting of the African Institutions Initiative Wellcome Trust Committee in December 2008 and an award was recommended at a level of £5 million over five years. The committee considered that a strength of the SACORE application was the proposed partnership between low-income African countries (Malawi, Zambia, Zimbabwe), with middle-income countries (South Africa with Stellenbosch University and University of Cape Town and Botswana with Botswana Harvard Partnership) and UK partners (London School of H&TM, Liverpool SH&TM, UCL, Barts Univ), for provision of PhD and Masters training with mentoring for existing staff and professional development. Furthermore, the committee highlighted that the strength of the application was that the PhD programmes would be based in Africa with quality maintained through an outstanding system of supervision. This five-year grant will also provide seed money that will help to build new research support centres in low-income countries and enhance existing centres in middle-income countries.

Selected training services of CID members

The International Partnership on HIV (IPH) between the CID of Stellenbosch University, HIVCENTER of the Johann Wolfgang Goethe University in Frankfurt am Main, Germany and the KARABONG Clinic in Mafeteng Government Hospital in Lesotho aims to contribute to the international containment of HIV/Aids and related diseases. It links the diverse sources of knowledge and expertise on HIV/Aids available within an international network to optimise treatment, care and prevention of HIV/Aids and associated diseases in a way that is best suited for local conditions. The strengthening of international knowledge and expertise takes place through training programmes such as annual summer schools focusing on the management of new emerging and reemerging epidemics with specific focus on HIV/Aids and associated diseases.

Themes for the summer schools include:

- The global binding site – connecting individualised therapy and public health approach in the treatment of HIV/Aids
- HIV as a family health problem
- Scaling up or breaking down – treating HIV in many with little resources
- International management of emerging, reemerging and chronic epidemics – lessons learnt from AIDS to SARS.

Project leaders:

Prof. Jean Nachega

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Centre for Infectious Diseases, Faculty of Health Sciences

THE HUMAN IMMUNODEFICIENCY VIRUS AND CANCER IN CHILDREN

In 2005, the AIDS pandemic claimed an estimated 2.8 million lives of which 570 000 were children. A third of these deaths are occurring in sub-Saharan Africa. Southern Africa has the largest number of HIV patients in the world and it is estimated that almost 300 000 children in South Africa are infected. Immunodeficiency increases the risk of certain, but not all, types of cancer. A common feature of these malignancies is that specific infectious agents appear to be important in their aetiology, not only in immunodeficient subjects but also in the general population.

More than 40 million people are now infected with the human immunodeficiency virus (HIV), the majority in sub-Saharan Africa, and this has provided an opportunity to investigate the role of the immune system in the aetiology of cancer as well as possibly identifying as yet unknown cancers with an infectious cause. Furthermore, an infectious cause of cancer might more easily be identified in the immunosuppressed than in the immunocompetent using current technology, because for certain viruses, such as HHV-8, viral genomes and gene products are more easily detected in an individual as immune function declines. Therefore, information gained from the study of HIV associated cancers is likely to be relevant to the HIV uninfected population as well.

Infection with HIV is causally associated with Kaposi's sarcoma, non-Hodgkin's lymphoma, and with conjunctival squamous cell carcinoma. For each of these malignancies, other known viruses, notably human herpes viruses and papilloma viruses are believed to be important causes. Moreover, similar associations between these viruses and cancers have been found in people who are not immunosuppressed. The great majority of HIV infected children acquire the virus in the first months of life, while the immune system is developing and prior to exposure to many other immunological challenges. The role of this particular phenomenon in the etiology and clinical manifestation of cancer in children infected with HIV has not yet been studied.

Despite the fact that HIV infection is more prevalent in parts of sub-Saharan Africa than elsewhere, there is only one published

study from Africa that investigated the scale of the excess risk of cancer in HIV infected as compared to uninfected children: a small case-control study of childhood cancer in Uganda showed that HIV infection increased the risk both of Kaposi's sarcoma and of the African endemic form of Burkitt's lymphoma. Results for acute lymphoblastic leukaemia were suggestive of an association with HIV infection, but were not significant.

The aim of this study is to identify types of childhood cancer that are associated with HIV infection in South Africa. Other aims are:

- to examine socioeconomic and demographic risk factors for childhood cancer, relevant to the transmission of, and exposure to, infectious disease; and
- to establish a repository of data and biological material from southern African children with cancer, for future studies of infectious and genetic causes of childhood malignancies.

This research is being undertaken by Stellenbosch University in collaboration with York – Oxford University. Dr D. Cristina Stefan, Head of Paediatric Oncology at Stellenbosch University, is the principal investigator; she coordinates all sites in South Africa. The United Kingdom team is coordinated by Dr Rob Newton. Ethical approval has been obtained and over 100 mother-child pairs (with laboratory confirmed cancer in the child) have already been recruited and tested for infection with HIV in pilot studies. Biological samples were collected on all children and their mothers and blood and saliva samples are currently stored in an alarmed freezer in Tygerberg Hospital, Cape Town, ready for shipment on dry ice to the UK.

Project leader:

Dr D. Cristina Stefan
Department of Paediatrics and Child Health,
Faculty of Health Sciences
Email: cs@sun.ac.za

Project members:

Prof. D. Stones, J.E. Poole, M. Kruger, Dr L. Wainwright.

INTERNATIONAL RESEARCH TRAINING GROUP SUPPORTS YOUNG RESEARCHERS

Research Training Groups (Graduiertenkollegs) are university training programmes established to support young researchers in their pursuit of a doctorate. Funded by the German Research Foundation (Deutsche Forschungsgemeinschaft), they provide doctoral students with the opportunity to work within a coordinated research training programme run by a number of university teachers. While incorporated into the research work at the participating institutions, the study programme aims to complement and extend the doctoral students' individual specialisations and to provide a structure for cooperation. An interdisciplinary focus of the research and study programme is desired.

Doctoral students are given the opportunity to work within a coordinated research training programme run by a number of university teachers.

Twelve research groups from the Universities of Stellenbosch and Cape Town in South Africa have recently embarked on the first ever International Research Training Group (IRTG) for the whole of Africa. Scholarships for the South African PhD candidates and joint activities are funded by the National Research Foundation. The IRTG provides unprecedented opportunities for engaging in joint doctoral training between the South African group (speaker: Wolfgang Preiser) and their partner group at the University of Würzburg in Germany (speaker: Axel Rethwilm).

The IRTG's topic is "HIV/Aids and associated infectious diseases in Southern Africa". Its scientific topics focus on translating clinical into basic research on infectious diseases. The PhD students work on HIV molecular epidemiology and drug resistance, *Staphylococcus aureus*, pathogenic fungi, Plasmodium and HIV, and Leishmania. In addition, projects on the immunology of infectious diseases, on general mechanisms of virus-induced immunosuppression and on clinical HIV medicine are conducted.

The research and study programmes are jointly developed and supervised. Doctoral students in the programme complete a six-month research stay at the respective partner institution. They will also be given the opportunity to attend retreats and summer schools on relevant topics.

Project leader:

Prof. Wolfgang Preiser
Department of Pathology, Faculty of Health Sciences
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The following researchers at the Faculty of Health Sciences, SU, are involved:

Paul Carey, Psychiatry, Mark Cotton, Paediatric Infectious Diseases, Susan Engelbrecht, Medical Virology, Bernd Rosenkranz, Pharmacology, Jantjie Taljaard, Adult Infectious Diseases, Gert van Zyl, Medical Virology, Gerhard Walzl, DST/NRF Centre for Excellence in Biomedical TB Research, and Elizabeth Wasserman, Medical Microbiology.

HIV-1 MOLECULAR EPIDEMIOLOGY AND DIVERSITY

One of the major features of HIV-1 is the extreme genetic diversity. The strains of HIV-1 are classified into three groups: the major group M, the outlier group O and the new group N. More than 95% of HIV-1 infections worldwide are caused by HIV-1 group M that is subdivided in genetically distinct subtypes (subtypes A, B, C, D, F, G, H, J and K).

Stellenbosch University is conducting a longstanding research programme into the molecular diversity of the HIV-1 epidemic and the characterisation of the virus in South Africa.

A feature of HIV-1 is also genetic recombination and at least 43 circulating recombinant forms (CRFs) have been described. The HIV-1 subtypes and CRFs are unevenly distributed throughout the world, with the most widespread being subtypes A and C. Subtype C is the predominant subtype of HIV-1 in South Africa and it is also responsible for more than 50% of all HIV-1 infections in the world. HIV-1 subtype diversity has been implicated as an important factor in the transmission and pathogenesis of the virus; the accuracy of diagnostic laboratory assays; antiretroviral treatment and the development of antiretroviral resistance; and also possible vaccine development.

Stellenbosch University is conducting a longstanding research programme into the molecular diversity of the HIV-1 epidemic

and the characterisation of the virus in South Africa, with six different projects currently running. One project aims to characterise non-subtype C viruses and recombinants using polymerase chain reaction (PCR) amplification, cloning and sequencing of the complete viral genomes. Cutting-edge computational analysis is done to investigate diversity and evolution of the strains. Another project is the first subtype analysis of HIV-1 in the Eastern Cape, from where no HIV-1 subtypes have been described yet.

The vpr protein of HIV-1 interferes with different cellular pathways and is crucial for HIV-1 pathogenesis. Most international publications on the functions of the vpr protein were done with HIV-1 subtype B strains. We are investigating genomic diversity in subtype C strains and its influence on vpr function. Studying the vpr protein and its influence on cells may elucidate not only HIV-1 pathogenesis but also cellular processes and lead to the development of novel anti-HIV-1 therapeutics.

The HIV-1 env gene plays an important part in the viral life cycle and pathogenesis. Functional env genes have been used for vaccine design, neutralisation assays and pathogenesis studies. The env pseudotyped viruses can also be used for studying antiviral agents that interfere with virus entry into the target cells. The purpose of another project is to set up an HIV-1 single cycle pseudovirus assay and to use this assay to characterise env genes obtained from different HIV-1 subtypes.

Project leader:

Dr Susan Engelbrecht

Department of Pathology, Faculty of Health Sciences

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Preventing

HIV/Aids

AFRICA CENTRE FOR HIV/AIDS MANAGEMENT

The Africa Centre for HIV/AIDS Management was established in January 2003 and today it offers one of the most comprehensive HIV training programmes in the world, empowering people to take control of the epidemic and to reach out to those affected by HIV and AIDS. These include the Postgraduate Diploma in HIV/AIDS Management (PDM), as well as a masters programme (MPhil). These programmes are a true reflection of the philosophy of the Centre that academic institutions must help transform society and that academic programmes must have a real-life impact. There are numerous examples of current and past students who are already making a difference in the management of HIV and AIDS in their workplace or environment.

The Centre is an independent unit for teaching, research and community service related to the management of HIV/AIDS in the workplace at Stellenbosch University. The Centre believes academic institutions must play a creative and active role in social, political and economic transformation and aims to:

- offer postgraduate teaching programmes and conduct research on the problematics with respect to HIV/AIDS in the workplace, and the publication of research findings in the appropriate media;
- develop and implement community service projects that are related to the management of HIV/AIDS in the workplace and community;
- develop expertise and infrastructure in order to maintain the highest possible standards in teaching, research and service provision and make the expertise in the field of HIV/AIDS available to individuals and organisations that require it; and
- control and manage external funding that has been obtained with a view to performing the Centre's functions.

The Centre and its teaching/research results have been widely accepted as a benchmark and model for the African continent. It enjoys strong government support and is a UNAIDS collaborating centre on capacity building, community mobilisation and research dissemination.

The Centre's flagship community mobilisation prevention programme – in the form of educational theatre – focuses specifically on the Afrikaans-speaking, coloured communities on the farms and the outlying areas of the Western Cape. This program has proved to be a very successful HIV/AIDS prevention tool and one of its main aims is to get people tested. The Artists for AIDS Awareness concert series is presented quarterly and culminates in the Centre's annual World AIDS Day gala concert on 1 December each year. With these concerts, the Centre strives to further promote HIV/AIDS awareness and prevention.

Together with the academic programmes and community mobilisation, research is one of the foundational pillars of the Africa Centre. The Centre conducts research with respect to HIV/AIDS in the workplace and publishes the findings in academic journals and appropriate media.

The Centre assists Stellenbosch University to plan strategically for the impact of HIV/AIDS on students and staff via its Comprehensive Institutional HIV Response Programme. This programme aims to integrate and coordinate all existing HIV/AIDS functions within the University's structures in order to mainstream HIV/AIDS issues through all aspects of the University's core business activities.

Project leader:

Prof. Jan du Toit
Africa Centre for HIV/AIDS Management
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PREVENTION OF HIV TRANSFER FROM MOTHER TO CHILD

Most children living with HIV become infected through perinatal mother-to-child-transmission. In 2005 the global prevalence of HIV among children younger than 15 years was 2.3 million and of those 80% was in sub-Saharan Africa. Even with the implementation of prevention strategies the new infections in children came to 350 000 in 2007. In developed countries the transmission rate has dropped to less than 2% (0.99% in some), which is proof that an effective Prevention of Mother-to-Child-Transmission (PMTCT) programme will reduce the number of perinatal acquired HIV infections.

In order to improve the quality of PMTCT programmes in South Africa, we need to overcome a number of challenges, many of which are avoidable. The studies that we have conducted and will conduct focus mainly on prevention of PMTCT. We trust that the results of these studies will be received and implemented with much enthusiasm.

The Department of Obstetrics and Gynaecology, together with the Department of Pediatrics, are involved in several HIV related research projects of which the following examples are relevant:

Mother infant rapid intervention at delivery (MIRIAD)

The exact management of women who enter the labour ward with an unknown HIV status is still unsure. There have been numerous debates on the ethics of counselling and testing women for HIV during labour. The purpose of this study (P1031A) was to determine whether this practice is feasible and acceptable to women.

Women who entered the labour ward at two study sites were randomised to be counselled and tested either during labour (intrapartum) or after delivery (postpartum), with calendar weeks being the unit of randomisation. Staff was on duty 24/7 and in two years 7 238 women were screened, of whom 3 596

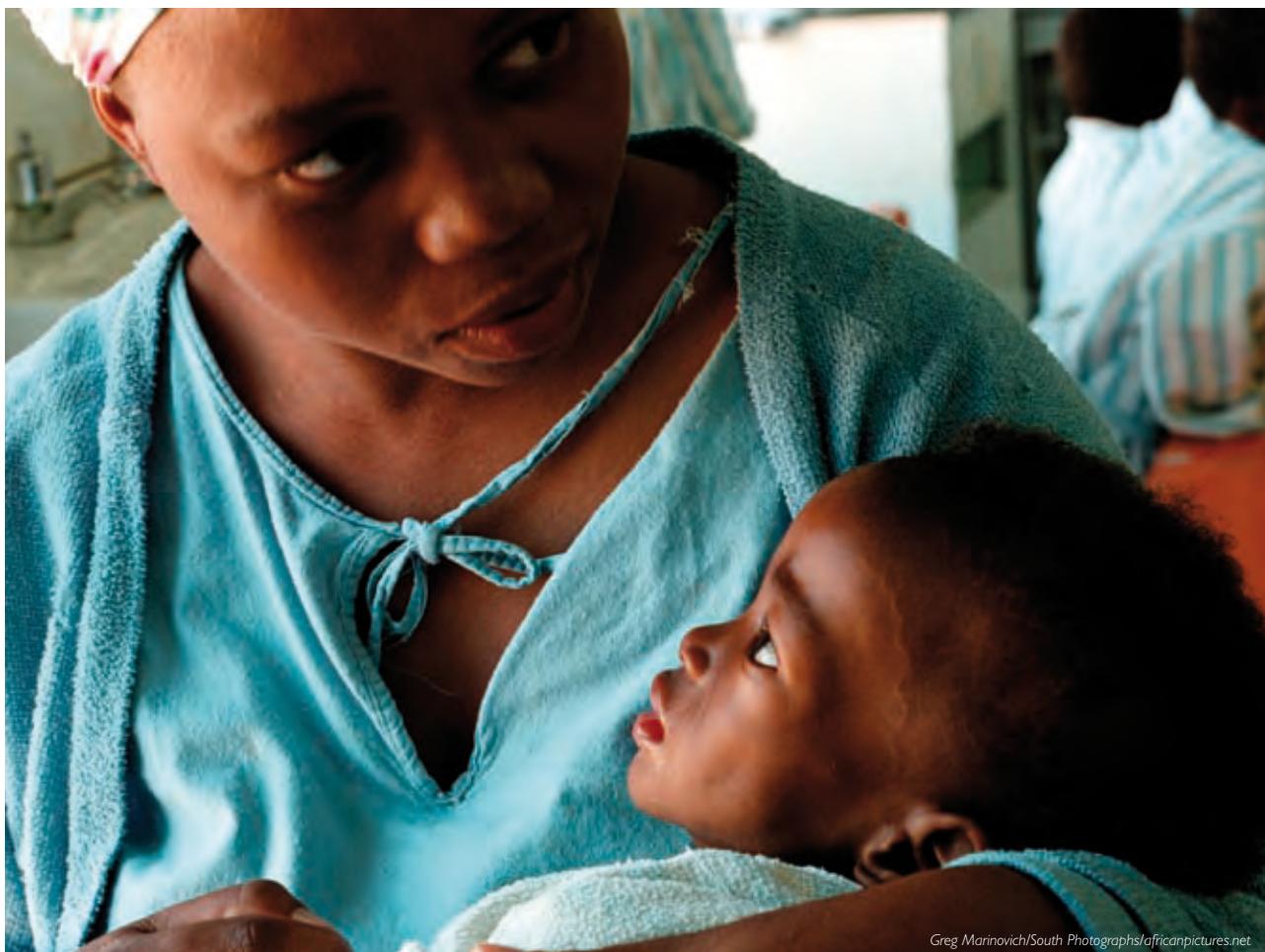
were intrapartum, and 3 642 postpartum. Of these women 542 were eligible and 343 were enrolled (intrapartum = 161; postpartum = 182). It was found that testing women intrapartum was both acceptable to the women and feasible. All women received treatment well in time of the delivery after being tested during labour.

In order to improve the quality of PMTCT programmes in South Africa, we need to overcome a number of challenges, many of which are avoidable.

The safety and efficacy of three neonatal antiretroviral regimens for prevention of intrapartum HIV-1 transmission

Many HIV-positive women deliver their babies without receiving antiretroviral therapy for prevention of mother-to-child-transfer of the virus during pregnancy and delivery. In most cases this is because the HIV status is unknown. About 10% of women still do not attend antenatal clinics or they simply “fall through the system”. The purpose of this study (HTPN 040/P1043) is to identify these women, test them for HIV after delivery and randomise their babies to receive one of three treatment options (one regimen includes a protease inhibitor). The efficacy and safety of these three antiretroviral regimens will be compared.

To date we have tested 690 women of whom 104 tested positive and were enrolled in the study. The research programme will continue until the end of 2009.



Greg Marinovich/South Photographs/africanpictures.net

Comparison of HIV transmission from mother to child in highly active antiretroviral therapy (HAART) and in dual therapy respectively

Most children living with HIV become infected through perinatal mother-to-child-transmission. The aims for this retrospective case control study were to determine whether there is a difference in perinatal HIV transmission between mothers who received HAART therapy during pregnancy and mothers who received the standard provincial dual therapy

regimen and to determine if the CD4+ count of the mother plays a role in perinatal HIV transmission.

Files of all HIV positive women who delivered at Cape Town's Tygerberg Hospital between January 2007 and April 2008 were obtained after discharge. The antiretroviral treatment, which could be either HAART or dual therapy, received during pregnancy was recorded, along with other related data. A total of 581 HIV positive women were delivered during the

Many HIV-positive women deliver their babies without receiving antiretroviral therapy for prevention of mother-to-child-transfer of the virus during pregnancy and delivery. In most cases this is because the HIV status is unknown.

study period. The study group was the 73 patients on HAART. The dual therapy group comprised of 508 patients, from which the control group of 146 were randomly selected. The difference in transmission rates in the study 2/58 (3.4%) and control group 12/119 (10.1%) was not significant ($p=0.15$). If the CD4 count was <250 the transmission rate was 6/21 (28.6%) in the control group. The high transmission rate (10.1%) in the dual therapy group is due to a very high transmission rate in the group with a CD4 count <250 (28.6%). A CD4 count of <250 seems to be a reasonable cut-off for initiation of HAART as the transmission rates at higher counts do not improve markedly. A larger study is required to compare whether HAART and dual therapy have an equivalent transmission rate at a higher CD4 count cut-off than 250.

Promoting maternal and infant survival

This study (promiose impact 1077) will aim to determine the best practice for preventing transmission of HIV from mother to child, during pregnancy, delivery and breastfeeding. Pregnant women who are HIV positive with CD4 counts of >350 will be randomised to receive dual therapy or HAART therapy during pregnancy. Another important question that will be answered is whether HAART solely for the purpose of PMTCT should be stopped after delivery or continued. The women randomised to the HAART arm will again be randomised after delivery – to either stop or continue HAART. Babies will receive the standard PMTCT treatment. The mother-infant pairs will be followed up for two years after the last enrollment. We anticipate enrolling 180 women per annum. The study will be one of the largest projects undertaken in this field.

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THE PHILANI MENTOR MOTHER PROJECT

The Philani Mentor Mother Project (PMMP) is a study which has emerged in response to the growing need in South Africa for the development and implementation of evidence-based health interventions which are cost effective in addressing the nation's most pervasive health concerns – primarily illnesses related to HIV, TB, alcohol and malnutrition. These are co-occurring epidemics that collectively account for substantial proportions of infant mortality and morbidity, as well as poor maternal health and quality of life, and fragmentation of the family.

The home visits are intended to empower pregnant mothers to better protect the health of their families by accessing available clinic services, implementing preventive behaviours in daily life routines, and sustaining preventive behaviours over time.

A randomised controlled trial, the PMMP is concerned with the implementation and evaluation of a community-based home-visit intervention programme, whereby unemployed mothers from study neighbourhoods are employed and trained as Mentor Mothers to deliver a series of home visits to all pregnant and new mothers in their neighbourhoods. The visits take place from the time each mother is pregnant until her infant is six months old. Mentor Mothers are selected based on the principle of positive peer deviants – they are mothers who themselves

come from the same adverse circumstances as other mothers in their community, yet they have still managed to raise a healthy child despite their often impoverished circumstances. The Mentor Mother training is an intensive three to four week course which is composed of theory, group work, discussion, demonstration, counselling skills, and practical case work relating to a diverse range of topics, including but not limited to: the prevention and management of HIV, antenatal and neonatal care; maternal and infant nutrition and feeding; alcohol related behaviour; and child health.

The home visits are designed to be both supportive and educational in nature. They are intended to empower pregnant mothers to better protect the health of their families by accessing available clinic services, implementing preventive behaviours in daily life routines, and sustaining preventive behaviours over time. The home-based delivery strategy addresses the cluster of behaviours necessary to deal with chronic conditions simultaneously, as opposed to individually. This is a significant shift from existing prevention models, which typically address only one health behaviour at a time. A further advantage of this intervention model is that by integrating programmes for HIV with TB, alcohol and nutrition – primarily by improving parenting – we are mainstreaming HIV prevention into a broader framework of non-stigmatising, community level support.

The study is taking place in 26 neighbourhood clusters which are located across two peri-urban settlements on the outskirts of Cape Town. Certain study areas are serviced with basic infrastructure, while in others there are no tarred roads or clinics, the dwellings consist only of corrugated iron and wooden waste materials, and the water and sewage systems are limited to public facilities which are deeply inadequate in number to serve the great number of people they are being used to support. The 26 neighbourhoods are stratified into 13 matched pairs of neighbourhood clusters – each pair matched in size, infrastructure and government services. Each pair is

randomly divided across intervention and control conditions, resulting in a control group of 13 neighbourhood clusters where pregnant mothers and children simply have access to the standard government clinic services which are available and an intervention group of 13 neighbourhood clusters where mothers receive the community-based home-visit intervention in addition to standard government services.

These mothers are called Mothers at Risk, and are women who are either HIV positive, have TB, use alcohol during pregnancy, or who have given birth to a low birth weight child/children previously.

To evaluate the effectiveness of the home-visit intervention, longitudinal health outcome data is collected by an independent team of researchers who conduct assessments and interviews with all mothers and infants from both intervention and control neighbourhoods. A baseline assessment is taken of all pregnant mothers initially during pregnancy, a follow up assessment is made six days post birth, and again when the infants are six and 18 months old.

While the study invites all childbearing women from the intervention study neighbourhoods to join the intervention programme, the main outcomes of the research will be measured by the degree to which Mentor Mothers are able to improve the health of those mothers who are most at risk to begin with. These mothers are called Mothers at Risk (MAR), and are women who are either HIV positive, have

TB, use alcohol during pregnancy, or who have given birth to a low birth weight child/children previously. Should we find the intervention to have a notable impact on the health of mothers and infants in the intervention areas, the intervention programme is developed in such a way that it could be scaled up to a national level and implemented across South Africa to address the intersecting epidemics of HIV, TB, alcohol use and malnutrition.

The project is funded by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and operates in partnership with University of California, Los Angeles.

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HOW “INFORMED” IS THE MOTHER’S DECISION REGARDING INFANT FEEDING OPTIONS?

A comprehensive package of care for the Prevention of Mother-To-Child Transmission (PMTCT) of HIV (National Department of Health, Operational Plan for Comprehensive HIV and AIDS Care, Management and Treatment for South Africa. Pretoria, 19 November 2003) states that all mothers participating in the PMTCT Programme should receive education that will enable them to make informed decisions about infant feeding options. Rapid, same-day HIV testing and results that are available immediately, cause health care workers to be responsible for providing pre- and post-test counselling (which includes infant feeding options) on the same day. This could place a tremendous workload and time pressure on the health care workers.

The aim of this study was to determine how informed the decisions of the literate mothers regarding infant feeding options are in the Gert Sibande District. Data was collected from health care workers and mothers who participated in the PMTCT Programme’s 23 PMTCT sites in the Gert Sibande District, Mpumalanga, South Africa. This was done with the help of six field workers and the PMTCT site manager at each PMTCT site, by means of a once-off, self-administered questionnaire.

Health care workers’ attitude towards the PMTCT Programme was positive, although some (14%) indicated that what was expected of them is not achievable in their working environment. The most prominent change relating to the personal preferences of health care workers regarding infant feeding options for HIV-infected mothers, after attending the five-day PMTCT course, was from formula-feeding to breast-feeding. Most (65%) indicated it is possible to stay neutral in a counselling session regardless of personal preference for infant feeding and 60% of those who could not, still thought it was in the mother’s best interest to be counselled by them. One health care worker did not agree that mothers had the right to make informed decisions and 80% agreed that mothers were able to make such a decision. Most (67%) health care workers indicated

that not enough staff was stationed at PMTCT sites, only 53% used the feeding option cards when counselling mothers and indicated that more educational material were needed. Sixty one percent of the health care workers demonstrated the preparation of the formula to the mothers and allowed the mothers to demonstrate back to them. Between 49-82% and 37-56% of the health care workers knew the correct answers to knowledge questions relating to breast-feeding and formula-feeding, respectively. Not one health care worker, nor mother, knew all the steps in preparing a formula feed. Most (80%) mothers made decisions based on information provided to them by health care workers and only a small (13%) percentage were influenced by the community to practise a different feeding option than what they had chosen.

The attitude, personal preferences, knowledge of and resources available to health care workers influenced the decision made by mothers regarding infant feeding. It is thus concluded that mothers can only make an informed decision about infant feeding options if they are advised appropriately by well trained, equipped and informed health care workers.

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Treating

HIV/Aids

THE CHILDREN'S INFECTIOUS DISEASES CLINICAL RESEARCH UNIT (KIDCRU)

The research unit was established in August 2002 at Tygerberg Academic Hospital as it became clear that care was inadequate and that there were many research questions relevant to sub-Saharan Africa that needed to be answered in a prospective systematic fashion. The research is done in collaboration with other academic institutions both inside and outside South Africa. The mission is to improve care through research. The focus areas are HIV and tuberculosis (TB).

The close proximity to the HIV Family Clinic (the second oldest in Africa) and the good working relationship with its clinicians allows us to provide a comprehensive service to families. That the unit is situated within Tygerberg Academic Hospital gives our children the best available special investigations and expert opinion when needed.

Currently, the unit has a staff of more than 60 people and we are conducting eight studies involving more than 600 children. The studies include antiretroviral trials, TB prevention, and Prevention of Mother-To-Child-Transmission (PMTCT) trials.

Current clinical trials include:

IMPAACT (International Maternal Pediatric Adolescent AIDS Clinical Trials Group)

The mission of IMPAACT, which is worldwide in scope, is to significantly decrease the mortality and morbidity associated with HIV disease in pregnant women, children, and adolescents.

It is funded by the National Institute of Health (NIH) in the USA and Secure the Future. The regulatory body is Division of AIDS. Clinical trials are done in several countries including RSA, Malawi, Zimbabwe, Zambia, Uganda, Thailand, Brazil and USA. IMPAACT provides all resources and financial support to do the clinical trials. Three studies are currently underway:

- A trial comparing a nevirapine-based antiretroviral therapy regimen to a lopinavir/ritonavir-based regimen in infants

who have and have not been exposed to nevirapine as part of (PMTCT) programme.

- A trial to determine the efficacy of isoniazid (INH) in preventing tuberculosis in infants with perinatal exposure to HIV. This study is now closing down as interim analysis has unexpectedly shown that there was no benefit (or harm) from isoniazid.
- Infants of mothers who are newly diagnosed with HIV infection at the time of delivery are randomised to receive one of three post-natal antiretroviral regimes to prevent HIV infection. This trial will help infants at highest risk for HIV infection.

It became clear that care was inadequate and that there were many research questions relevant to sub-Saharan Africa that needed to be answered in a prospective systematic fashion.

The following new trials will be started soon through the IMPAACT group and pharmaceutical companies:

- A multi-national trial will look at what the best methods of PMTCT are for both the health of the mother and the infant. It will also assess the best feeding practice in infants of HIV-infected mothers.
- Pharmacokinetic, safety and efficacy studies will also be done on a new formulation of nevirapine, on a CCR5 antagonist, on an integrase inhibitor and on efavirenz in children younger than three years of age with and without TB.

CIPRA (Comprehensive International Programme for Research in AIDS)

CIPRA is another NIH funded project at KIDCRU and the Perinatal HIV Research Unit at Chris Hani Baragwanath Hospital in Soweto.

Children's Early Antiretroviral Therapy (CHER) trial:

CHER is comparing three treatment strategies in infants with perinatally acquired HIV-1 infection diagnosed between six and 12 weeks of age. This study has resulted in the World Health Organization recommending in April 2008 that all HIV-infected infants younger than one year of age be started on antiretroviral therapy, irrespective of their CD4 count or clinical status. We are also evaluating the feasibility of temporary discontinuation of medicines once the infant is older and the immune system more mature. There is also a comparative linked study evaluating the safety and efficacy of the pneumococcal conjugate vaccine (PncCV) and of the *Haemophilus influenzae* vaccine (HibCV) administered as combination vaccines together with other routine immunisation (national immunisation programme) in HIV-infected children, HIV-1 unexposed-uninfected children, and HIV-1 exposed-uninfected children. The HIV-infected patients are co-enrolments with CHER.

Sub-studies: With Dr Barbara Laughton, a neurodevelopmental paediatrician we are evaluating neurodevelopment in the children and with Prof. Soraya Seedat, psychiatric morbidity in the mothers.

Pharmaceutical Studies

Three pharmaceutical studies are also underway, looking at the safety, efficacy and pharmacokinetics of novel antiretrovirals (ARVs) in infants and children.

It is important to study new ARVs and new formulations of ARVs in children as more children start failing second line treatment. It is also important to develop more child-friendly formulations that have a better taste, are once daily and are in a syrup formulation. We also need to develop ARVs that are effective when given with concomitant tuberculosis treatment. As children are potentially going to be on ARVs life-long we need to develop ARVs with fewer long-term side-effects.

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IMPACT OF HAART ON BODY COMPOSITION AND OTHER ANTHROPOMETRIC MEASURES OF HIV-INFECTED WOMEN

An understanding of the effect of HAART on different aspects of health, including nutritional status, of HIV-infected individuals in South Africa is needed to ensure that appropriate population-specific guidelines and policies can be developed. This study aimed to investigate the impact of HAART on nutritional status, focusing on changes in anthropometric measures, and to explore the relationship between these measures and immunological and virological response to HAART.

A prospective study of 30 adult females was carried out at a primary healthcare setting – a clinic in Cato Manor, KwaZulu-Natal. Anthropometric measurements, including weight, mid-upper arm circumference (MUAC), waist circumference, hip circumference, body mass index (BMI) and waist-to-hip ratio (WHR) were performed at baseline and 12 and 24 weeks after commencing HAART. Laboratory values, including CD4 lymphocyte count, viral load, albumin and haemoglobin as well as bioelectrical impedance analysis data, including lean body mass (LBM), fat mass (FM) and body fat percentage (BF%), were collected at baseline and after 24 weeks on HAART.

Overall, there was a statistically significant increase in all anthropometric measures, except WHR and LBM. The mean weight change was 3.4 ± 5.8 kg ($p=0.006$). Fifty percent of the subjects had a BMI above normal at baseline and mean BMI increased from 25.6 ± 5.7 kg/m² to 27.3 ± 5.6 kg/m² ($p=0.007$). Seventy percent of subjects gained weight, 18.5% had a stable weight and 11.1% lost weight. The weight gain in most subjects was attributable to a gain in FM while in subjects who lost weight; the loss consisted mainly of LBM. Some patients with stable body weight experienced changes in the relative proportions of fat and lean mass. Six patients showed evidence of disproportionate gains and losses in body circumference measurements which may be indicative of fat redistribution. Subjects with lower CD4 lymphocyte counts experienced greater increases in weight, BMI, FM and BF%. The strongest

correlation was observed with FM ($rs=-0.53$; $p=0.00$). Greater increases in weight, BMI, MUAC, waist circumference, hip circumference, FM and BF% were seen in those with lower baseline haemoglobin. Baseline viral load and albumin did not correlate significantly with changes in any anthropometric variables. Change in CD4 count was only significantly associated with baseline MUAC ($rs=0.40$; $p=0.04$). Change in viral load was significantly correlated with baseline weight, LBM, FM, BF% and MUAC with the strongest correlation being with weight ($rs=0.44$; $p=0.01$). No significant association was found between anthropometric changes and changes in CD4 count and viral load between baseline and the 24-week visit.

Overall, subjects experienced a significant increase in most anthropometric measures. There appears to be a relationship between some anthropometric and laboratory measures but this needs clarification. The findings of this study demonstrate the value of including circumference measurements and body composition techniques as part of nutritional status assessment and demonstrate the need for studies to determine the prevalence and significance of overweight and obesity in the HIV-infected population. Research is needed to determine the best methods of bringing about the most favourable anthropometric changes to enhance the health of patients on HAART.

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MOLECULAR GENETIC ANALYSIS OF VARIED CLINICAL RESPONSES TO ANTIRETROVIRAL DRUG COMPOUNDS

The scale of the HIV/AIDS epidemic and the consequent levels of need and usage of antiretroviral (ARV) drugs in South Africa necessitate clinical and cost-effective treatment programmes. Despite the benefits offered by combination antiretroviral therapy (ART), it is widely recognised that all of the antiretroviral drug classes have multiple effects other than the intended suppression of HIV replication. A significant proportion of patients experience a loss of immunological, virological or clinical benefit from current regimens, while others can experience adverse drug reactions (ADRs).

An improved understanding of the genetic influences on ARV drug response within South African ethnic groups could lead to improved therapies with fewer side-effects and minimised drug resistance.

Variations in ARV drug efficacy and the occurrence of related ADRs are influenced by numerous factors, but are believed to be largely attributable to DNA sequence variants within genes responsible for drug metabolism and transport. For example, a variant in the enzyme encoded by the CYP2B6 gene is correlated with the plasma levels of an ARV drug, efavirenz, that it metabolises. There is also evidence that plasma drug levels correspond to treatment outcomes. Furthermore it has been shown that significant differences exist in the frequency of DNA sequence variants between ethnic groups, which can lead to marked differences in drug response between such groups. An improved understanding of the genetic influences on ARV drug response within South

African ethnic groups could lead to improved therapies with fewer side-effects and minimised drug resistance, while valuable health resources could be applied most advantageously.

Numerous genes involved in ARV drug metabolism and transport have been implicated in variable ART efficacy and ADRs. In a pilot study we investigated the genetic basis for any observed differences in ART response, in terms of both drug efficacy and ADR occurrence, in the South African isiXhosa and mixed-ancestry ethnic groups by examining selected DNA sequence variants within the CYP2B6, CYP3A4 and multi-drug resistance (ABCB1) genes in patients undergoing ART. This pharmacogenetics study identified no apparent effect of ethnicity on immune recovery in response to ART, but did detect an association between immune recovery and specific variants in the ABCB1 gene.

Currently we are collaborating with researchers at the University of California, San Francisco to expand the genetic study to include variants in an additional seven genes that have been implicated in drug transport and metabolism. Our collaborators have previously shown that ART drug levels in hair provide a more accurate picture of drug exposure than that acquired through blood level testing. Additionally, due to the invasive nature of plasma drug level tests, the use of hair offers a more attractive option. Through this collaboration we therefore plan to assess the influence of genetic variants on measured drug levels in hair. Given that we are attempting to implement a novel approach to therapeutic drug monitoring, the cultural acceptability of this method will be carefully studied. Ultimately we envisage that this research will contribute to a potentially cost-effective approach to enhancing ART treatment outcomes in a myriad of settings.

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ANTIRETROVIRAL DRUG RESISTANCE

More than 300 000 HIV-1-infected people are currently benefiting from South Africa's national antiretroviral roll-out programme. Treatment of HIV infected patients is based on combination antiretroviral therapy (ART) which consists of a combination of nucleoside/nucleotide (N(t)RTI) and either a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI). Although ART has meant enormous progress also in resource-poor settings, a number of problems may occur. These include antiretroviral drug resistance, as a result of selective pressure exerted by antiretroviral agents, HIV-1 easily develops mutations that render the virus drug-resistant and can thus cause treatment failure.

Detection of drug-resistant viruses is technically demanding and expensive. We have developed and validated a cost-effective in-house genotypic resistance test that is now used routinely. Current sequencing-based technologies also have other limitations to their clinical usefulness. We are exploring alternative techniques that will allow us to detect minor HIV-1 resistant variants that are not detected with more expensive genotyping methods but may be important to understand a patient's resistance situation.

A major study funded by the South African Department of Health seeks to determine factors affecting the evolution of antiretroviral drug resistance in the HIV family clinic at Tygerberg Academic Hospital. It studies patients failing ART, gathering clinical data – using a PEPFAR-funded patient database which includes clinical patient outcomes, therapy and adherence monitoring – and conducting a pilot study to assess the impact of resistance testing on outcomes both clinically and with regard to drug resistance. Factors associated with ART failure and emerging drug resistance are investigated.

Other research activities on antiretroviral drug resistance include monitoring of antiretroviral drug resistance in mothers that received antiretrovirals to prevent mother-to-child transmission (PMTCT); it could be shown that a dual PMTCT

regimen as used in the Western Cape province approximately halves the risk of resistance emerging in mothers, which is a major improvement over single-dose nevirapine PMTCT with its resulting high resistance risk.

As ART programmes expand in southern Africa, individuals newly infected with HIV may increasingly be at risk of becoming infected with resistant HIV strains that have developed in patients on ART.

We also conduct sentinel surveillance for transmitted resistance: as ART programmes expand in southern Africa, individuals newly infected with HIV may increasingly be at risk of becoming infected with resistant HIV strains that have developed in patients on ART.

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STRUCTURAL BARRIERS TO ADHERENCE TO ANTIRETROVIRAL TREATMENT (ART)

When ART was first made available in South Africa in the late 1990s and early 2000s, patients were carefully selected so that they could benefit maximally from the then new life-saving drugs. Sustained virological suppression of HIV requires high adherence to ART to ensure positive treatment outcomes and to prevent the development of drug resistance. By all accounts, inadequate adherence contributes to treatment failure which may result in frequent opportunistic infections, an increased number of hospitalisations, frequent absenteeism from work, and early death. At a public health level as well, poor adherence may lead to the development of treatment resistant forms of the HI virus.

This research project aims to identify the ways in which structural barriers affect adherence levels, with a view to developing a future intervention programme to help patients overcome these barriers.

Most of the literature on ART adherence thus far has focused on individual level determinants. This research however focuses on structural barriers to ART adherence. Structural factors are particularly salient in low income countries settings where economic, social and political realities are often more constraining on individual behaviour than in wealthy industrially-developed nations. Relevant examples are difficult living conditions such as community violence; inadequate housing; poor access to transport to clinics; food insecurity; lost wages; overburdened health care facilities; and AIDS-related stigma that force patients to conceal their status.

This research project aims to identify the ways in which structural barriers affect adherence levels, with a view to developing a future intervention programme to help patients overcome these barriers. The ultimate result of this line of research is to maximise the effectiveness of health interventions, thus contributing to patients' well-being and quality of life and maximising optimal usage of the already overburdened South African health care system. The study is unique in that it seeks to triangulate data obtained from various stakeholders, including patients, patient advocates, counsellors, nurses, and doctors. Participants have engaged in focus group discussions and individual interviews and were asked specifically about the way they think structural factors act as barriers to adherence. This elicitation research will form the basis for a future study in which workgroups of key stakeholders will be convened to develop a counselling intervention programme. It is envisaged that the counselling intervention will be administered by patient advocates in patients' homes in a future investigation to test its feasibility and effectiveness.

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STELLENBOSCH UNIVERSITY HIV RESEARCH UNIT

The Stellenbosch University HIV Research Unit was founded in 1997 and is located within the Infectious Diseases Clinic, Tygerberg Academic Hospital. The Clinic provides care for approximately 1 500 HIV infected patients of which 1 000 are on antiretroviral treatment. Co-infection with tuberculosis occurs in 60% of these patients at some time during the course of their disease. The outpatient care has a holistic approach with team members representing the medical and nursing field, counsellors, social workers and dietitians. The inpatient consultation unit provides the 1000 bed institution with tertiary level care.

The Research Unit has developed its own interactive database which serves as clinical aid during patient consultation as well as a research tool during research activities. The focus of research done at the unit is of a clinical nature. Initially established to participate in international pharmaceutical drug development to provide antiretroviral medications to clinic attendees, the scope has broadened since the start of the Government-funded treatment programme and largely moved toward self-initiated research.

Dr Jantjie Taljaard is the head of the Infectious Diseases Unit since 2002 and is currently engaging in two areas of research: tuberculosis/HIV and Hepatitis B/HIV co-infection. Active projects include a prospective study to assess the incidence and presentation characteristics of TB disease in HIV-1 infected patients with fever to evaluate the yield of the various diagnostic methods; as well as a retrospective cohort study which will assess the outcome and prognostic indicators of HIV positive patients admitted to the TBH medical ICU.

Working at the Department of Internal Medicine from 1992, Dr Hans Prozesky joined the Infectious Diseases Unit in 2001. He is participating in several national and international collaborative efforts investigating ARV treatment programmes in resource-limited settings under the banner of IeDEA-SA and ART-LINC. Focus points of this research are determinants

of mortality and loss to follow-up in transfer-out; prioritising prevention strategies; determinants of waiting times for ARV therapy; gender differences in clinical outcomes; switching to second-line antiretroviral therapy and mortality; long-term immunologic response to ARV therapy; early loss of HIV-infected patients on potent ARV therapy programmes; and risk factors for being lost to follow up.

Dr Michele Zeier has been associated with the Infectious Diseases Unit since 1994 and has been acting as Principal Investigator in numerous trials, including industry-sponsored antiretroviral studies. Current areas of interest include “SHARECARE” which investigates an alternative referral system by which the care of patients who are clinically stable on antiretroviral therapy is transferred to general practitioners in private practice. She is initiator of E-TREAT, which focuses on the development, implementation and management of an interactive electronic patient consultation management system for active onsite and distant participation by health care workers. Another focus of research is HPV in a collaborative effort with the Department of Gynaecology in a prospective descriptive study of the effect of HAART on cervical cytological abnormalities and HPV Infection in HIV infected women.

Dr Ingrid Eshun-Wilson has been working at the Unit since 2004. Her focus of research is TB immune reconstitution disease. She has constructed a descriptive cohort titled “Mycobacterium Tuberculosis Infection in HIV patients on ART;” a retrospective study, evaluating radiological and clinical manifestations of TB associated immune reconstitution inflammatory syndrome and incident tuberculosis infections on antiretroviral therapy.

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Care and management of

HIV/Aids



HIV/AIDS RESEARCH AT THE DESMOND TUTU TB CENTRE

The Desmond Tutu TB Centre (DTTC) is a Collaborating Centre of the International Union against TB and Lung Disease and contributes significantly to the control of tuberculosis (TB) and HIV/Aids in southern Africa, the African continent and global communities through:

- original, basic and applied research,
- education and training,
- fostering and facilitating appropriate collaboration between all possible role-players at every level of the community in the Western Cape, southern Africa and abroad,
- active participation in policy making processes and
- supporting and advocating care provision for the communities with whom we conduct research.

Although the DTTC focuses its research questions on TB, all its activities involves HIV/Aids as well, as these two diseases cannot be separated.

ZAMSTAR study

The Zambia South Africa TB and AIDS Reduction (ZAMSTAR) study is a community randomised trial evaluating the impact of public health interventions on TB and HIV. The primary outcome measure will be the prevalence of TB and HIV in all 24 communities. Secondary outcomes include the incidence of HIV, stigma and transmission of infection to children. The interventions take place in 24 communities and cover 1.2 million people. Eight communities are in South Africa and 16 in Zambia.

The interventions consist of:

- Optimal TB and HIV programmes in the clinics.
- Enhanced case finding in the community where local residents are trained to raise awareness of TB and to collect sputum samples for TB testing. Outreach activities take place in schools and communities, and via drama performances.
- Household intervention where trained counsellors visit the households of TB cases and motivate the family to support the person with TB to complete his/her treatment.

In the communities where the enhanced case finding occurs, up to 30% of all sputum samples collected are collected by the drama groups directly from individuals at community level. At the end of 2007, the inhabitants of 4096 households in total (1304 in South Africa) have received TB and HIV counselling in their houses. These household members are motivated to complete TB treatment, to have an HIV test and to get prophylactic treatment to prevent TB in HIV positive individuals.

Although the DTTC focuses its research questions on TB, all its activities involves HIV/Aids as well, as these two diseases cannot be separated.

TB-HIV Integration project

The TB/HIV Integration Project is implemented by the Desmond Tutu TB Centre in partnership with the Provincial Government of the Western Cape, City Health Directorate and local NGOs. This project has three broad components: the first is the establishment of community non-medical VCT centres; the second encompasses a range of health systems strengthening initiatives within the 22 high burden clinics around Cape Town; while the third goal looks at better integration of HIV and TB services at two large midwife obstetric units and five well-baby clinics in Khayelitsha (this takes place within the Prevention of Mother-To-Child-Transmission (PMTCT) programme. The eight NGO-lead, non-medical community VCT centres were established in Nyanga, Philippi, Khayelitsha, Kayamandi, Mfuleni, Tafelsig, Somerset West and Capricorn Park. These centres enable clients to know their HIV status in a secure and comfortable environment.

Those diagnosed HIV-positive are referred to clinics for care and are followed up to ensure that care has been accessed.

By August 2008, 4458 clients were counselled (pre-test), of which 4157 consented to an HIV test (93% uptake). As males are one of our target population groups, to date 1924 (43%) of our clients were male. Of the 448 (10%) of clients who tested positive for HIV, 421 (94%) were referred for HIV care. Confirmation was received of 149 people receiving care. Follow-up of clients therefore remains one of the challenges at the VCT centres and is an area that is receiving much attention at present.

Addressing gender issues is an important part of the TB-HIV integration project. In particular, the VCT component of this project addresses male norms and behaviours by targeting men for health promotion and VCT. Objectives include encouraging responsible sexual behaviour, for men to know their HIV status and to take appropriate action. Access to VCT services for men is a challenge and it is predominantly women who are tested in health facilities (with 67% of VCT attendees in the last quarter being women). The Community VCT centres outreach activities specifically target men and data are collected on the proportion of men tested so as to monitor this.

The @ Heart site is situated in Kayamandi, which is an informal settlement on the outskirts of Stellenbosch, in the heart of the Cape Winelands. The personnel at the site have taken advantage of their location and targeted the many wine farms in the area, which has allowed them to counsel and test predominantly males.

Interferon gamma Release Assays, IgRA

Progress is made with new diagnostic tests (Interferon gamma Release Assays or IgRAs) to allow for a more rapid detection of TB infection in children, especially those who are also HIV positive. Current research focus areas of the DTTC group include several large community-based studies in four

communities which aim to improve the diagnosis of TB infection and disease in HIV-infected and uninfected children using these new immune diagnostic tools. These large studies follow cohorts of approximately 1 200 children over five years in communities with high burdens of HIV and TB.

TB as principle cause of early death for people with HIV/Aids is well known as the most deadly opportunistic infection, i.e. the leading cause of death related to AIDS in southern Africa.

TB vaccine, BCG

The DTTC research group is also evaluating the effectiveness of the current TB vaccine (BCG) in infants born to HIV-infected and uninfected mothers in 800 infants, with the aim to be involved in larger vaccine trials in the future.

e-Nose

The electronic nose (e-Nose) study focuses on the development of the electronic nose to “smell” tuberculosis. The same technology is used in the wine and the perfume industry and depends on the identification of volatile substances. The aim of the study is to compare the results of electronic nose technology with conventional diagnostic tools in the diagnosis of TB in children, especially those who are HIV infected. The development and improvement of the electronic nose technology is done in phase 1 at the Royal Tropical Institute in Amsterdam, Netherlands. Phase 2 of the study include investigations into the ability of the electronic nose to detect

TB in sputum, blood and urine of adult TB patients at clinics in Elsiesrivier, Adriaanse, Ravensmead and Uitsig. Phase 3 repeats this process in the paediatric wards of the Tygerberg Children's Hospital.

RENEWAL study

The Renewal study has now been completed and examined food security in people affected by TB and HIV. The study specifically looked at the converging impact of tuberculosis, food insecurity and HIV, the efficacy of food aid, other forms of external welfare support in reducing the impact in households with strong rural-urban linkages. TB as principle cause of early death for people with HIV/Aids is well known as the most deadly opportunistic infection, i.e. one third of AIDS deaths worldwide and the leading cause of death related to AIDS in southern Africa.

Education and training

The Desmond Tutu TB Centre adds value through training in different ways including:

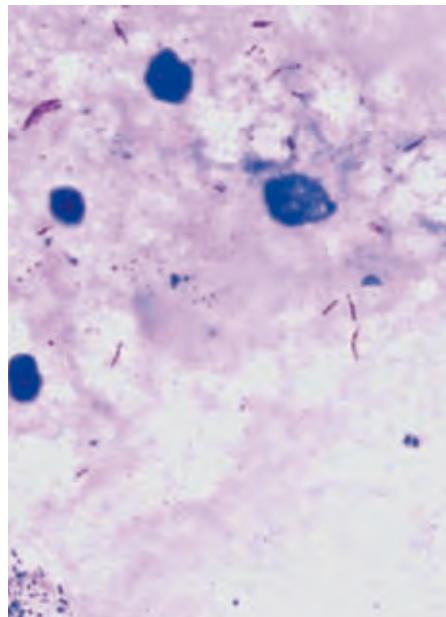
- accommodating twelve post-graduate students in master or doctoral studies;
- training courses to professionals and para-professionals in the health sector; and
- internal training to DTTC staff.

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CHRONIC PHYSIOLOGICAL CONDITIONS ASSOCIATED WITH LONG-TERM ARV USE

Although the use of potent antiretrovirals (ARVs) has improved mortality and morbidity associated with HIV-1 infection, full physiological recovery may not occur and ARV side effects may lead to other chronic diseases. In addition, the double burden of TB and HIV is prevalent in South Africa. Wasting and inflammation are consequences of both diseases and prior wasting or chronic low levels of inflammation may predispose patients to less optimal recovery. The broad goal of this project is to investigate the recovery process in an attempt to determine which early indicators may predispose patients to poor long-term health conditions despite low HI-viral load. A further aim is to determine whether daily physical activity or additional supervised physical activity may impact positively on recovery and quality of life.

In 2010 a new study will be initiated to monitor growth and physical activity in school-going children on ARV treatment.

This study is taking place in a semi-rural clinic setting in conjunction with the West Coast/Winelands HIV/Aids management staff. The proximity of the Idas Valley Day Clinic to Stellenbosch University also provides opportunities for experiential learning for final year undergraduate students with research assistantships and postgraduate research from Hons to PhD level.

A syndrome associated with highly active ARV treatment, is lipodystrophy or body fat redistribution. We are currently investigating this in adult women on ARVs. Despite recovery of body mass on ARVs, peripheral wasting of fat is apparent and paradoxically central fat accumulation. Changes in body fat distribution are both visible and uncomfortable and may influence adherence to the ARV regimen.

Normal aging and unhealthy lifestyle habits may predispose susceptible individuals to central fat accumulation, abnormal blood lipids, glucose and insulin which increase risk for cardiovascular disease or Type II diabetes, or both. These conditions may occur at an earlier age in HIV/Aids patients on ARVs. In collaboration with the Lipidology Division of the Medical Research Council Cape Heart Group we are also studying specific sub-types of low density lipoproteins known to be more associated with cardiovascular disease. Such adverse health profiles may be related to metabolic derangement as a consequence of chronic low grade inflammation.

Our study on adult women will in future include quantitative monitoring of daily physical activity and acute glucose and lipid clearance assessments. International collaboration has been secured with the International Health division in the Medical Faculty of Copenhagen University, Denmark. Our preliminary data indicate several differences between published data on Western cohorts, and our semi-rural South African cohort.

In 2010 a new study will be initiated to monitor growth and physical activity in school-going children on ARV treatment as well as potential abnormalities in the maturation process in adolescent girls on ARVs. These studies will be done under the auspices of the Centre for Human Performance Sciences which was awarded SU strategic funding to investigate physical activity in youth, girls and women belonging to special populations.

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ETHICS AND AIDS IN AFRICA: preventing and managing the pandemic

The Centre for Applied Ethics and its Unit for Bioethics have, over the past decade, been actively and successfully involved in research on the ethical problems raised by the prevention and management of the AIDS pandemic, particularly in Africa and the developing world.

Apart from a number of articles published in international journals on the moral issues related to AIDS, two major books have been produced on this research. The first, *Aids in context: a South African perspective* (Ed. Anton van Niekerk) was published in the early 1990s when awareness of the moral dimensions of the AIDS problematic was relatively new. More recently a much more comprehensive book, *Ethics and Aids in Africa: the challenge to our thinking* (Eds. Anton van Niekerk and Loretta M Kopelman, published by David Philip in 2005) drew together some of the most important, cutting-edge work on ethics and AIDS in the current African milieu.

Themes that were covered in this publication included data and uncertainty in the AIDS debate, the economic and moral challenges of rolling out antiretroviral treatments, the socio-political complexities of the pandemic (including the problems related to denialism in policy-making circles), the AIDS pandemic as a sign of instability in a complex global system, the way in which AIDS illuminates the need for principles of global distributive justice, problems of access to affordable drugs for AIDS (especially the role of the multi-national pharmaceutical corporations in this regard), moral problems raised by the treatment of mother-to-child-transmission of AIDS, HIV vaccine trial participation by both adults and children (particularly issues of informed consent), and many more. Contributions to this volume were also made by pre-eminent, internationally acclaimed bioethicists.

The Centre's work on moral problems related to AIDS continues. Problems that are currently being investigated include the alleged need to criminalise the deliberate spread of the HI-virus, issues related to pre-test counselling, inducement

and HIV testing, the moral justifiability of routine HIV testing, whether HIV positive pregnant women must receive mandatory treatment, ethical issues related to contaminated needle infections of HIV, and issues about rationing.

HIV/Aids is a disconcerting fact of our time, place and situation in the world. The research done in the Centre has shown how disease is a function of our total human condition – biomedical, yet also social, political and behavioural. Above all, HIV/Aids has demonstrated, not only our vulnerability, but also the limits to our powers. Even though the disease may one day be conquered, its message in an age of unprecedented medical power and technological prowess remains singularly appropriate: we are human, and our humanity is a function of the dialectic between limited insight and as yet inconceivable opportunity and creativity.

This research programme has been led by the Director of the Centre, Prof. Anton van Niekerk, assisted by Prof. Keymanthri Moodley, Head of the Tygerberg Division of the Unit for Bioethics, as well as a wide range of post-graduate students and colleagues, both in South Africa and abroad. The Centre for Applied Ethics and its Unit for Bioethics have divisions located in both the Department of Philosophy and the Faculty of Health Sciences, SU.

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GLOBAL HIV VACCINE RESEARCH CRYOREPOSITORY

The CAVD Consortium on Global HIV Vaccine Research Cryorepository (GHRC), funded by the Bill and Melinda Gates Foundation, has as its aim the establishment of a global HIV specimen collection using a state-of-the-art repository. Specimens comprise clinical samples (serum, plasma, PBMC, virus isolates) and key reagents from CAVD consortia (vectors, candidate vaccines, peptides, antibodies, recombinant proteins).

The cryolaboratory allows to process and cryopreserve specimens under optimal conditions, before they are transferred to the central facility.

The project is led by Dr Hagen von Briesen of the Fraunhofer Institute for Biomedical Engineering (FhG-IBMT) in Germany. FhG-IBMT has high competence in the areas of medical engineering and cryobiotechnology and is part of the Fraunhofer Society, a leading organisation for applied research and development in Europe. FhG-IBMT has established a highly sophisticated specimen repository where biological samples can be stored under optimally controlled low-temperature conditions, for long-term preservation and for sharing among collaborating laboratories. The reagents generated, as well as all new technology developed by this network, are being made available for HIV/Aids vaccine development throughout the whole Global HIV/Aids Vaccine Enterprise.

There are several international GHRC partner sites, representing regions of the world where different HIV strains are circulating, that contribute clinical samples, particularly from patients with early HIV infections, to the global HIV specimen collection. The Division of Medical Virology at the Faculty of Health Sciences at Tygerberg Hospital is one of these partner sites and was the first site within the GHRC consortium to start collecting patient samples. These are processed in the Division's biosafety level 3 laboratory and then cryopreserved according to standardised optimal procedures.

Recently, Tygerberg Hospital became the first GHRC partner site at which highly specialised, unique cryoequipment was installed. This tailor-made equipment was designed, developed and manufactured specifically for GHRC, according to high specifications. The cryolaboratory allows to process and cryopreserve specimens under optimal conditions, before they are transferred to the central facility at FhG-IBMT. The cryolaboratory comprises a storage tank with a special access tower for computer-controlled deposition and retrieval of specimens and a workbench allowing handling and processing of specimens under a controlled environment. The associated infrastructure consists of a central cryobank information and specimen administration system, the specimen preparation workflow management system "ChameleonLab" and the GHRC web portal with online registration of HIV specimens.

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BRAIN FUNCTION AND IMAGING IN HIV

In the developed world, the widespread availability of highly active antiretroviral therapy in the management of HIV disease has made significant inroads into the life-expectancy and quality of life of many people living with HIV/Aids. Despite this, the unabated growth of the worldwide HIV epidemic has led to an increase in the number of people with cognitive impairment and HIV associated dementia (HAD). Nowhere is this more true than in the developing world regions which remain the worst affected by the HIV epidemic. There are no evidence-based additional interventions for arresting cognitive decline in HIV. The question is what clinical, brain imaging and biochemical markers pose the greatest threat to long-term maintenance of high quality of life in HIV/Aids?

As such, the need to identify and if possible treat early clinical signs that herald later development of HAD is ever more acute.

Work in psychiatry began some years ago in which we characterised psychiatric disease in a recently diagnosed HIV cohort. Very high rates of psychiatric disease and associations with poor understanding of risks associated with the illness were found. We also found persistence of risky sexual behaviour in the presence of ongoing psychiatric disease. With this, concerns about the behavioural contributors to non-adherence to ARV therapy arose. In this area, an association with inevitable disturbances in body image with progressing illness and poorer adherence to ARV regimes was recently found. This body of work has highlighted the critical importance of identification and early intervention for psychiatric disease co-morbidity if HIV treatment programmes are to be optimised.

Ongoing investigations are examining the value of early clinical markers of dementia such as depression and apathy in early detection and eventually treatment. A series of clinical, neuropsychology, and brain imaging studies are assessing the correlations with changes in brain structure and function in reference populations. We have recently shown that subtle brain

changes exist in white matter in medial frontal brain areas of the corpus callosum in non-cognitively impaired patients with Stage III HIV disease who are on ARVs. Longitudinal studies to examine the value of preliminary findings for predicting subsequent HAD are planned.

Pharmacological challenge studies to examine brain functional responses using functional magnetic resonance imaging are envisaged to help elucidate the role of neurotransmitter systems putatively involved in the pathophysiology of HIV associated cognitive impairment. This work will involve collaboration with European partner institutions. Doctoral studies are envisaged which will use proteomic analysis as well as chemistry assays of the cerebrospinal fluid to examine the integrity of the dopamine system in HIV. The latter has been implicated in HIV associated cognitive decline invoking a number of theoretical explanatory models which involve host and viral contributors to risk. We plan to examine the relationship of these variables to the early and seemingly asymptomatic changes in brain function, and in so doing describe possible mechanisms of HIV related cognitive changes. Clinical brain imaging and biochemistry studies in this arena ideally require investigators skilled in a variety of basic sciences. This multidisciplinary approach to this programme contributes to the excitement we share in this work going forward.

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Social and cultural aspects of

HIV/Aids

RESEARCH THAT NEEDS TO DANCE TO AFRICAN RHYTHM

To address the HIV/Aids pandemic in this continent you'll have to learn to dance – the African way! The “them” under the scrutiny of the research microscope needs to become the “us” with whom we can dance. In the Faculty of Theology the apt term to describe this change in attitude may well be conversion.

The project focuses on the role of faith communities (congregations) and how they can provide local home-based care units.

The conversion story that infiltrated our research methodology goes like this: the Faculty of Theology joined a network formed by its students, the Network for African Congregational Theology (NetACT). This network of theological institutions in eight sub-Saharan countries was formed to assist these institutions in preparing leaders that can live up to and address the challenges they face. HIV/Aids was centre-stage from the very first meeting. All NetACT board members attended the first AIDS course and learned about the basics. It was a matter of time before intense research got underway, at this stage mostly in the form of MTh and DTh research programmes. The first step in a research programme is to build relationships, to learn to dance – only then can research and results follow.

The Global World Value Survey research constantly indicates that the church is the most trusted institution in Africa. Theology is in the privileged and responsible position of having access to the church. Annually, over the last 15 years, on average 38 masters and doctoral students from other African countries are studying at the Faculty. More than 100 degrees were awarded, revealing the scope of the research.

From this came the MTh programme in Clinical Pastoral Care: HIV Ministry. The project is funded by SIDA, an organisation of the Swedish government in cooperation with the Swedish churches. It is a joint attempt with the School of Theology, Pietermaritzburg KwaZulu-Natal, Makumira University Tanzania, and the Ethiopian Graduate School of Theology, Addis Ababa.

The overall aim of the project is to establish research units along the eastern Coast of Africa. Most of the research is done from an empirical perspective. It indicates that more should be done within the realm of human identity, norms and values, cultural and philosophical paradigms, and the linkages between these concepts and religious and spiritual issues. This can be illustrated by the current (one-sided) emphasis on condomising in prevention strategies. The notion of embodiment, its link with human sexuality and the connection with the human quest for meaning (spiritual dimension) and trusting relationships is lacking or underplayed.

The project focuses on the role of faith communities (congregations) and how they can provide local home-based care units. One possible outcome is to equip Christian leaders in order to take responsibility for the wider community and in doing so to network with different institutions. Its further objective is to address the problem of stigma and discrimination.

Dancing together change attitudes. This is reflected in the title of our next publication, available in July 2009: *Our church has AIDS – preaching in the context of HIV/Aids in Africa*.

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HIV/AIDS AND THE ARMED FORCES

Initially this research project on HIV/Aids attempted to ascertain whether the disease poses a security threat. By analysing the impact HIV/Aids has on individual, national and international security, the argument is made that although the disease does not pose a security threat per se, it may become so where it undermines the armed forces' ability to deal with the social, political and economic consequences. In this research, concern is raised that the high infection rates among African militaries not only weakens their capacity to maintain civil order or defend national interests, but to provide qualified personnel for peacekeeping and other humanitarian aid missions.

Concern is raised about the high infection rates among African militaries.

Research in this field has since moved on to examine the impact this disease is having on the South African National Defence Force (SANDF) as regional military power. In the article *Facing a Merciless Enemy* published in the journal *Armed Forces and Society*, 2003, 29 (2) the various policies, human rights, human resources, health, and educational challenges this disease presents to the SANDF, are assessed. Subsequent publications on this topic have focused more specifically on how this disease impacts on the operational capacity and capability of the SANDF by examining the potential impact at various levels, namely force procurement, force preparation, force deployment and force sustainment. Reference is made to the costs this disease poses in terms of recruitment, training and preparing operationally ready forces and of meeting the demands of expensive AIDS treatments.

The SANDF's policy of excluding applicants who are HIV-positive from enlistment and from deployment on international missions have been challenged by trade unions and AIDS activists. A recent court judgement has obliged the SANDF

to review its policies in this regard. In this study, due to be published in the *Journal of Human Rights* (forthcoming), the legal position in terms of HIV testing in the military are examined by referring to the current testing policies of the SANDF, as well as various other international court cases that have challenged the consequences of HIV-testing for military personnel. The research attempts to answer the question as to "whose rights are paramount – the human rights of individual soldiers, or the state's obligation to ensure that the armed forces are operationally effective to safeguard the interests of society, or the international community". This research was conducted together with Lt Col Michelle Nel, a military lawyer from the Faculty of Military Science, Stellenbosch University.

A future continuation of the project intends to look more closely at the impact this disease has on military recruitment. The SANDF is one of the few, if not only institution within South Africa which tests the youth for HIV on a regular basis as part of their pre-employment criteria. The information collected on the health assessment forms includes not only health status, but the age, race, gender and level of education of applicants. Should funding and permission be obtained to conduct this study, the intention is to process the data collected to determine prevalence trends among the youth. Monitoring how this disease is affecting our youth based on data collected by the SANDF during the testing process will be of immense value not only to the SANDF, but nationally as no other institution in the country has such longitudinal data on HIV-infection rates among the youth in the age cohort 17–22 years.

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RESPONDING TO THE HIV CRISIS: research on the success of peer education programmes

During July 2004 Stellenbosch University's Office for Institutional HIV Coordination piloted a HIV peer education training programme for students. The aim of this programme was to promote HIV awareness and knowledge and to encourage safer sexual practices amongst students at Stellenbosch University. The outcomes of the programme were to effect change at the individual as well as the professional level through modifying knowledge, attitudes and behaviour of students, as well as through the development of skills in students as future professionals to manage HIV prevention and care in the workplace environment. The training programme further intended to empower students to serve their peers as informal educators, role models, referral sources and activists.

A research study was consequently conducted to evaluate the success of the programme in achieving its intended outcomes. The main objective of the research was to determine whether the peer education training programme had achieved its stated outcomes, and has had a positive effect on the participants, especially with regard to their knowledge, attitudes and behaviour.

Purposeful selection was chosen as sampling method for this study. Research instruments included questionnaires, focus group interviews, individual interviews, portfolios and observation. A mixed-methods research approach was employed, combining both qualitative and quantitative methods of data collection and analysis, using both parallel and sequential forms of data collection in two separate phases. The quantitative data collection and analysis employed a quasi-experimental research design.

For the purpose of this study the quantitative questions in the pre- and post training questionnaires were analysed with the use of Statistica Version 7.1 computer software, employing the ANOVA test for the analysis of the Likert-scale data and the McNemar test for two-level questions. Both descriptive and inferential statistics were applied. The qualitative data was analysed by means of content analysis. The findings of the

research study showed that, even though certain limitations were identified and recommendations for improvement could be made, the programme was successful in achieving its stated short-term outcomes. Changes in the participants' knowledge as well as reported changes in attitudes and behaviour, in line with the desired programme outcomes, were indicated.

“I began to understand the multi-dimensions of HIV and AIDS; I began to understand that HIV is not about being ill, it is about people...about life.”

The findings further showed that knowledge of the basic facts regarding HIV as well as HIV-related services (especially regarding services on campus) increased immensely. These increases in knowledge led to personal feelings of empowerment as well as increased confidence to discuss these topics with peers. According to the research findings, the participants felt empowered and capable of fulfilling their roles as peer educators. They felt increased confidence through the knowledge gained and by being part of a supportive group.

The following statements from peer educators clearly indicate the success of the programme in helping students understand the HIV epidemic better, as well as motivating them to do something about it:

- “I had the motivation, now I also have the tools and determination to make a difference.”
- “Our goal is simple...we want to change the world, one person at a time, through knowledge, example, support and caring.”

- “I talked; I got to know myself; I got to know other people; I learned not to just tolerate other people’s views, but to respect them.”
- “I began to understand the multi-dimensions of HIV and AIDS; I began to understand that HIV is not about being ill, it is about people...about life.”

The results from the evaluation were used in planning, changing and improving further programmes. The peer education programme for students has been successfully implemented at Stellenbosch University since 2004 and has grown in numbers. During 2008 the programme was extended to the Tygerberg Medical campus and with appropriate funding we would like to also expand to the other satellite

campuses during 2009. The peer education concept has also been adapted and implemented for the staff of Stellenbosch University, with the first group of HIV staff peer educators trained during 2008.

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WOMEN'S PROPERTY RIGHTS, HIV/AIDS AND DOMESTIC VIOLENCE

Strengthening women's property rights has been identified as a key area of intervention in the development literature, both as a public good in itself and because it is increasingly recognised that the empowerment of women is positively linked to broader social and economic goals around poverty reduction and improved well-being in developing countries. As the devastating effects of the HIV/Aids pandemic on social and economic development in sub-Saharan Africa have become more apparent, there has been renewed interest in understanding more clearly the complex linkages between gender equality around land rights and the empowerment of women, as well as the extent to which stronger property rights for women could contribute both to prevention of the spread of HIV and to mitigation of its adverse economic consequences for individuals, households and communities. High levels of gender-based violence have also been implicated in the spread of HIV.

Against this background, this study was designed to explore this extremely complex terrain in South Africa and Uganda, where these issues are pressing matters for policy attention but the economic and political contexts in which they are being addressed are quite distinct. In addition to the two countries being at very different stages in the fight against HIV, there are also marked differences between them in terms of the importance of land-based livelihoods and levels of economic development and urbanisation.

The study adopted a qualitative approach, recognising that gender relationships around land in the context of HIV/Aids and high levels of domestic violence are embedded in dynamic social relationships that play themselves out over time over the life cycle of individuals and households. While the study was circumscribed in terms of its scale and generalisability, it confirmed that the linkages between the different variables in the specific contexts in which they were explored are highly mediated. While secure land rights and mechanisms for enforcing these rights, if threatened, emerged as important resources for women, they do not in themselves guarantee improved livelihoods or empowerment vis-à-vis intimate partners and other male relatives. Furthermore

the importance of land as a productive resource for women was far less significant in the Amajuba district in KwaZulu-Natal, South Africa, than in the far more rural Ugandan case-study district, although the importance of land and housing as a base from and within which social networks are negotiated and relationships within and across households enacted, is high (albeit differently shaped) in both sites.

The research was conducted during 2005 and 2006. A research monograph detailing the findings in both districts as well as the comparison between them was published in 2008 (ICRW, HSRC and AfD (2008) *Women's Property Rights, HIV and AIDS*, and *Domestic Violence: Research from two districts in South Africa and Uganda*. Cape Town: HSRC Press). Discussions are taking place about the feasibility of conducting a follow-up study that would extend the South African study by deepening the understanding of the gendered impact of HIV/Aids on land rights and property relations over time and also paying more attention to the perspectives and experiences of men with regard to women's land rights and sexual and personal autonomy.

This research was conducted under the auspices of the International Center for Research on Women (ICRW, Washington, USA), with funding from the Ford Foundation (New York, USA), in partnership with the Human Sciences Research Council (HSRC) in South Africa and Associates for Development (AfD) in Uganda. The South African case study was conducted in the Amajuba district, KwaZulu-Natal.

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LANGUAGE AND IDENTITY OF CULTURE: narratives on HIV/Aids

While the African continent arguably has become even more marginalised from a political and economic point of view after the collapse of the Berlin wall, the end of the East-West conflict and in the advent of the latest wave of globalisation, Africa as an ‘idea’, offering an alternative (“exotic”) way of life seems to have increasingly grasped the imagination of German writers. Besides numerous travelogues, quite a number of popular or main stream novels featuring Africa or the so-called African way of life have been published which, if judged by their sales figures, have reached a wide reading audience. There are, however, also those narratives that seek to explore alternative and alternate realities. They do this in terms of a consciousness that acknowledges and salutes difference, while examining conflict, change and cultural hybridity.

The assumption about the effects of storytelling is an extension of the belief that ideas can, and often do, have a material impact, and that people are not simply determined by their circumstances.

This ongoing research project examines contemporary German novels and narratives that are specifically set in South Africa, not primarily in terms of their participation in an intercultural dialogue that is structured around the North-South axis, but in terms of their (dis-)engagement with contemporary South Africa, its cultural specificities as well as in relation to South African literature and with a special focus on the writings of German author Lutz van Dijk.

After the publication in 1999 of his first book on South Africa on the Truth and Reconciliation youth hearings (*Between Anger and Hope*, 2001) van Dijk chose Cape Town as his permanent residence. Subsequently van Dijk wrote two youth novels set in the Western Cape published in their English translations respectively as *Stronger than the Storm* (2001) and *Crossing the Line* (2006). Both feature young protagonists coming to grips with having contracted HIV after having been subjected to violent crimes of rape. Van Dijk’s books primarily address young people and tell stories about young adults who are different from the majority (e.g. people living with HIV/Aids, Jews and gays) who fight for their rights, anywhere and at any time.

This project is also premised on the notion that literature (i.e. storytelling) is an effective means of breaking the silence about violent invasions of a person’s life (the ‘unspeakable’): this bringing to consciousness of new ways of seeing can influence and change the behaviour of both perpetrator and rape survivor and by extension the impressions, perceptions and behaviour of young readers. Changes in consciousness and behaviour could potentially cause a transcendence of the historical relationship of oppressed and oppressor, rape survivor and rapist, such that they are able to accept each other, even reconcile with one another. The assumption about the effects of storytelling is an extension of the belief that ideas can, and often do, have a material impact, and that people are not simply determined by their circumstances. Van Dijk’s well researched writings thus depict realistic settings and tell realistic stories that show an interest in forms of social organisation, which create the socially local within the global, exploding any notion of a bounded social, cultural, and political space.

This study hypothesises that authors such as van Dijk produce what could be called ‘immersion’ texts. His narratives explore issues such as identity and cultural practices in relation to language, violence and reconciliation. In their translations (English, Afrikaans and isiXhosa) the two youth novels have been prescribed at numerous schools in the Western Cape and

have thus become part of, engage with and contribute to the South African debate on these issues.

Through a critical analysis of van Dijk's writings, an interrogation into the status of their translations and their reception within a school context, through interviews with the author and by situating and relating his texts within the context of the South African literary scene, this research project seeks to investigate to what extent and if so how contemporary German narratives contribute to the

debate on the AIDS pandemic in South Africa, issues of violence (particularly rape) and finally how and in what manner literature can be productively used within an educational context.

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