

WELCOME TO THE CAPRISA NEWSLETTER

The success of any ongoing venture, certainly one with a national and international profile like CAPRISA requires not only commitment on the part of the scientists, researchers and leading role players, but a high level of partnership and networking.

In the establishment of a regular newsletter that's exactly what we aim to do, bringing news and views on key processes as they unfold on the Aids front and keeping team members in touch with one another.

Scattered as the multi-disciplinary team are across South Africa often beyond our borders, it will therefore become vital to establish an ethos of sharing whether in the field of knowledge and information or from a more personal perspective.

It was also important that we opened the communications channels as soon as possible so that everyone involved in the programme can be kept up to date as the initial stages of the projects get underway.

Designs for the logo, letterheads etc are presently being worked on - these will be up and running by next month's edition of the newsletter. So too will the new offices on the edge of the University campus in Francois Road (see story on the next page).

One of the aims of the newsletter is to provide information that will not only be of interest, but of use to members.

Among the subjects highlighted from month to month will be progress reports from the various CAPRISA centres, the setting up of research studies, training programmes, published data, best practices and ways to streamline our efforts for the best outcomes.

Clearly as the way forward becomes more focused there may be other issues of equal importance that need to be profiled.

So don't hesitate to let us know what you as a member of the CAPRISA team would like to see included in your newsletter.

To ensure that material of meaningful interest is selected, the director of CAPRISA Professor Salim Abdool Karim has agreed to oversee the project and to field any enquiries or suggestions that come in.



LOOKING TO THE FUTURE: *The CAPRISA Executive Committee meets at Natal University for the inaugural meeting. From left: Lynn Morris (NICD), Salim Abdool Karim (NU), Cathal Seioghe (UWC), standing in for Win Hide, Marian Swart (NU), Carolyn Williamson (UCT), John Matjila (NU), Umesh Laloo (NU) Sharon Cassol (NU), Quarraisha Abdool Karim (NU), Gavin Churchyard (AngloGold), Clive Gray (NICD)*

URGENT UPDATE

As at September 6, the CAPRISA funds have still not been received from NIH. We have assumed that the cheque sent to us by NIH in July has gone astray. We have asked NIH to stop payment on that cheque and to issue a new cheque. The problem is that the cheque was sent via regular mail. Rod Hoff and his team are doing everything they can to resolve the problem. Please bear with us as we cannot proceed with staff appointments until the money has been received.

The CAPRISA mission is launched

A warm winter's day heralded the first meeting of key leaders in the collaborative Centre for the AIDS Program of Research in South Africa (CAPRISA) held in the auditorium of the Natal University research block.

After a welcome address by Capriska's principal investigator, Professor Salim Abdool Karim, there was no doubt about the level of excitement and enthusiasm from the 40 or so multi-disciplinary team of scientists and health and medical specialists (pictured above) who each offered their personal endorsements for the five year mission.

As Professor Karim put it: The Capriska grant creates new opportunities for South African AIDS researchers to contribute to global efforts to contain the spread of the disease."

Commenting on the grant Lynn Morris, project leader of the Laboratory Core, and Clive Gray, both professors at the National Institute of Communicable diseases said the Capriska funds would make an important contribution to enhancing laboratory capabilities in South Africa.

"It will enable us to do precision-



based investigations," she said. Dr Gavin Churchyard, director of the AngloGold Health Research Unit added that CAPRISA's research had the "exciting potential" to have an impact on the control of both AIDS and TB.

Leader of the bioinformatics sector based at the University of the Western Cape, Winston Hide, said that the state-of-the-art Cray Supercomputer would be able to analyse volumes of genetic data to better understand how the virus is able to escape the human body's immune responses." As he pointed out this information was crucial to the development of new AIDS therapies and vaccines for use in Africa.

Above all the initial meeting was a commitment to the research aims of the National Institute of Health in America whose R110 million funding will inject vital resources to finding the solutions to the AIDS

pandemic, particularly in sub Saharan Africa.

The program's three goals were very much at the heart of the proceedings being:-

- *To undertake globally relevant and locally responsive prevention and treatment research that contributes to understanding HIV pathogenesis, evolving epidemiology and developing strategies for AIDS care provision in resource-constrained settings

- *To build local research infrastructure and capacity in virology, immunology, clinical infectious diseases, bioinformatics, epidemiology and biostatistics

- *To enhance and strengthen the critical mass of skilled researchers in South Africa, particularly young scientists from historically disadvantaged communities, through well-established training links with Columbia University in New York.

New home at

Intuthuko

Junction

Drive up Francois Road, past the University of Natal campus and down the other side. That's where you will find the nerve centre of CAPRISA housed in a bright, multi-coloured building at the western edge of the campus grounds.

At the moment the newly constructed offices are filled with rows of desks, computers, books and files - all waiting to be placed in their new surroundings.

At the centre of all this activity is Marian Swart, CAPRISA's new administrative manager who under

the circumstances is remaining remarkably calm. "In a couple of weeks we will be all set and ready," she says brightly, holding a pile of books in her arms. Intuthuko Junction will house 18 members of the core CAPRISA team, including researchers and administrative and finance personnel. Facilities will include a modern boardroom, research centre and video conferencing room which will eventually link with all the CAPRISA centres in the rest of the country. There will also be a facility for telephone conferencing which will be up and ready within the next few weeks.

"The big day is when Telkom switches us on," said Marian. "As soon as we know our new numbers we will inform everybody. Hopefully that will be very soon."

**The word Intuthuko in Zulu means development*

Overview of the START (TB/ARV) project

This is a NIH funded research project within the CAPRISA research program led by Professor Salim Abdool Karim at the University of Natal



Rationale for the Project

ARV therapy is largely unavailable in the public sector hospitals in South Africa (apart from the use of nevirapine in PMTCT programs). Identification of persons most likely to benefit from HAART is problematic as majority of infected people are unaware of their HIV status and do not have access to laboratory

markers of immune decline eg CD4 count. Because of the high prevalence of HIV infection in people with tuberculosis this population represents an easily identifiable group of individuals with HIV who are most likely to benefit from ARV therapy. Furthermore, TB programs have an established infrastructure to provide supervised directly observed treatment (DOT) to patients with tuberculosis. If antiretroviral therapy is initiated with tuberculosis treatment, the DOT infrastructure provides a unique opportunity to promote antiretroviral adherence which is a critical determinant of success of ARV treatment.

Overview of the project design

The aim of the project is to assess the effectiveness of integrating TB and HIV care, including antiretroviral therapy on survival in HIV-infected patients with active TB using the established DOT program. It is a randomized control trial where participants in the intervention arm will get both anti-TB treatment and antiretroviral therapy through the DOT program at the Cyril Zulu Clinic for six months. Upon completion of TB therapy the participants will receive their ARV at the HIV clinic at King Edward Hospital. No DOT will be provided at the hospital.

The control arm will receive only anti-TB medication at the Cyril Zulu Clinic for six months (ARV therapy is deferred in this group until the completion of TB therapy). Upon completion of TB treatment, the participants in the control group will receive HIV care (including ARV therapy) at the same clinic as the intervention arm

Survival at 18 months after enrollment will be assessed as the primary end point in both groups. Secondary outcomes include impact of the intervention on the TB control efforts at Cyril Zulu Clinic.

The study will enroll approximately 300 participants and is expected to run over three years. It is anticipated the project will start recruitment of participants in early 2003. It will employ about 15 staff from varied disciplines including clinicians, nurses, field workers data managers and social scientists.

The combination of ARV drugs to be used in the project has not been finalised yet in view of the number of potent once-daily regimens that are becoming available. In the pilot project of this study, 3TC, DDI and efavirenz is being used.

START poster presented at the Barcelona Aids Conference

The groundwork for a pilot project of START (Starting TB and Antiretroviral Therapy) began last year when members of the CAPRISA team looked into the possibility of using a combined regimen of TB medication and HAART in a resource poor setting where a TB Clinic using the DOTS system was situated.

The poster presented at the Barcelona AIDS Conference by Dr

Chris Jack of the Nelson Mandela School of Medicine profiled the first pilot site using this combination therapy.

Eighty Five TB patients were identified at the Prince Cyril Zulu Chest Clinic in Durban's Warwick Avenue in February of this year. Fifty four (58%) of the patients were HIV positive. And of those 16 with an average CD4 count of 233 and high viral loads were chosen as suitable candidates for the study.

"We needed to look into the feasibility of combining TB and HIV therapies," explained Dr Jack. "Until now published studies on this aspect of treatment is scant". The aim of the pilot START study is to establish whether the taking of drugs for both TB and AIDS would increase toxicity levels in the co-infected and whether the

toxicity profile was an important issue to be studied.

"The efficacy of the medications when taken together needs to be urgently assessed", said Dr Jack. "In this regard it is also important to know whether TB therapy is less effective when combined with antiretrovirals and vice versa". Patients in the pilot study were monitored on a weekly basis for any side effects. Routine blood tests were conducted for liver toxicity. The monitoring was done by Dr Jack and a dedicated TB doctor at the Cyril Zulu Clinic ensuring that both disease profiles were accurately documented.

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The combined dosage of 14 tablets was administered once a day - five TB tablets daily taken Monday to Friday together with nine ARVs daily for the first two months. The TB dosage was then reduced to three tablets daily, Monday to Friday with the same amount of ARVs.

Larger doses in the tablets could reduce the number of tablets required. However unlike Western countries, there was no apparent reluctance from patients about the number of tablets consumed at one time.

In the ongoing patient studies the combined regimen was generally well tolerated. None of the study patients

had any noticeable liver toxicity profiles. A few developed rashes while in some Efavirenz caused dizziness. All symptoms settled within a few weeks. One of the significant outcomes, said Dr Jack, was the improved well-being of the patients.

"There was a marked difference in the levels of despair and dejection that is so apparent with many TB/HIV patients," he said. "Although a great deal more research and evaluation needs to be done there are signs that the combined therapy could be one of the ways forward."

Close monitoring of the patients in the combined therapy study will continue for the rest of the year.

CAPRISA'S ACUTE INFECTION PROJECT

Learning about protocols

The acute infection project which forms a major part of the NIH's funding allocation could well become the catalyst for the setting of defined protocol standards for South African.

Explaining the ongoing establishment of the project study manager Francois van Loggerenberg said that working closely with Westat, the US based research company associated with NIH had been an "enormously valuable" exercise.

"In South Africa we are still new to the writing of detailed and comprehensive study protocols which adhere to every provision of international regulations," said van Loggerenberg.

"Now we are beginning to see a detailed analysis of exactly what needs to be done. Once the initial protocol 'recipe' is in place, I think we will all benefit from the experience."

He said that Westat's protocol template which itemised each research requirement in depth was a useful tool in that gaps in the protocol procedures could be more easily identified.

SOME KEY POINTS IN THE RESEARCH PLAN

Under the leadership of Carolyn Williamson, the acute infection project will look at the viral set point in HIV-1 subtype C infection: role of host and factors

Specific Aims

The overall aim of the project is to elucidate the host and viral factors that influence the set point in heterosexually acquired HIV subtype C infection. While the viral set point has been extensively studied in subtype B infections, there is little data on subtype C infection.

Since the set point is currently the best available predictor of progression of HIV infection to clinical disease and death, it is an important primary outcome of trials of HIV therapy and HIV vaccines, at least for those vaccines that do not provide sterilizing immunity. This project proposes to provide essential information on the viral set point that inform both the design and analysis of future therapeutic and vaccine efficacy trials in southern Africa.



Contact details

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