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Newsletter of the Federation of Infectious Diseases Societies of Southern Africa

Contents

Historic UN Declaration on Antimicrobial Resistance

21st September 2016 was an historic day for the global movement to combat antimicrobial resistance (AMR). A high-level meeting of heads of state formally adopted a resolution on AMR, endorsing the primacy of the WHO Global Action Plan, and calling for the formation of a high-level inter-agency coordination group, co-chaired by the Executive Office of the Secretary-General and the World Health Organisation. This is a huge step forward and we congratulate the South African Minister of Health and Director-General on the prominent roles they played in bringing this declaration into being.

First National Antibiotic Stewardship Train-The-Trainer Course kicks off in Cape Town

In line with the Antimicrobial Resistance National Strategy Framework (2014-2024), 7 clinicians and 5 pharmacists from the Eastern Cape (EC) participated in the first 'Antimicrobial Stewardship Train-The-Trainer course' in Cape Town at the end of July. It was an intensive week-long program run by a team of experts from the Western Cape. The strategy behind this is for the provinces with developed antimicrobial stewardship (AMS) programs i.e., Western Cape and Gauteng, to train champions from nearby provinces, who can then develop AMS in their provinces. The EC team was drawn from Port Elizabeth, East London, Queenstown, Umtata and Lusikisiki. The training was a good balance of interactive lectures and discussions, interspersed with practical AMS ward rounds in various contexts around the Metropole eg ICU, tertiary medical, surgical, secondary level, district level, and obstetric.

One of the highlights was a session by Prof. Ivan Joubert from Groote Schuur Hospital ICU, who demonstrated how aggressive AMS, together with the implementation of 'Best care always' infection control bundles, has dramatically reduced their overall antibiotic consumption, use of colistin, prevalence of *Acinetobacter* infection, and even average length of stay in ICU. The ray of hope that we took away in the doom and gloom of rising antimicrobial resistance is that changes in practice can start to reverse resistance rates. An additional boost to the team in East London is the appointment of Dr Harsha Lochan as the paediatric infectious diseases specialist at Frere Hospital, a first for the province.

AMS ward round at Mitchell's Plain district Hospital.

A 'plate – round' in the microbiology lab helped the trainees get to grips with resistant Enterobacteriacae.

STDSSA - Improving the Effect of HIV Drugs by Use of the Tat Vaccine – Marcelle le Roux

South Africa has a high HIV burden, with steadily increasing numbers of HIV-infected patients on combined antiretroviral therapy (ART). This poses an enormous challenge to the public health system due to a growing work overload and associated economic burden. Although ART has been very successful, it is incapable of full immune reconstitution and virus eradication. The rates of HIV morbidity/mortality are still high; with a 14% annual increase of HIV drug resistance related to insufficient treatment compliance, which hampers an effective suppression of virus replication, a prerequisite to reduce virus transmission.

The transactivator of transcription (Tat) is a regulatory protein that drastically enhances the efficiency of viral transcription. Tat is expressed and released early by infected cells and in this form promotes excessive and improper immune stimulation, preparing target cells for virus propagation. It therefore disables effective immune control, leading to chronic loss of immune homeostasis in HIV infected patients. This continues even in patients on ART. The presence of anti–Tat antibodies is rare in natural infections and they do not persist. They restore neutralization of the virus (*in-vitro*) and are associated with reduced disease progression. This suggested that induction of anti-Tat antibodies represents a pathogenesis-driven intervention to block progression and to intensify ART, making it a good candidate for a therapeutic vaccine.

An open-label, randomized phase II clinical trial conducted in 168 ART-treated volunteers in Italy has shown the Tat-based vaccination to be safe, immunogenic and capable of immune restoration. To assess whether B-clade Tat immunization would be effective also in patients with different genetic background and infecting virus (clade C), a phase II trial was conducted in South Africa. The trial, conducted at the Clinical Research Unit of the Sefako Makgatho University (MeCRU), enrolled 200 participants on ART with undetectable viral load. The study aimed to characterise the anti–Tat Ab for cross clade recognition, cross clade neutralization of entry into dendritic cells and to determine the relationship between neutralization and CD4 cell counts.

Patients on controlled ART were screened and enrolled with the following inclusion criteria: between 18-45 years of age; viral loads below 400 copies/ml; CD4 ≥200 cells/µl and negative for anti-Tat Ab. The participants were randomly assigned to two "blinded" groups to receive three intradermal injections of 30 µg of the vaccine or placebo one month apart. After 48 weeks from vaccination, the codes were broken. Anti–Tat B clade Ab was induced in 97% vaccinees and 20% placebo. There was a reduction of Tat/Env complex entry into dendritic cells: > 60% of vaccinees versus 37% of placebos ($p < 0.0001$). The vaccinated participants showed significant increases of $CD4^+$ T cells over placebo. The gain of $CD4^+$ T cells was particularly significant in participants with low $CD4^+$ T cells at study entry. The vaccine acts by inducing protective antibodies capable of neutralizing the HIV Tat protein from different viral subtypes, including the A, B and C clades circulating in Asia, Europe, America and Africa. The Tat vaccine promises to improve the effectiveness of current treatments against HIV and the expectancy of life of people living with HIV worldwide.

The trial in South Africa is part of a large cooperation program with the South African Department of Health and the Medical Research Council in the fight against HIV/AIDS, signed by the Governments of Italy and South Africa, directed by Dr Bensoli (Principal Investigator), in close collaboration with the South African counterparts. Moving to phase III studies toward vaccine registration with financial support from international organizations is advocated.

https://retrovirology.biomedcentral.com/articles/10.1186/s12977-015-0151-y

http://retrovirology.biomedcentral.com/articles/10.1186/s12977-016-0261-1

ICSSA
INFECTION CONTROL SOCIETY OF SOUTHERN AFRICA

Yolanda van Zyl has joined the ICSSA executive committee as the new Secretary following the resignation of Briette du Toit. Briette has been a valuable asset to the committee and our heartfelt thanks go to her for many years of dedication.

We continue to await the way forward with regards to curricula development from the South African Nursing Council (SANC), with particular reference to the Advanced Diploma in Infection Prevention and Control Nursing and

All Chapters with the exception of KZN and East London are functioning well.

There is a 'new face' of the Gauteng Infection Control Society (GICS): the new Chairperson, Marietjie du Toit has large shoes to fill and together with an enthusiastic committee, She has already made an excellent start to ensuring that the Infection Prevention and Control message continues to be spread far and wide.

- A GICS website has been developed where topical articles are published and members are encouraged to submit news and photographs.
- One Infection Prevention and Control Specialist has been partially sponsored to attend the Infection Control Africa Network conference (conference fees) and a similar sponsorship will be awarded for the FIDSSA 2017 conference.
- Study days continue 4 times a year and the September study day includes an international key note speaker. Thea Daha, a hospital hygiene and environmental specialist from the Netherlands, will contribute to the theme: "Nightingales Environmental theory – does it still work".
- FIDSSA is strongly advocated and it is recommended that all GICS members who attend study days are paid up FIDSSA members.

More news on the other Chapters next quarter.

sascm
South African Society for Clinical Microbiology

SASCM hosted a successful workshop at the Protea Hotel, Wanderers on 26-27 May 2016.

On the first day, the move from CLSI to EUCAST susceptibility testing was discussed. We were fortunate to have Professor Gunnar Kahlmeter, Past President of ESCMID and Past Chair of EUCAST, who shared his vast experience. Discussions focused on the rationale behind the change in methodology and the challenges that need to be overcome.

Suppliers were present at the meeting and have committed to working together to make the transition as efficient as possible. Training across the country, in both public and private laboratories, will be a major undertaking, and is essential for success. It is hoped that the target date for implementation, set at January 2017, will be achieved.

On the second day, SASCM members discussed strengthening surveillance for antimicrobial resistance in SA, which is a key deliverable for SASCM and SAASP. The discussions included getting line list data from public & private sectors, generation of antimicrobial resistance maps and priority surveillance areas. It was decided that the GLASS policy would be used for drug-bug combinations. Antimicrobial resistance maps for 2015 (public-sector data only) will be available on NHLS website in pdf format soon.

The surveillance meeting was followed by the SASCM AGM. New guidelines for the surveillance, treatment and control of Carbapenem-resistant Enterobacteriacae and diagnostics for *Clostridium difficile* are priority areas and will be addressed shortly by the SASCM working groups.

SASCM Chair, Dr Chetna Govind (left) with Prof Kahlmeter and Prof Olga Perovic, Chair of NAC

SASCM members at surveillance meeting

Report of the 2nd HIV Exposed Uninfected (HEU) Infant and Child Workshop

Amy Slogrove (UCT)

The first HIV Exposed Uninfected (HEU) Infant and Child workshop was held in Vancouver in July 2015 and brought together enthusiastic clinicians, epidemiologists and basic scientists to review what is known about HEU infants and their clinical course, immunologic differences and risk for neurodevelopmental and infectious morbidity. This 2nd Workshop, held at the KwaZulu-Natal Research Institute for Tuberculosis and HIV (K-RITH) at the University of KwaZulu-Natal in Durban, built on the 1st Workshop. Methodological challenges were considered to facilitate the generation of high quality evidence translatable into action for HEU infants and children. The tone for the day was set by Mo Archary (UKZN) urging us to think more broadly about PMTCT aims and, instead of just preventing vertical HIV infection, we should be striving for **P**romotion of the health of **M**others and **T**heir **C**hildren **T**ogether (PMTCT).

Infant Feeding

Landon Myer (UCT) led an engaging panel discussion on how to optimally measure and compare feeding exposures in HIV exposed and unexposed infants raising the tension between measurement for routine surveillance purposes, that needs to be pragmatic and focused on a few key questions, versus measurement for research purposes that may require more nuanced detail and sophisticated analytic techniques to understand the role of breastfeeding in reducing HEU infant morbidity. Nigel Rollins (WHO) highlighted the

lack of reliable information on rates of breastfeeding in HIV infected women, a critical piece of information in accurately estimating postnatal HIV transmission rates. Moleen Zunza (Stellenbosch University) shared her qualitative work showing that infant feeding choices are ongoing for mothers' despite having made an initial decision and that healthcare providers who are highly influential in these initial choices often lack the skills to adequately transfer messages to HIV infected mothers about the risk-benefit ratio of infant feeding choices. Daya Moodley (UKZN) reminded us of the reality that whatever we have observed about infant feeding in a well supported clinical research setting is unlikely to be achieved in the real world setting.

Infant HIV diagnostics

Jean Maritz (Stellenbosch University) discussed HIV diagnostic dilemma's that are becoming apparent in the presence of prolonged infant postnatal prophylaxis and declining vertical HIV transmission. These include reduced sensitivity of standard HIV PCR tests and extended persistence of maternal antibodies beyond 18 months of age in up to 14% of HIV exposed but confirmed uninfected infants.

Specific HEU challenges

Nigel Klein (University College London) took a critical look at the evidence for immune differences in HEU infants. With little evidence for quantitative differences in major lymphocyte subsets, there is fairly strong evidence for increased immune activation in HEU compared to HIV unexposed (HU) infants. Much of this evidence though comes from the pre-antiretroviral therapy (ART) era and there is yet to be a study that attempts to link immunological aberrations to clinical manifestations to better understand the relevance of these immune changes. A large prospective study that evaluates immunological differences in conjunction with clinical outcomes in the era of universal maternal ART is needed. Kate Powis (Harvard) shared her work in Botswana, indicating that in the context of maternal ART HEU infants are experiencing impaired length growth that is only partly mediated by the higher prevalence of low birth weight in HEU infants. This indicates the urgent need to develop large scale pharmacovigilance and antiretroviral (ARV) safety surveillance that can keep up with the pace of expanding universal ART and changing regimens. Claire Thorne (University College London) discussed the challenges in establishing a consented cohort of HEU children for safety surveillance in the United Kingdom and how this has not been a feasible strategy even in a well-resourced setting. As an alternative, routine national data is being used to monitor death and cancer in children born to HIV-infected mothers. Mary-Ann Davies (UCT) described efforts in the Western Cape leveraging the province wide patient unique identifiers to establish a provincial cohort of all pregnancies that can link mother-baby pairs to digitally available exposures including pharmacy records for ARV and other drugs. This will allow for evaluation of birth outcomes in relation to ART *in utero* exposure, hospitalizations for infectious and other events and future association with rare events such as malignancies. Paige Williams (Harvard) took us through the advances being made in statistical methods to appropriately evaluate the safety of individual ARVs in the context of changing ART regimens over time, multiple concurrent ARV drug exposures and confounding by indication. Collaboration and pooling of data is going to be needed to achieve sufficient numbers of ART-exposed HEU infants to confidently establish safety. On this note Amy Slogrove (UCT) proposed that harmonization of outcome measures, particularly birth outcomes and infectious morbidity, could aid HEU researchers in more rapidly resolving pending questions through better comparability of studies across different settings.

The way forward

A small group will be taking this effort forward and aim to have a framework of harmonized outcomes to present to the HEU community at the 3rd HEU Infant and Child Workshop. Mark Cotton (Stellenbosch

University) closed the workshop by reminding us of the importance of fathers and families in the PMTCT equation (PMTCT F^2 = **P**romotion of the health of **M**others and **T**heir **C**hildren **T**ogether with the support of **F**athers and **F**amilies).

We thank UKZN for hosting this Workshop, Merck for sponsorship, SASPID and AfSPID for endorsements and all participants for their lively engagement. The 3rd Workshop is planned for Sunday the 16th of July 2017 in Paris prior to the International AIDS Society Conference. All are welcome!

CALLING FIDSSA MEMBERS: ALL YOU NEED TO KNOW ABOUT TRAVEL MEDICINE AND MORE IS COMING TO THE BOARDWALK CONFERENCE CENTRE, PORT ELIZABETH, STARTING ON 28TH SEPTEMBER 2016. SEE THE SASTM WEBSITE FOR MORE DETAILS