43rd Annual

MEDICINE RESEARCH DAY · MENTORSHIP

Wednesday 5th October 2-6pm

Thursday 6th October 8am-6pm

UNIVERSITY OF CAPE TOWN & GROOTE SCHUUR HOSPITAL DEPARTMENT OF MEDICINE

LECTURE THEATRE 2 New Groote Schuur Hospital

DEPARTMENT OF MEDICINE
43rd ANNUAL RESEARCH MEETING

DATE: 5-6 OCTOBER 2016
VENUE: LECTURE THEATRE II, NEW GROOTE SCHUUR HOSPITAL
Programme

Wednesday 5th October 2016

14:00 – 15:45
Session I

Chair **Prof Karen Sliwa**

14:00 – 14:20	**Prof Simon Stewart** Mentorship & Research
14:20 – 14:40	**Prof V Mizrahi** How to write a grant
14:40 – 15:00	**Prof K. Dheda** How to write a paper
15:00 – 15:20	Parenting and research: joys and challenges A Mother's point of view: **Dr Liesel Zuhlke** A Father's point of view: **Dr Tom Boyles**
15:20 – 15:40	**Dr Joel Dave (Con)** vs **Dr Ntobeko Ntusi (Pro)** "Should we be encouraging young clinicians to do PhDs?"
15:40 – 16:00	**Tea/Coffee**

Session II

16:00 – 17:30	Poster presentations and adjudication (Klein Schuur) Posters will remain on display in Klein Schuur on the 6th October

Poster Abstracts

Set A

A human lung-orientated approach to correlates of risk in tuberculosis – Preliminary results

Malika Davids, Anil Pooran, Richard Meldau, Fawziyah Thompson, Phillippa Randall and **Keertan Dheda***

Introduction: Currently tested vaccines against tuberculosis have been ineffective. Evidence suggests that a robust Th1 immune response is insufficient to prevent disease progression. Immunological correlates of risk are poorly understood within the human lung, the organ of initial contact with *M. tuberculosis*. We evaluated a comparative, first in man, lung antigenic challenge model (PPD and live BCG) to investigate local *in vivo* pulmonary immune responses in HIV-uninfected individuals with different risk susceptibility profiles based on clinical, radiological and immunodiagnostic profiles (immunodiagnostic test -ve despite exposure, LTBI, previous active TB, recurrent TB, and self-cured TB).

Subjects and Methods: PPD, live BCG, and saline (control) were instilled into separate lung segments via bronchoscopy. Initial experiments were performed to determine the immuno-mechanical effect of saline installation and to optimise BCG and PPD concentrations. Bronchoalveolar lavage was performed prior to antigenic challenge (baseline) and 72 hours post-challenge. Peripheral blood samples and BCG challenged skin biopsy samples were concurrently collected. Flow cytometry was used to analyse BAL and peripheral blood cells for cell surface markers and cytokine/chemokine expression profiles associated with innate and cell-mediated immune pathways.

Results: The bronchoscopic instillation of saline in healthy controls (n=4) induced an immune response. Antigenic challenge using BCG (10^4 CFU) and PPD (5TU) was optimal in generating measurable alveolar immune responses [increase in total cell numbers from baseline: (BCG, p= 0.03; PPD, p=0.004)]. PPD challenge in those with previous TB showed significantly increased TLR2+IL6+ co-expression in macrophages (p=0.01) but decreased biomarker-specific T cell expression [CD4+TNFα (p=0.05), CD8+TNFα (p=0.02), and Th17 homing cells i.e. CD4+IL17+CCR6+; p=0.004]. However, a high degree of inter-patient variability was observed.

Interpretation: These preliminary findings demonstrate the feasibility of using an *in vivo* mycobacterial-specific human lung antigenic challenge model. The emerging data will likely have significant implications for the design of vaccines and immunotherapeutic interventions.

Clinico-pathological features of the re-biopsy in patients with lupus nephritis at Groote Schuur Hospital, Cape Town

S. Kajawo*, F. Botha and I.G. Okpechi

Introduction: Repeat biopsies are often performed for patients with lupus nephritis (LN) to guide treatment or to establish disease chronicity. The aim of this study is to provide a report on the clinico-pathological features of repeat renal biopsies in patients with LN treated at Groote Schuur Hospital, Cape Town.

Subjects and Methods: Ethical approval was granted by the Ethics committee of the University of Cape Town. All patients with biopsy proven LN who had a repeat biopsy between Jan 2003 and Dec 2014 were recruited. Electronic, paper records and histological slides were retrieved and reviewed. The data was analysed using SPSS version 22 for windows

Results: A total of 44 patients had at least 2 biopsies done during the study period. The average age at first biopsy was 25.7 (13.7 – 58.3) years and 28.4 (14.4 – 60.4) years at 2nd biopsy. Most patients were females (81.8%) and elevated proteinuria was the main indication at 1st and 2nd biopsy (43.2% and 29.5%). There was significant worsening eGFR (p=0.001) and proteinuria (p=0.019) between both biopsies suggesting disease progression. At 2nd biopsy, 27.3% had the same class of LN while 72.7 % had switched class. Of the patients with proliferative LN at reference biopsy (40.9%), 14/18 (77.8%) remained as proliferative LN. There was significant increase in chronicity score at the second biopsy from 1 to 3.5 (p<0.0001). Surprisingly the activity index was also significantly higher at the time of second biopsy 3.9 to 7 (p=0.005). Most patients (17/26 i.e. 65.4%) with a non-proliferative LN transformed into a proliferative class. The second biopsy prompted escalation of therapy in 72%, reduction / discontinuation of treatment in 12% dose reduction and no treatment change in 15%.

Interpretation: This study highlights the importance of a repeat renal biopsy in patients with LN and suggests earlier intervention to halt disease progression.

Risk Factors of Colorectal Cancer in Zimbabwe

Katsidzira L*, Gangaidzo IT, Makunike-Mutasa R, Manyanga T, Rusakaniko S, Thomson SR, Matenga JA and Ramesar RS

Introduction: Colorectal cancer incidence is increasing in Africa, and is characterised by frequent early-onset disease, with morphological features associated with inherited syndromes. The explanation for these observations remain speculative. This community based case-control study aimed to determine the risk factors for colorectal cancer among the black African population of Zimbabwe.

Subjects and Methods: Incident cases of colorectal cancer diagnosed between November 2012 and December 2014 were recruited through pathology laboratories, public hospitals and clinicians in Harare. Age and sex-matched controls were randomly recruited from corresponding communities using the 2012 census maps. All participants were interviewed using a standard risk factor questionnaire. Baseline characteristics were compared between cases and controls using the student *t*-test or χ^2 test and potential risk factors were analysed using conditional logistic regression.

Results: A total of 101 cases and 202 controls were recruited. Cases were more likely to have a tertiary education (32.7% vs 13.4%, $p < 0.001$), diabetes mellitus (9.9% vs 3.5%, $p = 0.022$), a history of bilharzia (43.6% vs 26.2%, $p = 0.002$) or a history of cancer among first degree relatives (18.8% vs 9.4%, $p=0.020$). After conditional logistic regression, diabetes mellitus [OR 4.7, (95% CI 1.3-17.4)], having lived in an urban area [OR 4.05, (1.2-13.3)], a history of bilharzia [OR 2.5 (1.4-4.5)] and cancer in a first degree relative [OR 3.3 (1.4-7.8)] remained independently associated with colorectal cancer.

Interpretation: The key risk factors for the development of CRC include factors associated with westernisation such as diabetes, and genetic factors which offers opportunities for targeted prevention. The influence of schistosomiasis is a novel finding requiring further confirmation.

Type 1 hereditary angioedema: a descriptive study of an adult cohort in the Western Cape, South Africa

Khalid M. Coovadia*, Paul C. Potter, Sheila Baker, Di Hawarden, Mogamat-Yazied Chothia and Jonny Peter

---

Introduction: Type 1 Hereditary angioedema (HAE) is a rare autosomal dominant condition, caused by a deficiency in the C1 esterase inhibitor protein, resulting in increased levels of circulating bradykinin. It presents clinically with recurrent attacks of angioedema. Few cohorts from sub-Saharan Africa have been reported. The objective of this study was to describe the clinical spectrum, natural history, treatment and outcomes of a large cohort of type 1 HAE patients from South Africa.

Subjects and Methods: A retrospective descriptive study was conducted on a case series of 60 cases of probable HAE, seen between 2010 and 2015, at the Allergy Diagnostic and Clinical Research Unit (ADCRU), University of Cape Town Lung Institute and the allergy clinic at Groote Schuur Hospital. Forty-four patients were confirmed as type 1 HAE (age >18 years) with low C1 esterase inhibitor protein levels. Important co-variates considered included: age, gender, laboratory tests, age of diagnosis, duration of illness, family history, identifiable triggers, average duration of attack, number of attacks per year, and type of attack. Ethics approvals were obtained from both Stellenbosch and Cape Town University Human Research Ethics Committee.

Results: A total of 44 type 1 HAE patients were reviewed. Sixty-six percent were female. Median (IQR) age at diagnosis was 20 (10-27), while the median (IQR) duration of illness was 10.5 (6-22) years. People of mixed race ancestry were the predominant race affected (61%) while Caucasian and black patients made up 34% and 5% respectively. Fifty nine percent (26/44) of patients were index cases, with the remainder (41%, 18/44) family members. Median (IQR) duration of an attack was 48 (24-72) hours. The anatomical distribution of attacks was as follows: limbs (88%), abdomen (71%), face and upper airway (64%) and external genitalia (14%). Fourty eight percent (21/44) of patients used danazol for long term prophylaxis, while 5 patients used recombinant C1 esterase inhibitor for short term prophylaxis or for acute attacks; life-threatening acute attacks were treated with fresh frozen plasma in 34% (15/44). A single death occurred in the cohort during the study period.

Interpretation: The majority of HAE patients require long-term care and experience life-threatening acute attacks. Despite limited resources to access newer therapies such as icantibant and recombinant C1 esterase inhibitor for acute attacks, mortality in this cohort is less than 5% with half the cohort tolerating danogen prophalyxis therapy and a third of patients successfully treated with FFP for acute attacks.

Cases of antiretroviral-associated gynaecomastia reported to the National HIV & Tuberculosis Health Care Worker Hotline in South Africa.

Christine Njuguna*, Annoesjka Swart, Marc Blockman, Gary Maartens, Briony Chisholm, Annemie Stewart, Anri Uys, Karen Cohen

---

Introduction: Gynaecomastia is associated with exposure to antiretroviral therapy (ART), in particular efavirenz. There is limited data on clinical characteristics of patients with ART-associated gynaecomastia in resource-limited settings and little guidance on the optimal management of this adverse drug reaction (ADR). We describe the clinical characteristics, management and outcomes of gynaecomastia cases reported to the National HIV & Tuberculosis Health Care Worker Hotline in South Africa.

Subjects and Methods: We identified all gynaecomastia cases in adolescent boys and men on ART reported to the hotline between June 2013 and July 2014. We collected follow-up data telephonically at monthly intervals to document clinical management and outcomes.

Results: We received 51 reports of gynaecomastia between June 2013 and July 2014; 11% of the 475 patient-specific ADR queries to the hotline. All patients were on efavirenz-based ART. Mean age was 34 years (standard deviation 12) and 7 were adolescents. The median onset of gynaecomastia was 15 months after efavirenz initiation (interquartile range 6 to 42). Gynaecomastia was bilateral in 29 patients (57%) and unilateral in 16 (31%). Serum testosterone was quantified in 25 of 35 patients with follow-up data, and was low in 2 (8%). Efavirenz was replaced with an alternative antiretroviral in 29/35 patients (83%) and gynaecomastia improved in 20/29 (69%).

Interpretation: Gynaecomastia was a frequently reported ADR in our setting, occurring with prolonged efavirenz exposure. Testosterone was low in the minority of tested cases. Most clinicians elected to switch patients off efavirenz, and gynaecomastia improved in the majority.

Genetic and phenotypic correlates of colorectal cancer in an African population

Katsidzira L*, Vorster A, Gangaidzo IT, Makunike-Mutasa R, Manyanga T, Rusakaniko S, Matenga JA Govender D, Thomson SR and Ramesar RS

Introduction: Colorectal cancer in sub-Saharan Africa has distinctive features, the most remarkable of which is a high frequency of early onset disease. There is a lack of prospective studies with comprehensive phenotypic information to explain the underlying causes of this pattern.

Subjects and Methods: One hundred and one incident cases of colorectal cancer were prospectively recruited from pathology laboratories, hospitals and clinicians in Harare between November 2012 and December 2014. Patients were interviewed for phenotypic information particularly, previous cancer, family history of colorectal cancer and associated cancers. Immunohistochemistry for *MHL1*, *MSH2*, *MHS6* and *PMS2*, analysis for microsatellite instability and copy number variation were performed.

Results: The mean age was 53.3 (±14.8) and 20 (20%) were younger than 40 years. Mucinous and signet ring cell morphologies accounted for 14% and 9% of the cases respectively and 13% had associated adenomatous polyps. Eleven percent of cases had microsatellite instability and mutations consistent with Lynch type syndrome (MSH2 Ex 6 deletion, MLH1 Ex 17-Ex 19 deletion, MSH2 Ex 11) were identified in 4.5% (3/66) of our cohort.

Interpretation: The proportion of hereditary colorectal cancers in an African population mirrors high incidence countries. The early onset cancers in this population are likely sporadic, and the risk factors for this sub-group requires further study.

The effect of beta-blockers on fetal birth weight in pregnancies with structural cardiac disease

Johann Baard*, Karen Sliwa, John Anthony, Ayesha Osman and Wentzel Dowling

---

Introduction: Data of birth weight outcomes following beta-blocker usage during pregnancy is limited. The objective of this study was to determine the influence of beta-blocker usage on birth weight and other fetal outcomes in woman with structural heart disease during pregnancy.

Subject and Methods: Birth weight and fetal outcomes were attained from pregnancies seen in cardiac maternity clinics within Grootte Schuur Hospital, Cape Town from 2013 to 2016. All pregnancies had structural heart disease including congenital, cardiomyopathy, infiltrative, valvular and ischaemic heart disease. Beta-blockers (Atenolol or Carvedilol) were used by 36 women for various lengths during the pregnancy as compared to 87 in the control group. Birth weight was adjusted according to gestational age and the two groups were compared using the Mann-Whitney U test using the statistical software SPSS.

Results: Fetal weight outcomes for patients on beta-blockers were not significantly less as compared to controls (2765 versus 2842 g, $p = 0.304$). Thirty percent of patients on beta-blockers had small for gestational age (SGA) babies. A trend of decreasing birth weight with prolonged use of beta-blockers was shown.

Interpretation: As opposed to previous studies this study shows no significant decrease in birth weight for patients with structural heart disease using beta-blockers during pregnancy.

Cape Town: How age friendly is the city? An exploratory study

Tarryn Blouws*, Sebastiana Kalula and Monica Ferreria

Introduction: Worldwide population ageing calls for a growing need to integrate older people in social life and enable them to live active healthy lives. The living environment of the majority of older citizens of Cape Town remains characterised by infrastructural and developmental deficits. This study investigated older citizens' experience and perceptions of the "age friendliness" of their communities in the City of Cape Town.

Methods: The study employed research methodology advocated by the WHO's project on "Age friendly Cities," based on the Vancouver Protocol 2006. Low-income suburbs of Cape Town were selected and qualitative research methods (ten focus groups with members and interviews with managers of service centres) were used to collect and analyse the data.

Results: A sample 97 participants, mean age 70 years (range 54-83) were recruited. Eight domains constructed for the assessment of age friendliness were: physical environment, transport, housing, social participation, respect and social inclusion, civic participation, community support and health services, and communication and information.

Interpretation: Barriers to social inclusion and participation were: Government restriction in income generating activities for social pensioners; features of the physical environment particularly uneven, poorly lit and unsafe sidewalks; short timing at traffic light for pedestrian-crossings; public transport services that was inaccessible to commuters with disability and younger commuters not offering their seats to them. Ageistic attitudes of personnel and the unfriendly services at public healthcare facilities were widely reported. Services and support from religious and other community agencies and travel concessions from government were greatly valued. Lack of exposure and inability to access pertinent electronic information was a concern for a large number.

A productive and inclusive society calls for stakeholders to address the concerns

Impact of transthoracic echocardiography at district hospital level

WF Bedeker,* AS Lachman, M Borkum, D Hellenberg and CS Cupido

---

Background: The use and demand of echocardiography has increased worldwide. In developed countries, this has not been translated into improved access outside tertiary centres. Previous studies have favoured the appropriate use of echocardiography over its clinical impact, limiting generalisability to resource-constrained settings.

Objectives: To assess the impact of an echocardiographic service at district hospital level in Cape Town, South Africa.

Methods: A prospective, cross-sectional study was performed. A total of 210 consecutive patients, referred to the echocardiography clinic over a five-month period, were recruited. Transthoracic echocardiography was evaluated by its indication, new information provided, correlation with referring doctor's diagnosis and subsequent management plan. Impact included the escalation and de-escalation in treatment, as well as usefulness without a change in management.

Results: The results show that 84% of the patients' management was impacted by echocardiography. Valvular lesions were the main indication. The most frequent contribution was information provided towards the diagnosis of heart failure and assessment post-myocardial infarction. Fifty-six per cent of the echocardiograms confirming the referring doctor's diagnosis still had a significant impact. The rational prescription of medication had the major impetus, followed by de-escalation of therapy and screening patients for referral to tertiary facilities.

Conclusion: Echocardiography has a positive impact on patient management outside tertiary settings, where the definition of impact appears to be different. The value of a normal study, screening prior to upstream referral and usefulness irrespective of change has been established. This should alert policy makers towards the risk of restricted access and promote training.

The impact of vascular calcification among dialysis dependent South African CKD patients: A five year follow up study

K. Simba*, M. Borkum, R. Freercks and B.L. Rayner

Background: Cardiovascular disease is prevalent in CKD patients attributed mainly to vascular calcification. Studies in Western countries suggest a survival advantage among blacks on dialysis however there is little data on this in Sub-Saharan Africa.

Methods: A 5-year follow-up study of dialysis patients recruited to assess vascular calcification. Participants were recalled for: anthropometry, vascular stiffness measurement using a Sphygmocor device and an electrocardiogram (ECG). Medical records were reviewed.

Results: 66 (22 male, 42 female) of 74 participants were located.12 of 34 (36.4%) blacks died and 12 of 32 (37.5%) non-blacks (p=0.686). 11 of 37 (30%) patients with coronary artery calcium (CAC) score ≥1 died versus 13 of 29 (45%) with CAC score of 0 (p=0.147). 2 of 37 with CAC score of 0 had a parathyroidectomy compared to 7 of 29 with CAC score ≥1 (p=0.036). Central aortic systolic pressure (CASP) at baseline and after 5 years was 134.0±25.81mmHg versus 133.6±22.25mmHg (p=0.592). Alive participants with a CAC score of 0 had a CASP of 131.6±20.82mmHg versus 136±24.88mmHg (p=0.491) in those with CAC score ≥1. Pulse pressure at baseline and after 5 years was 53.5±41.5-62.0mmHg versus 38±33.0-52.0mmHg (p<0.001). Augmentation index was 82(70-92.5) at baseline and 24(14.0–31.0) at 5 years (p<0.0001). Subjects with baseline CAC score of 0 had a PVW of 7.8±2.19 versus 7.8±1.33 in those with CAC score ≥1 (p=0.983). Left ventricular hypertrophy (LVH) by Cornell score was 2208 (1584-2976) at baseline versus 1474(1064-1936) at 5 years (p=0.005). Those alive at follow up had a higher BMI 28.0±5.69kg/m^2 versus baseline 23.7±4.31kg/m^2 (p<0.0001). 8 of 35 (23%) transplanted developed diabetes (p=0.028).

Conclusion: There was an unexplained dissociation between CAC and vascular stiffness parameters. A regression in LVH on ECG was not explained by improved CASP. Previous parathyroidectomy was significantly associated with CAC. BMI significantly increased at follow-up as well as diabetes incidence in transplant patients.

The Liver Clinic experience with Direct Acting Antiviral Therapy for Hepatitis C - the first year

Mark W. Sonderup*, Neliswa Gogela and Wendy Spearman

Introduction: All oral DAA therapies have revolutionized hepatitis C management. In the pre-DAA era, cure rates ranged between 40-60%. Through access programs, DAAs are increasingly affordable and accessible in South Africa. We review our experience in the first year of DAA use.

Subjects and Methods: Patients sequentially treated with all oral DAA therapy were included in a registry. A variety of DAA combinations were used as per availability, cost and genotype (GT). Patient data and virological outcomes were documented.

Results: 50 patients were evaluated, 32 men, 18 women; men significantly younger than women; median age 51 [IQR 44-58], 59 [52-66]; p=0.05, respectively. GT distribution included 19 GT 1a, 13 GT 1b, 1 GT 2, 6 GT 3, 9 GT 4 and 2 GT 5a. 14% were HIV co-infected, 28% were treatment experienced. Baseline fibrosis scores were 24% F1; 22% F2; 20% F3 and 34% F4. Baseline median HCV viral load was log 6.1 [IQR 5.5-6.6]. Treatment regimens included Paritaprevir(PTV)/Ombitasvir(OMB)/Dasabuvir(DSV) n=15; PTV/OMB n=7; Sofosbuvir(SOF)/Ledipasvir(LDV) n=15; SOF/Daclatasvir(DCL) n=6; SOF/Ribavirin n=5; SOF/Simeprevir(SIM) n=2. Baseline, week 4 and end of treatment (EOT) median ALT was 103 [65-145]; 26 [19-31] and 2 2[17-30], respectively. HCV RNA was undetectable/LLOQ in 82% at week 4; in all at EOT. One patient died whilst on therapy. Of those with end of follow up results available to date (n=42), sustained virological response (SVR) rates for regimens include 100% for PTV/OMB/±DSV; 93% for SOF/LDV; 83% SOF/DCL; 60% SOF/RBV; 100% SOF/SIM.

Interpretation: In our initial first year experience, DAA therapy was highly effective in our setting in achieving SVR in a diverse pangenotypic population with advanced fibrosis. Treatment availability should be expanded.

SET B

High prevalence of metabolic syndrome in South African SLE patients

NA Nkabane*, IG Okpechi and B Hodkinson

Introduction: Against a background of urbanisation and widespread poverty, the prevalence of the metabolic syndrome (MetS) is increasing in South Africa, and atherosclerotic cardiovascular diseases are emerging as a major cause of mortality. Patients with systemic lupus erythematosus (SLE) are at increased risk of the MetS and its complications, but there are no published studies of the prevalence or associations of the MetS amongst sub-Saharan Africans with SLE.
OBJECTIVES: To investigate the prevalence and associations of the MetS amongst recent-onset SLE patients.

Subjects and Methods: A cross-sectional study of baseline features of an inception cohort of recent onset (<5 years' disease duration) SLE patients. All patients met the SLICC SLE classification criteria and were attending the rheumatology clinic at Groote Schuur hospital. The MetS was defined by Joint Interim Statement criteria1.

Results: Of 90 patients, the mean (SD) age was 36.7 (12.2) yrs, disease duration was 24.7 (22.9) months, 81 (87.8%) were female, and of these 67 (82.7%) were premenopausal. In terms of ethnicity, 70.0% were of mixed ethnic ancestry and 25.6% were Black Africans. Patients were of poor socio-economic status: 31.1% were unemployed, with a mean (SD) schooling of 10.2 (2.6) yrs. The mean (SD) SLEDAI score was 5.9 (3.4), and 94.4% were ANA positive, and 15 (16.7%) had lupus nephritis. The majority of patients were prescribed chloroquine (97.8%) and low dose corticosteroids (67.1%). The mean (SD) BMI was 26.2 (6.8) kg/m2, and 53.3% were smokers. The overall prevalence of MetS in this cohort was 33.3%, and increased waist circumference and reduced HDL- C were the most frequently observed features (Table). There was a trend toward more females having MetS (OR 0.2 (95%CI 0.02-1.4, p=0.09), but there was no association between the MetS and age, menopausal status, disease duration, ethnic group nor with SLEDAI score, presence of dsDNA, hypocomplimentaemia, or with organ involvement including nephritis. Surprisingly, neither the use of corticosteroids nor their dose was associated with MetS.

Interpretation: South Africans with recently diagnosed SLE are at particularly high risk of atherosclerotic cardiovascular disease due to the high prevalence of the MetS and cigarette smoking. This calls for aggressive primary prevention strategies.

PK/Tumor size modelling of a Kinase Inhibitor in Cancer patients

Miné de Kock*, and Guillaume Baneyx

Introduction: Ovarian cancer has the highest mortality rate of the gynecologic malignancies [1], due to late diagnosis and high recurrence rate (80%) [2]. Thus, there is a pressing need to find the efficacious therapy for the ovarian cancer patients. Akt is a protein kinase that participates in multiple pathways and abnormal activation is present in almost every type of human malignancy suggesting that selective inhibition of this pathway represents a promising therapeutic approach [5]. The compound included in this analysis is an oral low nanomolar pan-Akt kinase inhibitor developed for the treatment of hematological and solid tumor malignancies. CA125 protein has been shown to be a good surrogate of treatment response (tumor shrinkage).

Subjects and Methods: The PK data was collected in three clinical studies whereas the PD data (absolute tumor size and CA125) was collected in only one. PK analysis consisted in identifying (i) structural model and random effects and then (ii) covariate effects among Body size, Race, Sex, Age, Study, and Type of malignancy. PK-tumor size analysis was performed using a sequential approach where (i) individual PK parameters were added to the dataset as regressors and then (ii) the impact of treatment on absolute tumor size was evaluated.

Results: PK was described by a 2-compartment disposition model with 1st order absorption and elimination, BSV on all parameters except bioavailability, and a combined error structure. Inclusion of covariate effects decreased BSV in CL, V2, and Q by 1.6%, 8.8%, and 9.7% respectively. Tumor size was described with a PK effect compartment to introduce delay in treatment response, a first order net growth rate and drug effect including treatment resistance.

Interpretation: PK-Tumor size modelling is used to show the impact of treatment regimens on tumor size and the emergence of treatment resistance.

Physiological phenotyping for personalised therapy of resistant hypertension in Africa

Adeseye Akintunde M.D., Justus Nondi M.D., Kennedy Gogo M.D., Erika Jones M.D., Ph.D., **Brian Rayner*** M.D., Ph.D., Daniel G. Hackam, M.D., Ph.D. and J. David Spence M.D.

Introduction: Genome-based medicine has been recommended for treatment of hypertension and other conditions. African and African-American hypertensives tend to have lower levels of plasma renin, and retain salt and water. We tested the hypothesis that physiological phenotyping with plasma renin and aldosterone would improve blood pressure control in resistant hypertension in Africa.

Subjects and Methods: Patients at hypertension clinics in Nigeria, Kenya and South Africa with a blood pressure >140 mmHg systolic or 90 mmHg diastolic despite three drugs including a diuretic were randomized to usual care (UC) versus physiologically individualized care (PhysRx). Plasma renin and aldosterone were measured using ELISA kits. Patients were followed for one year; the primary outcome was the percentage of patients achieving blood pressure <140 mmHg and diastolic <90 mmHg.

Results are presented for the 94/105 participants who completed the study. Systolic control was achieved in13.9% of UC vs. 60.3% of PhysRx ($p = 0.0001$). Diastolic control was achieved in 36.1% of UC vs. 67.2PhysRx, vs. ($p = 0.003$). Control of both systolic and diastolic pressures was obtained in 11.1% of UC vs. 50.0% of PhysRx ($p = 0.0001$). Number of visits and total number of medications were not significantly different between treatment groups, but there were differences across the sites. There were important differences in prescription of spironolactone and amiloride as specified in the PhysRx algorithm.

Interpretation: PhysRx based on renin/aldosterone phenotyping significantly improved blood pressure control in African patients with resistant hypertension. This approach should be tested in African-American and other patients with resistant hypertension.

Diabetes mellitus and non-traumatic lower extremity amputations in four public sector hospitals in Cape Town, South Africa, during 2009 and 2010

Dunbar GL [*]**,** and Levitt NS

Background: Diabetes mellitus (DM) is the most commonly reported cause of non-trauma related lower extremity amputations (LEAs) worldwide, but there is a dearth of such information for South Africa (SA).

Objectives: To examine the proportion of LEAs due to DM and to describe the associated characteristics of these patients.

Methods: A retrospective analysis of all LEAs was performed in four public sector hospitals in Cape Town, SA, for 2009 and 2010. Operating theatre records were reviewed to identify all patients who had a LEA. Patient records were perused and information extracted using a structured questionnaire.

Results: Records for 941 of 1 134 patients identified as having a LEA were found (recovery rate of 82.9%). Of the 867 patients with 1 280 LEAs included in the study, 925 LEAs were in 593 patients with DM and 355 LEAs in 274 non-DM patients. Therefore 72.3% (95% confidence interval (CI) 69.8-74.7) of LEAs were in people with DM, while 68.4% (95% CI 65.2-71.4) of the total patients had DM. The DM group underwent more multiple LEAs (42.0% v. 23%, $p<0.001$) and had more multiple admissions (14.3% v. 7.7%, $p<0.005$) than the non-DM group. Infection (85.7% v. 63.5%, $p<0.001$) and ulcer (25.3% v. 15.3%, $p=0.001$) were the leading causes for LEA in the DM group compared with the non-DM group. Ischaemia was the dominant cause in the non-DM patients (49.3% v. 23.3%, $p<0.001$) as was smoking (69.7% v. 43.5%, $p<0.001$), compared with the DM patients.

Conclusions: These data demonstrate an alarming burden of LEAs due to DM in the public sector in Cape Town. Given that the majority of LEAs are preventable with adequate education, screening, treatment and follow up, effective interventions are needed.

South African medical students' perceptions and knowledge about antibiotic resistance and appropriate prescribing: are we providing adequate training to future prescribers?

Sean Wasserman*, Samantha Potgieter, Evan Shoul, William Msemburi, Annemie Stewart, Marc Mendelson and Tom Boyles

---

Introduction: Inappropriate prescribing behaviours by clinicians contributes to antimicrobial resistance (AMR), and may result from inadequate preparation at under-graduate level.

Subjects and Methods: We conducted a cross-sectional survey of all final year students at three medical schools using a 26-item self-administered questionnaire. The questionnaires recorded basic demographic information, perceptions about antibiotic use and AMR, sources, quality, and usefulness of current education about antibiotic use, and questions to evaluate knowledge. Hardcopy surveys were administered during whole class lectures.

Results: 289 of 567 (51%) students completed the survey. Ninety-two percent agreed that antibiotics are overused in South Africa and 87% agreed that AMR is a significant problem in the country, higher proportions than those who thought that antibiotic overuse (63%) and resistance (61%) are problems in the hospitals where they had worked. Most reported that they would like more education on appropriate use of antibiotics (95%). The domains for which students felt least prepared were interpretation of antibiograms, knowledge of dosing duration, performing de-escalation, and making the correct antibiotic choice (good or very good preparedness in 13, 30, 26, and 46% respectively). Only 29% felt confident to prescribe antibiotics, with similar proportions across institutions. There was an overall mean correct score of 50% on the knowledge questionnaire. The median number of correct answers was 6 (IQR 5 – 7, range 2 – 9) for institution A, and 4 (IQR 3 – 5, range 0 – 7) for institutions B and C.

Interpretation: There are low levels of confidence in antibiotic prescribing amongst final year medical students in South Africa. Perceptions that AMR is less of a problem in their local setting may contribute to inappropriate prescribing behaviours. Differences exist between medical schools in knowledge about antibiotic use, with sub-optimal scores across institutions.

Adverse drug reactions among hospitalised children in South Africa

JP Mouton*, N Jobanputra, U Mehta, K Technau, C Scott and K Cohen

---

Introduction: Paediatric pharmacovigilance data are scant, especially from developing countries. South Africa's high HIV and tuberculosis (TB) burden and massive antiretroviral therapy (ART) program may contribute to the local risk for drug-related harm. We describe the adverse drug reaction (ADR) burden among hospitalised children at two South African hospitals.

Subjects and Methods: We assessed 30 days' paediatric (age 1m to 18y) ward admissions (except oncology). We used a trigger tool to help identify adverse drug events (ADEs). A multidisciplinary panel assessed causality (using the WHO-UMC system), seriousness, and preventability.

Results: 922 patients had 972 admissions. 519/922 (56%) were male and 421/922 (46%) were ≤1y of age. Of 28 HIV-infected children, 21 were on antiretroviral (ARV) therapy. Of 80 HIV-exposed children, 34 were on ARVs to prevent mother-to-child transmission. We identified 205 ADEs in 134 children. We classified 132 as ADRs (18 certain, 33 probable, and 81 possible), 31 as unlikely, and 9 as unassessable. 33 ADEs remain under review. Forty ADRs were present on admission; ADRs caused 15/972 (1.5%) admissions. 92 ADRs occurred during admission, of which 13 were serious. Three near-fatal ADRs were: vancomycin-associated anaphylaxis, midazolam-associated respiratory depression, and enalapril-associated hyperkalaemia. The most common ADRs were diarrhoea (n=24, mostly antibiotic-associated), hypokalaemia (n=16, mostly diuretic-associated), and tachycardia (n=14, mostly β-agonist-associated.) 21/132 (16%) ADRs were preventable. ARVs, anti-TB therapy, and/or cotrimoxazole were implicated in 13/132 (9.8%) ADRs. 8/28 (29%) HIV-infected children had ADRs.

Interpretation: ADRs caused 1.5% of admissions in our survey, lower than a previous meta-analysis (2.9%, 95% CI 2.6% to 3.1%). ADRs occurred during 9.5% of admissions, within a previous systematic review's range (0.6% to 16.8%). Serious ADRs occurred during 1.3% of admissions. ART and anti-TB therapy contributed little to the ADR burden compared with other drugs, but HIV-infected children had a high incidence of ADRs.

Xhosa translation of the Internalised Stigma of Mental Illness Scale for use in South African Xhosa people with schizophrenia and rheumatic heart disease

O. Matshabane*, J. de Vries, P. Appelbaum, P. Marshall, B.M Mayosi, D.J Stein and M.M Campbell

---

Introduction: Standardised measuring instruments are commonly used in stigma research, however cultural and linguistic factors may be barriers to conducting such research with Xhosa-speaking South Africans. It is therefore important to apply a thorough translation design in preparing stigma measures for use with Xhosa speakers. The aim of this presentation is to describe the process of translating the Internalised Stigma of Mental Illness Scale (ISMIS) into Xhosa for use in a South African stigma study that compares stigma experiences across Xhosa people with Schizophrenia and those with Rheumatic Heart Disease.

Methods: The ISMIS was translated into Xhosa using a five stage translation design. First the measure was forward-translated into Xhosa by four Xhosa speaking healthcare professionals. Next the group met as a committee to discuss and debate the resultant translations and select preferred translation choices for each questionnaire item. The resultant ISMIS Xhosa translation was then quantitatively piloted in a sample of 50 Xhosa people with schizophrenia and 50 Xhosa people with rheumatic heart disease living in the Western Cape of South Africa, and qualitatively piloted in a smaller sub-sample of 5 Xhosa people with schizophrenia and 5 Xhosa people with rheumatic heart disease using cognitive interviewing. Furthermore, the tool was back-translated into English by an independent Xhosa speaking translator. The translation team met together to review the piloting data to resolve any discrepancies.

Results: The piloting process suggest that this translation design worked well, however some challenges included the difficulty in finding conceptually equivalence Xhosa vocabulary for English concepts relating to stigma and discrimination experiences.

Prevalence of Chronic Kidney Disease (CKD) in HIV Populations: A Systematic Review and Meta-Analysis

Ekrikpo UE*, Effa EE, Kengne AP and Okpechi IG

Introduction: With the advent of antiretroviral therapy, HIV patients now live longer and are prone to chronic non-communicable diseases including CKD. We undertook a systematic review/meta-analysis to determine the global prevalence of CKD in adult HIV populations, and assess the variation by region and major HIV/AIDS predictive characteristics.

Subjects and Methods: We searched multiple databases including Pubmed-Medline, Web of Science, EBSCO, Cochrane Library, ScieLO and AJOL from 1982 to 2016, for published and unpublished articles on CKD in people with HIV, using relevant key words and MeSH terms. Manual search of reference list of eligible articles and contact with relevant experts was also done. The pooled prevalence of CKD overall and by subgroup was computed using the random effects model meta-analysis and meta-regression used to identify study-level factors associated with variations in CKD prevalence. The protocol was registered with PROSPERO (CRD42016036246).

Results: Of the 1959 entries identified via searches, 41 met the inclusion criteria and were included in the final selection. CKD across these studies was diagnosed using MDRD-based eGFR (n=41 studies). These studies comprised 155,044 HIV positive patients from across the WHO regions. The pooled prevalence of CKD (eGFR<60ml/min/1.73m^2) was 6.5% (95% CI 5.8 – 7.3%) overall; 9.5% (7.6-11.4%) in sub-Saharan Africa, 3.1% (2.3-4.0) in Europe, 6.0% (4.6 – 7.4%) in North America, 6.5% (1.4 – 11.5%) in South America; 4.1% (2.7 – 5.5%) in Western Pacific; p<0.001 There was always evidence of heterogeneity (all p<0.001), partly explained by regional differences in meta-regression analyses. There was no evidence of publication bias.

Interpretation: There is a high prevalence of CKD amongst the HIV population globally, especially in SSA. Efforts to reduce disease burden through kidney disease screening amongst HIV positive patients and treatment to retard progression should be implemented. There is need for further research to identify further disease risk factors in SSA.

Optimizing participant retention in a longitudinal cohort of HIV- positive, ART-eligible adults in Gugulethu, South Africa

Courtney Ingrid*, Panda Regina, Orrell Catherine and Katz Ingrid

---

Background: Linkage of HIV-positive individuals to care in sub-Saharan Africa is sub-optimal with only 50% reported to be in care 12 months after an HIV-positive diagnosis. Innovative approaches to improve linkage are required in order to achieve the UNAIDS target of 90-90-90 by 2020.Our objective was to optimize retention, and keep loss to follow-up below 20%.

Description: We prospectively recruited 300 HIV-positive, ART-eligible adults identified through voluntary counselling and testing (VCT) between November, 2014 and June, 2015 at Gugulethu Day Hospital in Cape Town, South Africa. A single in-depth interview was performed by a trained researcher at the point of enrolment. The purpose of the questionnaire was to identify the modifiable determinants of ART refusal. To optimize study-retention, we requested that participants provide 2 contact numbers a home address. Researchers called participants monthly, and tracking was verified through verbal response. We utilized discrete language that did not mention HIV and privacy was maintained. Participants were followed longitudinally for 6 months, with 2 telephonic interviews performed at 3 and 6 months to compare medical outcomes and healthcare utilization in treatment "refusers" and "acceptors" as well as rates at which participants reversed their initial treatment decision.

Lessons Learned: Of the 300 enrolled participants; the median age was 35 years, 65% were female and the median CD4 count was 266 cell/mm3. We maintained 84.5% of the cohort for the 3-month interview, and 75.5% for the 6-month interview. There were no significant differences in age, gender, and median CD4 count or baseline rates of ART refusal between those who were retained and those who were lost to follow up.

Conclusions: Our data suggest that monthly phone calls to participants maintain communication and optimize retention in a disenfranchised population. Future studies should target this population and explore novel communication technology, such as "What's App," as a free messaging device that is less time-intensive and may be equally efficacious.

A Retrospective Cohort review of Time in the Therapeutic Range (TTR) for Patients on Warfarin at a dedicated Tertiary and District Level INR Clinic in South Africa

Ismaeel Ebrahim*, Alan Bryer and Marc Blockman

Introduction: South Africa has a lack of published data regarding the time within the therapeutic range (TTR) for patients receiving long-term warfarin anticoagulation. The high risk and cost of warfarin failure, as well as the lack of access to the direct oral anti-coagulants (DOACs) in the public health care sector, motivated this evaluation of the TTR for warfarin therapy at a tertiary and secondary level facility in the Western Cape. The primary aim of this study was to describe the International normalized ratio (INR) adjusted-dose level of anticoagulation using the internationally recognized Rosendaal TTR method in a group of patients on long term warfarin therapy at these two sites.

Methods: A retrospective folder review of patients attending the INR clinics at Groote Schuur Hospital (GSH) and Mitchell's plain (MP) clinic between 2009 and 2013 was undertaken. 466 patients were included; and were required to have a minimum of 27 months of INR readings following initiation of warfarin therapy. TTR outcomes were calculated using the Rosendaal method for both sites.

Results: Valvular heart disease (VHD) followed by Atrial Fibrillation, were the comments indications for warfarin. The mean TTR of our cohorts was 49.0% (SD 19%) over a 24-month observation period and only 20.2% had TTR's above the recognised 65% level. TTR control between the two sites was not significantly different; and mean INR readings were fewer in patients with TTR's >65%. The younger cohort (<50years) had a TTR 46.3% (SD 19.0%) and the older cohort a TTR 50.5% (SD 19.5%) these differences were statistically significant.

Conclusion: Our study reveals that despite patients attending a dedicated INR clinic, anti-coagulation control is poor. Interestingly there was no significant difference in control found between the tertiary or district level INR clinic. This has major ramifications for the continued prescribing of warfarin in our community and the South African context.

Clinical audit of suspected sodium benzoate-associated angioedema and/or urticaria

Tshego Mabelane*, and Jonny Peter

Introduction: Sodium benzoate is a preservative used widely to prevent yeast spoilage of acidic foods. It is the causative link and benefit of benzoate elimination diets for idiopathic angioedema and urticaria remains controversial.

Subjects and Methods: A clinical review was conducted of 100 patients with angioedema and/or urticaria in whom a preservative association was suspected and CAST testing to sodium benzoate (and other preservatives) was performed as part of the diagnostic work-up causing angioedema. A sample size of 100patients was reviewed using an extraction data form including (i) demographics; (ii) angioedema history and associated clinical features;(iii) atopy background and other chronic conditions associated with angioedema; (iv) chronic medical history; (v) relevant blood tests and treatment provided. A questionnaire was administered telephonically, within a year to follow up on efficacy of elimination diet.

Results: A total of 100 folders between 2013 and 2015 were reviewed. 70% of female and 30% male. Age range was 10% between 11-20yrs; 18% between 21-30yrs; 25% between 31-40yrs; 24% between 41-50yrs; 13% between 51-60yrs; and 10% above 60yrs. 50% of the patients had associated urticaria; 30% had other associated allergies (asthma, allergic rhinitis, eczema, food and drug allergies); and 20% had angioedema without other symptoms. All the patients had angioedema at two sites or more, 76% had periorbital and oral and 24% in other body parts. 18% of patients had associated chronic medical conditions. 46% of the patients gave a history of diet that consisted of canned food, sauces or drinks. 74% of the patients tested positive to sodium benzoate. 71% of the patients were managed with elimination diet, follow up appointment between 2-6 months.

Interpretation: Angioedema due to preservatives is increasing in South Africa. Patients with unknown angioedema aetiology need to be investigate for preservatives. An elimination diet is the most effective therapy tool.

Changes in high density lipoprotein composition in hypertensive patients

Nicholas Woudberg*, Richard James, Olusoji Billyrose, Dike Ojji, Sandrine Lecour and Miguel Frias

---

Introduction: Hypertension related complications account for 9.4 million worldwide deaths, causing at least 45% of deaths due to heart disease. Contributory pathophysiological factors include endothelial dysfunction and changes in high-density lipoprotein cholesterol concentrations but little is known about possible changes in HDL composition. We, therefore, aim to investigate HDL composition in 61 Nigerian healthy or hypertensive with/without heart failure patients admitted to the University of Abuja Teaching Hospital.

Subjects and Methods: Patients were divided into healthy controls with no pre-existing cardiac or metabolic conditions, hypertensive patients and hypertensive patients with heart failure. HDL functionality was assessed in isolated HDL from patient sera using differential ultracentrifugation. HDL composition was determined using Western blot techniques to quantify levels of apolipoprotein A1 (ApoA1) and M (ApoM) whilst mass spectroscopy was used to quantify levels of sphingosine-1-phosphate (S1P).

Results: There was no difference in ApoA1 content between groups. ApoM content was lower in hypertensive and heart failure patients compared to controls (3.57±0.37 AU vs 4.75±0.43 AU, p=0.05). Additionally, hypertensive and heart failure patients had lower HDL-associated S1P content compared to controls (178±9.9 pmol/mg vs 209±9 pmol/mg, $p < 0.05$).

Interpretation: Our data show that hypertension, particularly hypertension with heart failure is associated with changes in HDL composition. It is likely that the decrease in ApoM content results in a reduced binding of S1P to HDL, an important component for HDL to confer cardioprotection. Changes in HDL composition may therefore result in an alteration of HDL functionality in hypertensive patients with heart failure.

SET C:

Outcome of renal transplantation in patients with lupus nephritis: A single centre study in Cape Town.

A. Almradi*, U. Ekrikpo and I.G. Okpechi

Background: Lupus nephritis (LN) occurs in up to 50 - 70% of patients with systemic lupus erythematosus (SLE). Although most LN patients are suitable for renal transplantation when they develop end stage renal disease (ESRD), the risk of recurrence of LN post-transplantation can be as high as 30%. The outcome of transplanted LN patients has not been adequately studied in South Africa**.**

Methodology: The study was designed as a retrospective descriptive study of patients transplanted in the renal unit Groote Schuur Hospital, Cape Town from 1st January 2004 to 31st December 2013.

Results: There were 454 patients who were transplanted in the study period of which 15/454 (3.3%) had LN. The M: F ratio of LN patients was 1:14, mean age was 25±10 years, all were known with class-IV LN and 10/15 (66.7%) were transplanted from a cadaveric donor. Immunosuppression was initiated in 7/15 (46.7%) with combination of cyclosporine and azathioprine; in 2/15 (13.3%) with tacrolimus and azathioprine and in 6/15 (40.0%) with Tacrolimus and MMF. Recurrence of LN was seen in one patient (6.7%) who developed class V LN. Graft rejection was diagnosed in 10/15 cases (66.7%) with types of rejection noted to be acute cellular rejection in 6/15 (40%), antibody mediated rejection 1/15 (6.7%) and chronic rejection in 3/15 (20%). ESRD occurred in 3 patients (20%) with causes from antibody mediated rejection (6.7%), chronic allograft nephropathy (6.7%) and renal artery thrombosis (6.7%). Mean time to ESRD was 16.0 months. Five deaths (33.3%) occurred from sepsis in 3/15 (20%), pulmonary embolism; 1/15 (6.7%) and progressive ESRD after denial of dialysis; 1/15 (6.7%). Mean time to death was 44.1 months.

Conclusion: Outcome of transplanted LN patients is similar to those without LN. Further studies are needed to enable us improve outcomes and to better understand factors associated with outcome in these patients.

Cases of antiretroviral-associated gynaecomastia reported to the National HIV & Tuberculosis Health Care Worker Hotline in South Africa.

Christine Njuguna*, Annoesjka Swart, Marc Blockman, Gary Maartens, Briony Chisholm, Annemie Stewart, Anri Uys, Karen Cohen

---

Introduction: Gynaecomastia is associated with exposure to antiretroviral therapy (ART), in particular efavirenz. There is limited data on clinical characteristics of patients with ART-associated gynaecomastia in resource-limited settings and little guidance on the optimal management of this adverse drug reaction (ADR). We describe the clinical characteristics, management and outcomes of gynaecomastia cases reported to the National HIV & Tuberculosis Health Care Worker Hotline in South Africa.

Subjects and Methods: We identified all gynaecomastia cases in adolescent boys and men on ART reported to the hotline between June 2013 and July 2014. We collected follow-up data telephonically at monthly intervals to document clinical management and outcomes.

Results: We received 51 reports of gynaecomastia between June 2013 and July 2014; 11% of the 475 patient-specific ADR queries to the hotline. All patients were on efavirenz-based ART. Mean age was 34 years (standard deviation 12) and 7 were adolescents. The median onset of gynaecomastia was 15 months after efavirenz initiation (interquartile range 6 to 42). Gynaecomastia was bilateral in 29 patients (57%) and unilateral in 16 (31%). Serum testosterone was quantified in 25 of 35 patients with follow-up data, and was low in 2 (8%). Efavirenz was replaced with an alternative antiretroviral in 29/35 patients (83%) and gynaecomastia improved in 20/29 (69%).

Interpretation: Gynaecomastia was a frequently reported ADR in our setting, occurring with prolonged efavirenz exposure. Testosterone was low in the minority of tested cases. Most clinicians elected to switch patients off efavirenz, and gynaecomastia improved in the majority.

Renal Granulomatous Interstitial Nephritis: a presentation of TB-IRIS

Thania Kahn*, Erika Jones, Kathryn Manning, Rob Freercks, Jason Ensor, Bianca Davidson, Pheto Mangena, Jashira Naidoo and Nicola Wearne

---

Introduction: Tuberculosis immune reconstitution inflammatory syndrome [TB-IRIS] is a well described clinical entity in HIV infected patients that can affect multiple organs. There is however a paucity of information regarding renal involvement. This study aimed to illustrate the clinical and histopathological features of HIV patients with suspected renal TB-IRIS, an entity not to be overlooked as a cause of acute kidney injury in this population.

Subjects and Methods: Renal biopsies from HIV positive patients from Groote Schuur and Livingstone Hopsitals were reviewed for the presence of granulomatous interstitial nephritis [GIN]. Patients' folders and laboratory records were reviewed for evidence of TB and TB-IRIS. They were also reviewed for other causes of GIN ie drugs, fungal infection, sarcoidosis and bacterial ascending infection. The study was approved by the UCT research ethics committee.

Results: 68 HIV positive renal biopsies were assessed. The mean age was 37.5 ±9.14yr. There were 34 males (50%), 61 (89%) were Black, 7 (11%) were Non-black. GIN was caused by TB in 50 biopsies (75%), only one biopsy was AFB positive. MAC, cryptococcus and syphilis each accounted for one case of GIN and drugs were the cause in 3 cases. In 11 biopsies the cause was not identified. For those that had TB as the cause 17 (27%) had a clinical diagnosis of TB-IRIS, which presented at a median time of 5 weeks (IQR 4-8 weeks) after antiretroviral initiation. There was an association with TB-GIN and clinical IRIS p=0.024. Patients with TB-IRIS had a lower CD4 count 76.5 vs 160 [p=0.072]

Interpretation: There is a clinical entity of TB- renal IRIS that is associated with GIN on renal biopsy. This study is the largest series of renal TB-IRIS that adds to the very limited case reports in the literature

The successful development of a non-radioactive, hepatocyte uptake assay

Lloyd Tanner*, Birk Poller, Rowan Stringer, Caroline Rynn and Bernard Faller

---

Introduction: Human drug uptake transporters are membrane-bound proteins that facilitate the active cellular uptake of compounds (Kunze et al, 2014).
In vitro metabolic clearance data which is obtained using different liver fraction incubation assays are consistently used as measures for progressing compounds forward in the drug discovery pipeline (Giacomini et al, 2010). However, as the technology to measure these predicted values increases, a greater tendency to poorly predict the in vivo values has been reported in several papers (Ito and Houston, 2004; Riley, 2005; Stringer et al., 2008). It is increasingly recognized that the drug transporters could hold the key to explaining this lack of correlation between in vivo and in vitro clearance (Shitara et al., 2006).

Understanding the interaction between compound properties, hepatic metabolism and drug transport is crucial for accurate predictions of hepatic clearance especially for Novartis compounds, which highlights the imperative nature of this assay.

Subjects and Methods:
For this study:

- 6 compounds (mainly statins) chosen from the existing data in the paper (Novartis DMPK) using radioactive compounds (Riede et al., 2016).
- Inhibitors at varying concentrations also included in the assay (quantify active uptake for each compound)

Comparisons to DMPK results could then be made

Results:
Hepatocyte uptake results:

- The six compounds were completed in triplicate(n=3)
- Uptake kinetics calculated by normalizing the measured compound concentration (LCMS/MS measurement) to the incubation time and protein content.
- Ratios between the PSinf,act and PSinf,tot values are very accurate, 91-101% accuracy when compared with DMPK; except for atorvastatin (61%) and propranolol (148%).
- Reasoning behind the difference due to: difference in internal standard interaction with the compounds as well as a slightly different assay methodology.

Inhibitor experiments:
Five known inhibitors of active hepatocyte uptake were included in an inhibitor cocktail. These inhibitors were added to the same experimental procedure and significant inhibition of active uptake was seen

Interpretation:
In this study we have illustrated the usefulness of the assay based on the following outcomes:

- The results obtained in the non-radioactive experiments in this study agree with those obtained in radioactive studies (Riede et al., 2016).
- Assay allows for the measurement of compounds in a medium to high throughput fashion (12 compounds per day)
- The inhibitor inclusion illustrates the ability of the assay to measure active hepatocyte uptake
- This method is suitable for early drug discovery eliminating the costly labelling of compounds

Effect of new teaching methods on medical students' self-efficacy

Fiona Drummond*, Harold Amaler, Sean Waserman, Tasnim Bana, Stella Botha and Vanessa Burch

---

Introduction: Students' self-efficacy beliefs influence their learning and the likelihood of engaging with, and completing, complex tasks such as making a diagnosis. Strategies for organizing, prioritising and visualising information to facilitate clinical reasoning during patient consultations are not routinely used, and their impact on students' self-efficacy beliefs are not known. This study explored the use of diagnostic maps (DM), structured reflection charts (SRC) and algorithm-based treatment guidelines (PACK) to facilitate medical students' clinical reasoning during patient encounters and their effect on students' self-efficacy beliefs regarding their diagnostic reasoning ability.

Subjects and Methods: 4th year medical students completing a medical clerkship (January - June 2016) were invited to participate in the study. They spent 2 weeks in OPD using DM, SRC and PACK during patient consultations. A 9-item diagnostic reasoning self-efficacy scale was used to determine the self-efficacy effect of these methods, as compared to traditional bedside teaching (BT).

Results: 88 students participated in the study. Global ratings of clinical reasoning self-efficacy beliefs were significantly improved after completing the clerkship ($p<0.0001$). BT had a greater positive effect on self-efficacy beliefs for data gathering and analysis as compared to DM ($p<0.0001$), SR ($p<0.0001$) and PACK ($p<0.0001$). DM and SRC, as compared to BT, had an equivalent ($p>0.05$) or greater positive effect ($p<0.001$) on student' self-efficacy beliefs regarding data synthesis ability. PACK had a significantly greater positive effect on students' beliefs about their ability to develop basic management plans, as compared to DM, SR and BT ($p<0.001$ for all comparisons).

Interpretation: Cognitive strategies for organizing, prioritizing and visualizing clinical information had a positive effect on the self-efficacy beliefs of students' regarding their clinical reasoning ability during patient consultations.

Augmented reality - a new method for teaching clinical skills

Yin Yin Li,* Meron Lawissa, Maleke Moloi, Jonny Peter, Vanessa Burch

---

Introduction: Augmented reality (AR) is the integration of digital information with the user's environment in real time. Unlike virtual reality, which creates a totally artificial environment, AR overlays digitial information on top of an existing environment. This technology, used to enhance classroom-based teaching, has not been used to enhance learning in the workplace. This study was conducted to determine whether expert clinician-generated videoclips could be used to develop AR learning materials for medical students learning clinical skills and prepare for practical examinations in authentic clinical settings.

Subjects and Methods: Video recordings of the examination of the chest and abdomen were made using expert clinician tutors. These recordings were edited to produce 25 short (2-4-minute) clips, which were overlayed onto A0 posters and pocket-size A6 learning cards using customised trigger images. During a 6-week pilot study the posters will be placed in clinical skills training facilities and 66 sets of AR learning cards (A6) will be distributed to all 2nd year medical students currently learning abdominal examination skills. At the end of the pilot phase the educational utility of the AR learning material will be evaluated using a customised survey.

Results: The AR learning materials will be demonstrated and the results of the survey will be presented at Research Day.

Interpretation: Physical examination skills are an essential part of clinical practice. Learning these skills is challenging because teaching opportunities are limited. Capturing these events and making them 'portable', i.e. readily accessible at all times, is an important advance on traditional bedside teaching. AR teaching materials can also faciliate standardization of the training and assessment of clinical skills, which are important limitations of current clinical skills training programmes worldwide.

Predictors of Emergency Colectomy in Patients Admitted with Acute Severe Ulcerative Colitis

Nimrod Nnete Mokhele* and Gillian Watermeyer

Introduction: Acute Severe Ulcerative Colitis (ASUC) is a life threatening condition which requires urgent and aggressive medical therapy to reduce mortality, morbidity and avoid surgery. To facilitate this process, it is essential to identify patients at high risk of poor outcomes and emergency colectomy. Numerous such risk factors have described in the Western literature however there are no local data addressing this issue. As such it is unclear if these predictors are applicable in our setting. The aim of this study is thus to identify risk factors for emergency colectomy in patients admitted to Groote Schuur Hospital with ASUC.

Methods: A retrospective cohort study of 98 patients admitted with ASUC between January 2003 and January 2013 was performed. Clinical, demographic, laboratory and endoscopic factors on admission and 3 days thereafter were analyzed as predictors of colectomy by univariate and multivariate analysis.

Results: Twenty-five percent of the cohort underwent emergency colectomy. On univariate analysis factors predicting colectomy on admission were exposure to oral corticosteroids (p=0.01), megacolon (p=0.049) or mucosal islands (p=0.04) on abdominal X-ray, and a short duration from UC diagnosis until presentation with ASUC (p=0.04). The only variable that was significantly associated with colectomy on day 3 was serum albumin (p=0.01). This was also the only variable to remain significant on multivariate analysis (OR 0.79, 95% CI 0.65-0.97, p=0.01).

Conclusions: ASUC is a medical emergency and predicting colectomy risk aids in therapeutic management. The only variable significantly associated with the need for surgery in our study was hypoalbuminaemia on day 3. Given the small study numbers a larger prospective study would be of value

Infliximab as rescue therapy for patients with steroid-refractory acute severe ulcerative colitis: results from the Cape Town IBD register

Mirthe van der Valk*, Sandie Thomson, Abdul Cariem, Eduan Deetlefs, Nimrod Mokhele, Gillian Watermeyer and David Epstein

---

Background: Acute severe ulcerative colitis (ASUC) will affect up to 25% of patients with UC. Intravenous steroids are considered fi line management, but up to 30% of patients fail steroids and may require colectomy. Infliximab for steroid-refractory ASUC patients can help avoid colectomy, but there is limited data on the outcome in the South African population.

Aim: To analyze the colectomy-free survival and clinical remission at 3 and 12 months in patients with ASUC treated with rescue infliximab. Material and methods: For the current study, we selected all patients with ASUC (based on the Truelove and Witts criteria) who required hospitalization and failed treatment with intravenous steroids. Patients were selected from one public hospital and three private hospitals. Primary end points were colectomy-free survival and clinical remission at 3 and 12 months.

Results: In total 19 patients met the criteria of acute severe ulcerative colitis (mean age 37 years, 38% female). Patients were treated with infliximab rescue dose after a median (inter quartile range) of 5 (3-7) days of intravenous corticosteroids. The probability of colectomy-free survival at 3 and 12 months was 84% and 79% respectively. Steroid-free, clinical remission was achieved in 58% at 12 months.

Conclusions: Infliximab seems effective as a rescue treatment in a steroid refractory ASUC based on data of our IBD Cape Town register. A colectomy was avoided in almost 80% after 12 months of follow up.

Widening access to HIV testing for adolescents in an integrated youth centre in South Africa: a 5-year update

Rebecca Marcus*, Katherine Gill, Andrea Mendelsohn, Landisiwe Mzukwa, Eve Mendel, Dante Robbertze and Linda-Gail Bekker

---

Introduction: Young people account for over a third of new HIV infections in South Africa, yet HIV counselling and testing (HCT) uptake remains low. Non-traditional healthcare settings may promote health-seeking behaviour and facilitate prevention and screening opportunities among adolescents.

Subjects and Methods: The Desmond Tutu HIV Foundation Youth Centre in Masiphumelele, Cape Town was established in 2011. It provides incentivised adolescent-responsive health, educational and recreational activities, with the objective of widening access to HCT and sexual and reproductive health services. We analysed data on HCT over the past 5 years.

Results: Between May 2011 – January 2016 2,301 adolescents between 12-22 years old were seen at 10,656 visits (median 3 visits per adolescent, range 1-35). 89 percent of visits were by females. Total visits per year increased from 1,576 in 2012 to 2,771 in 2015, suggesting a high level of acceptability. Sixty-four percent of visits included contraceptive services, which is likely to account for the disproportionate no of female visits. 1491 (65%) of the 2301 clinic attendees had HCT at least once, with 61% of girls and 76% of boys ever testing. Of those attending only once, 40% of girls (189/470) and 66% of boys (185/280) received HCT. Repeat attenders were more likely to have HCT – the proportion testing at least once increased with number of visits, reaching over 80% for those visiting $\geq$8 times. There were 53 new HIV diagnoses (47 girls; 6 boys), the vast majority (51) among 16-22 year olds.

Interpretation: Increasing visit numbers suggest that the youth centre provides an adolescent-responsive environment. Many adolescents return for multiple visits with good overall HCT uptake. However, HCT should occur at the first visit to prevent missed testing opportunities and efforts to engage boys should be increased. Research is warranted to assess the degree of impact of specific programmatic methods on HCT uptake.

Baseline Galectin 3 plasma levels identifies poor clinical outcome in patients with peripartum cardiomyopathy

Feriel Azibani*, Wentzel Dowling, Olivia Briton, Tasneem Adam, Sarah Kraus, John Anthony and Karen Sliwa

---

Introduction: Peripartum cardiomyopathy (PPCM) is characterized by new onset of heart failure in late pregnancy and up to the first six months postpartum. Galectin 3 is a β-galactoside-binding lectin protein that is required for transforming growth factor (TGF)-β pathway-mediated myofibroblast activation leading to cardiac fibrosis. This matricellular protein was described as a prognostic biomarker in heart failure patients. We aimed to determine whether galectin 3 and cardiac fibrosis are associated with poor outcome in PPCM patients.

Subjects and Methods: In this single centre prospective study, we enrolled 37 consecutive patients with PPCM and 10 age-matched healthy subjects. All patients received ACE inhibitors and beta-adrenergic blocking agents. Plasma NT-proBNP and Galectin 3 levels were measured at baseline. Echocardiograms were performed at baseline and six months postpartum. Poor outcome in PPCM patients was defined by NYHA ≥3 or death at 6 month.

Results: At baseline, PPCM patients had significantly higher NT-proBNP and Galectin 3 levels than healthy controls ($p<0.001$ and $p<0.05$, respectively). Six months postpartum, four patients did not improve their cardiac function (EF, 26.7±7.4%) and seven died. Baseline NT-proBNP (3865.6±1039 vs. 1730.1±245 pmol/l, $p=0.035$) and Galectin 3 (15.72±0.91 vs. 8.75±0.69 ng/ml, $p=0.02$) levels were significantly higher in patients with poor outcome compared to patients that improved their cardiac function (EF, 45.7±11.3%).

Interpretation: NT-proBNP and Galectin 3 levels were increased in the plasma of PPCM subjects who had poor outcome 6 months after delivery. Galectin 3 may be a clinically useful biomarker that identifies a subset of PPCM patients at highest risk of myocardial dysfunction due to fibrosis. These findings should be confirmed in a larger cohort and could lead to specific therapeutic intervention.

Primary cutaneous malignancies in the Northern Cape province of South Africa: a retrospective histopathological review

K York*, N C Dlova, C Y Wright, N P Khumalo,P E Kellett, R Kassanjee, A Mosam,

---

Introduction: Excessive sun exposure and high human immunodeficiency virus prevalence increase skin cancer risk in South Africa. The objective was to describe the nature and extent of skin cancers presenting in public and private health sectors of the Northern Cape Province.

Subjects and Methods: A retrospective analysis of histologically-confirmed new primary cutaneous malignancies from 1/1/2008 to 31/12/2012 was conducted using public and private health sector databases. Types, quantity and distribution of common invasive malignancies by population group, age, gender, anatomical site and health sector were explored. One-year cumulative incidence was calculated and logistic regression models used to analyse incidence and melanoma thickness trends.

Results: 4270 biopsies (13 cutaneous malignancies) were identified. Most common were Squamous Cell Carcinoma (SCC), Basal Cell Carcinoma (BCC), Kaposi Sarcoma (KS), Cutaneous Malignant Melanoma (CMM) and Basosquamous carcinoma. The odds of a White male developing SCC increased by 8% each year (OR: 1.08; CI: 1.01-1.15; p-value: 0.022) whilst the odds of a Black male developing SCC and KS decreased by 9% (OR: 0.91; CI: 0.84-0.99; p-value: 0.033) and 18% (OR: 0.82; CI: 0.70-0.97; p-value: 0.022) each year, respectively. SCC and CMM were diagnosed at more advanced stages within public versus private sectors. CMM is being detected earlier, as indicated by low stage depth increasing by 72% annually (OR: 1.72; 95% CI: 1.04 -3.01; p-value: 0.042).

Interpretation: Results suggest that reported skin cancer patterns are changing. There is a need for further research and equitable appropriation of financial resources and effort toward developing primary skin cancer prevention initiatives in South Africa.

The research was not a community based project

Thursday, 6th October

Oral presentations

Thursday, 6th October 2016

08:00 – 08:05 **Opening remarks**
Prof Gary Maartens

SESSION I

08:05 – 10:00 **Chairperson: Prof Sandie Thomson**

08:05 – 08:17 **Liesel Zuhlke (Cardiology)**
Clinical Outcomes in 3343 Children and Adults with Rheumatic Heart Disease from 14 Low and Middle Income Countries: 2-Year Follow-up of the Global Rheumatic Heart Disease Registry (the REMEDY study)

08:17 – 08:29 **Amy Ward (IDM)**
Cytomegalovirus viraemia and 12-week mortality among hospitalised adults with HIV-associated tuberculosis in Khayelitsha Hospital, South Africa: a prospective Cohort Study

08:29 – 08:41 **Naomi Walker (IDM)**
Matrix turnover and inflammatory pathology in HIV-1-associated tuberculosis immune reconstitution inflammatory syndrome (TB-IRIS).

08:41 – 08:53 **Jason Limberis (Pulmonology)**
Programmatically incurable tuberculosis and transmission among home discharged cases in South Africa

08:53 – 09:13 **Division research highlights from Division of Infectious Diseases**
Prof Graeme Meintjes (20 mins)

09:13 – 09:25 **Udeme Ekrikpo (Renal)**
Clinical profile and outcome of biopsy proven Acute Interstitial Nephritis of native kidneys at the Groote Schuur Hospital: A 10-Year Review

09:25 – 09:37 **Ayanda Gcelu (Rheumatology)**
Prevalence of FAM111B gene mutations in systemic sclerosis

09:37 – 09:49 **Cascia Day (General Medicine)**
A “RACY” screening tool for delirium in general medical in-patients

09:49 – 10:01 **Thuraya Isaacs (Dermatology/Allergy)**
Characterization of efavirenz-associated cutaneous adverse drug reactions

10:01 – 10:20 **Tea/Coffee**

SESSION II

10:20 – 12:40 **Chairperson: Prof Mpiko Ntsekhe**

10:20 – 10:40 **DEBATE 1:**
Prof Rafique Moosa (Pro) vs. Dr Nichola Wearne (Con)
Should we be rationing dialysis in South Africa in the 21st century?

10:40 – 10:52 **Lauren Knight (Dermatology)**
Stevens Johnson syndrome and toxic epidermal necrolysis: maternal and foetal outcomes in twenty-two consecutive pregnant women.

10:52 – 11:04 **Bianca Davidson (Renal)**
Patient outcomes in a peritoneal dialysis first program in Cape Town South Africa

11:04 – 11:16 **Sumanth Karamchand (Pharmacology)**
Risk factors for incident diabetes in a cohort taking first-line nonnucleoside reverse transcriptase inhibitor-based antiretroviral therapy

11:16 – 11:28 **Rulan Griesel (Pharmacology)**
A Clinical Prediction Rule for the Diagnosis of Tuberculosis in Seriously Ill HIV-Infected Adults

11:28 – 11:48 **Division research highlights from Division of Neurology**
Prof Jeanine Heckmann (20 mins)

11:48– 12:00 **Sandie Thomson (GIT)**
Differentiating Crohn's disease (CD) and Intestinal Tuberculosis (ITB) at presentation in patients with tissue granulomas

12:00 – 12:12 **Tafadzwa Machipisa (Hatter Institute)**
Preliminary genealogical evidence for the Plakophilin-2 gene, *PKP2* c.1162C>T founder mutation in South Africans with Arrhythmogenic Right Ventricular Cardiomyopathy

12:12 – 12:24 **Gina Phindile (Pulmonology)**
The impact of new TB diagnostic technologies on community-based intensified case-finding: a multi-centre randomised controlled trial

12:24 – 13:24 **Lunch**

SESSION III **Jack Bock Lecture 2016**

13:24 – 13:54 **Chairperson: A/Prof Sandrine Lecour**

Speaker: Prof Vicki Lambert

The nexus between physical activity, obesity and food insecurity in LMICs: tackling "wicked problems" for public health

Professor Estelle Lambert is head of the Division of Exercise Science and Sports Medicine (ESSM), in the Department of Human Biology, Faculty of Health Sciences, and has been a fellow of the University of Cape Town since 2009. NIH, at the University of Cape Town. She is a National Research Foundation, B2-rated scientist, and is the author or co-author on over 205 peer-reviewed scientific publications. She is actively involved in research on physical activity and obesity and health, particularly in the Global South, and more underserved communities. She has acted as a consultant to the United States Centers for Disease Control and World Health Organization (WHO) on issues related to the Role of Diet and Activity in the Prevention of Non-Communicable Diseases, and Developing a Global Policy for Promoting Physical Activity for Health. She currently serves on the executive council of the International Society for Physical Activity and Health, and was a member of the Scientific Advisory Council for the International Obesity Task Force (2009-2014). At present, she is the chairperson of the global advocacy movement for physical activity, Agita Mundo, and the first chair-person of the African Physical Activity Network (2007-2013), with more than 200 members representing more than 10 countries. She is the in-country principal investigator for South Africa for the NIH-funded, Modelling the Epidemiological Transition study (METS), was the co-principal investigator for WDF- funded, school-based intervention, Health Kick, as well as the South African principal investigator for the ISCOLE study (International Study on Childhood Obesity, Lifestyle and Environment). She is presently the principal investigator of the STOP-SA Study (Slow, Stop or Stem the Tide of Obesity in the People of South Africa). She has been a co-author of 2 Lancet series concerning physical activity and health, and one on obesity and health. She recently served on the South African Department of Health National Obesity Task Force, the end result of which was the Strategy for the Prevention and Control of Obesity in South Africa, 2015-2020 She is also the lead researcher for the Healthy Active Kids South Africa Report Card consensus and advocacy initiative, having produced a report card in 2007, 2010, 2014 and now 2016. Her current area of research focus is the nexus between obesity and food insecurity, and factors that shape health decisions in choice-constrained settings.

Session IV: Chairperson: Prof Nonhlanhla Khumalo

13:55 – 14:07 **Keertan Dheda (Pulmonology)**
Anatomically distinct whole transcriptome-based pathophysiological map of pulmonary tuberculosis lesions

14:07 – 14:19 **Marlyn Faure (Medical Genetics)**
Genomics in the South African research context: human rights and the Discovery Genomics Initiative

14:19 – 14:31 **Michele Tomasicchio (Pulmonology)**
Development of a Th1-polarising dendritic cell vaccine driving cytotoxic T-lymphocyte-mediated killing of primary breast cancer cells in vitro

14:31 – 14:43 **Khalid Seedahmed (Endocrinology)**
The phenotype and natural history of ketosis-onset diabetes in Cape Town, South Africa

14:43 – 14:55 **Renee De Waal (Pharmacology)**
Changes in estimated glomerular filtration rate over time in HIV-1-infected patients receiving Tenofovir

14:55 – 15:15 **DEBATE 2:**
Dr Tom Boyles (Pro) vs. Dr Clint Cupido (Con)
Should South Africa legalize assisted dying?

15:15 – 15:27 **Stephen Kamuli (Hatter Institute)**
Validation of the *PARVA* c.392A>T variant in a South African family with severe Arrhythmogenic Right Ventricular Cardiomyopathy**.**

15:27 – 15:39 **Andrea Mendelsohn (Desmond Tutu HIV Centre)**
A Comparison of Adolescent Sexual Reproductive Healthcare Utilization at the DTHF Youth Centre vs an Adolescent-friendly City Clinic

15:39 – 15:51 **Mark Sonderup (Hepatology)**
The Liver Clinic experience with Direct Acting Antiviral Therapy for Hepatitis C - the first year"

15:51 - 16:03 **Robert Nel (Gastroenterology)**
Comparison of Full-spectrum endoscopy, magnetic endoscopic imaging and standard forward viewing colonoscopy

16:03 – 16:23 **Tea**

SESSION V

16:23 – 17:05 **38th Annual Bernard Pimstone Memorial Lecture**

Introduction of Speaker: Prof Karen Sliwa

Speaker: Prof Simon Stewart

Rediscovering the Heart of Africa

Professor Simon Stewart NFESC, FCSANZ, FAHA is dedicated to understanding the evolving burden of heart disease and developing innovative models of care to improve related health outcomes having published >300 journal articles and 10 books since he completed his PhD in 1999. The Director of the Mary MacKillop Institute for Health Research at the Australian Catholic University in Melbourne Australia, he is also an NHMRC of Australia Principal Research Fellow and leads the NHMRC of Australia Centre of Research Excellence to Reduce Inequality in Heart Disease. As Principal Investigator he currently leads projects worth more than $AU10 million in peer-review funding. This includes a number of multicenter, randomized trials of disease management that extend upon the findings of recently published trials - including the landmark SAFETY Trial of atrial fibrillation management published in The Lancet. In collaboration with Professor Karen Sliwa, Professor Stewart made a major contribution to the establishment and conduct of the world-renowned Heart of Soweto Study. He is senior Editor of a recently published book arising from his research collaborations in Africa (The Heart of Africa: Clinical Profile of an Evolving Burden of Heart Disease in Africa) and also co-led the Heart of the Heart Study of Indigenous heart health in Central Australia. He continues to undertake critical research in these vulnerable populations. Professor Stewart is also an Associate Editor of the International Journal of Cardiology and holds senior editorial positions in other prestigious journals including the Journal of the American College of Cardiology and Nature Reviews Cardiology

SESSION VI

Chairperson: **Prof Gary Maartens**

17:05 – 18:30 **Department of Medicine Cocktail Party and Awards ceremony**

- Best poster presentation Prize
- Department of Medicine Best Publication Award
- Bernard Pimstone Prize
- Department of Medicine Prize for Clinical Research

SESSION 1

Chairperson:
Prof Sandie Thomson

08:05am - 10:01am

Clinical Outcomes in 3343 Children and Adults with Rheumatic Heart Disease from 14 Low and Middle Income Countries: 2-Year Follow-up of the Global Rheumatic Heart Disease Registry (the REMEDY study)

Liesl Zuhlke,* Mark Engel and Bongani Mayosi for the Remedy investigators

---

Introduction: The World Health Federation has set a global target to reduce mortality from rheumatic heart disease (RHD) by 25% by 2025 in those under the age of 25. We aimed to estimate the RHD-associated mortality and morbidity in low and middle-income countries, and identify predictors of mortality.

Subjects and Methods: Between January 2010 and November 2012, we enrolled 3343 patients from 25 centres in 14 countries and followed them for two years to assess all-cause mortality and adverse events.

Results: Vital status at 24 months was known for 2960 (88.5%) patients. Although patients were young (median age 28 years, interquartile range 18 to 40), two-year case fatality rate was high (500 deaths, 16.9%). Mortality rate was 116.3/1000 patient-years in the first year and 65.4/1000 patient-years in the second year. Median age at death was 28.7 years. Independent predictors of death were severe valve disease (hazard ratio (HR) 2.36, 95% confidence interval (CI) 1.80-3.11), CHF (HR 2.16, 95% CI 1.70-2.72), New York Heart Association functional class III/IV (HR 1.67, 95% CI 1.32-2.10), atrial fibrillation (AF) (HR 1.40, 95% CI 1.10-1.78) and older age (HR 1.02, 95% CI 1.01-1.02 per year increase) at enrolment. Post-primary education (HR 0.67, 95% CI 0.54-0.85) and female sex (HR 0.65, 95%CI 0.52-0.80) conferred a lower risk of death. 204 (6.9 %) had new CHF (incidence, 38.42/1000 patient-years), 46 (1.6%) had a stroke or TIA (8.45/1000 patient-years) and 19 (0.6%) had ARF (3.49/1000 patient-years). Patients from low and lower-middle income countries had higher prevalence of predictors of mortality and higher age- and sex-adjusted mortality compared to patients from upper-middle income countries.

Interpretation: Young patients with symptomatic RHD have high mortality and morbidity; those from low and lower-middle income countries had a poorer prognosis associated with advanced disease and low education.

Cytomegalovirus viraemia and 12-week mortality among hospitalised adults with HIV-associated tuberculosis in Khayelitsha Hospital, South Africa: a prospective Cohort Study

Amy Ward*, David Barr, Charlotte Schutz, Rosie Burton, Andrew Boulle, Gary Maartens, Robert J. Wilkinson, Graeme Meintjes

---

Introduction: Mortality in hospitalised patients with HIV-associated tuberculosis remains high. Cytomegalovirus (CMV) organ disease is one of the co-infections found in autopsies of such patients. We investigated the association of CMV viraemia with mortality in this setting
Subject and methods: HIV-infected inpatients in Khayelitsha Hospital with CD4<350cells/µL and new diagnosis of tuberculosis were enrolled from January 2014-June 2015. Plasma CMV qPCR was performed and categorized as detectable (CMV+) or undetectable (CMV-). Endpoint was 12-week mortality.

Results: We included 256 patients with median age 36 years (IQR 31-44 years), 49% male, 35% on ART, median CD4=64 cells/µL(IQR 24-117) and 79(30.9%) CMV+. By 12 weeks, 26/77(38.0%) of CMV+ and 31/174(17.8%) of CMV- patients died (p=0.008); 5 were lost to follow-up. In CMV+ patients with <1000 copies/ml mortality was 12/36(33.3%) compared to 14/41(34.1%) in those with higher viral load (p=1.0).

Mortality was higher in older patients (≥36 years): 32.8% vs. 14.1%(p<0.001). Older patients were more likely to be CMV+ (38.0% vs. 23.6%, p=0.015) and a larger proportion of older patients had CD4 count<50 cells/µL (48.5% vs. 37.9%, p=0.106). In Kaplan-Meier analysis, CMV+ was associated with mortality in older, not younger patients. In multivariate Cox proportional-hazards regression, age (aHR=1.70, 95%CI=1.34-2.15 per 10years increase) was associated with mortality; CMV status was not

Interpretation: CMV viraemia was associated with higher mortality, but not after adjusting for potential confounders. Older patients had higher mortality and were more likely to have CMV viraemia. CMV viraemia is likely a marker of more severe immunodeficiency rather than a direct contributor to mortality.

Matrix turnover and inflammatory pathology in HIV-1-associated tuberculosis immune reconstitution inflammatory syndrome (TB-IRIS).

Naomi F Walker[*], Katalin A Wilkinson, Graeme Meintjes, Liku Tezera, Rene Goliath[1], Janique M Peyper, Rebecca Tadokera, Anna K Coussens, Robert J Wilkinson, Jon S Friedland, Paul T Elkington.

Introduction: Tuberculosis (TB) is the leading cause of death in HIV-infected patients. Anti-retroviral therapy (ART) reduces mortality but may be complicated by TB-IRIS. Diagnostic and targeted treatment strategies for TB-IRIS are lacking. We investigated the hypothesis that matrix metalloproteinases (MMPs), previously implicated in TB tissue destruction, associate with immunopathology in TB-IRIS.

Subjects and Methods: In a longitudinal study conducted at a HIV-TB clinic in Cape Town, HIV-infected ART-naïve patients, with CD4 counts <200 cells/mm3, presenting with TB, were followed from TB treatment initiation (TB0), for the first 3 months of ART. Serial induced sputum and plasma were collected. MMP and matrix degradation product procollagen III N-terminal propeptide (PIIINP) concentrations were quantified (pg/ml) at TB0, ART initiation (ARV0), week 2 (ARV2) and 4 (ARV4) of ART. Chest radiographs were scored for disease extent. Patients who developed TB-IRIS were compared with those who did not (non-IRIS controls) using Mann-Whitney U test. Correlations were assessed using Spearman's test.

Results: 29 (59%) out of 49 study participants developed TB-IRIS, after a median of 14 days of ART. Median plasma PIIINP was higher in TB-IRIS patients than non-IRIS controls, at TB0 (43600 vs 21651 pg/ml, p=0.036), ARV2 (6104 vs 1095 pg/ml, p=0.043) and ARV4 (46763 vs 22424 pg/ml, p=0.001). Plasma MMPs were elevated in TB-IRIS patients, most significantly MMP-8. Median plasma MMP-8 was higher in TB-IRIS at all timepoints, with the greatest difference observed at TB0 (4582 vs 526 pg/ml, p=0.002) and at ARV2 (6140 vs1095 pg/ml, p=0.0007). Plasma MMP-8 correlated with plasma PIIINP (r=0.435, p<0.0001), neutrophil count (r=0.617, p<0.0001), and C-reactive protein (r=0.67, p<0.0001). Plasma MMP-1 and MMP-3 were also higher in TB-IRIS.

Interpretation: These findings implicate systemic MMP dysregulation in TB-IRIS pathophysiology, suggesting that neutrophil-derived MMP-8 plays a key role and may be a therapeutic target. MMP-8 and PIIINP are also potential predictive and diagnostic markers of TB-IRIS.

Programmatically incurable tuberculosis and transmission among home discharged cases in South Africa.

Jason Limberis*, Elize Pietersen, Jody Phelan, Aliasgar Esmail, Maia Lesosky, Kevin P Fennelly, Julian te Riele, Barbara Mastrapa, Paul Spiller, Elisabeth M Streicher, Tania Dolby, Abdallah M. Abdallah, Fathia Ben Rached, John Simpson, Liezel Smith, Tawanda Gumbo, Paul van Helden, Frederick A Sirgel, Ruth McNerney, Grant Theron, Arnab Pain, Taane G Clark, Robin M Warren, Keertan Dheda

---

Introduction: Prospective data on patients with programmatically incurable tuberculosis are urgently needed to inform treatment and containment strategies.

Subjects and Methods: 273 South African patients with XDR-TB, or resistance beyond XDR-TB, were followed over 6 years. For patients from the Western Cape transmission dynamics, infectiousness, and drug susceptibility were interrogated using whole genome sequencing (WGS), cough aerosol sampling, and phenotypic testing for 18 drugs.

Results: The 5-year mortality was 68% and 84% of patients had unfavorable outcomes of either treatment failure, relapse, default, or death during treatment. 172/273 (63%) patients were home-discharged into the community. Unfavorable outcomes were recorded for 104/172 (60%) home-discharged patients, 54/104 (52%) having failed treatment. Median time to death following home-discharge was 9.9 months (IQR 4.2-17.4). 135/179 (75%) isolates were phenotypically resistant to ≥8 drugs, and 20/179 (11%) to ≥12 drugs. WGS suggested a high likelihood of transmission in 65/141 (46%) patients having ≤5 SNP differences and matching drug- resistance markers. Importantly, 35/104 (34%) home-discharged patients were smear-positive, and 5/12 expectorated infectious (culture-positive) respirable (<5µm) cough aerosols. WGS revealed that 18/90 (20%) home-discharged patients were likely to have caused a secondary XDR-TB case. Discharged patients reported inter-person contact with sub-optimal use of protective masks.

Interpretation: A considerable proportion of patients with programmatically incurable tuberculosis were discharged into the community where they had significant longevity, were highly infectious, and were a serious transmission risk. Urgent action, including appropriate containment strategies, is needed to address this situation. Access to newer drugs must be accelerated along with comprehensive drug susceptibility testing.

Clinical profile and outcome of biopsy proven Acute Interstitial Nephritis of native kidneys at the Groote Schuur Hospital: A 10-Year Review

Emmanuel Effa, Brian Rayner, **Udeme Ekrikpo*,** Ikechi Okpechi

---

Introduction: Acute interstitial nephritis (AIN) is a relatively common cause of acute often reversible kidney injury characterized histopathologically by inflammatory infiltrates and oedema in the interstitium as well as tubulitis. In South Africa, even with high prevalence of the human immunodeficiency virus (HIV) and tuberculosis infections and the resultant use of multiple medications, there are scarcely any studies on the clinical profile and outcomes of patients with biopsy proven AIN.

Methods: Retrospective audit of records of patients with biopsy proven AIN of native kidneys seen at the Groote Schuur Hospital, Cape Town between January 2006 and December 2015.

Results: Fifty-six patients consisting of 29 females and 27 males with biopsy proven AIN were reviewed. The majority were blacks with HIV and HIV-TB coinfection as the most common co-morbidities in 42.8% and 30.5% of patients respectively. Drug related AIN was seen in 38 (67.9%) patients with Rifampicin as the most often implicated medication. Probable drug-related AIN was seen in 3 (5.4%) patients, infection-related AIN in 8 (14.3%), and unspecified causes in 7 (12.5%). The diagnosis of AIN was suspected in 44.6% of all patients before biopsy. In terms of intervention, 18 (32.1%) patients had haemodialysis while 24 (42.8%) received steroids. Complete renal recovery at 30 and 90 days was seen in 11/44 (25%) patients and 11/30 (36.7%) patients respectively. There was no correlation between degree of interstitial inflammation and serum creatinine at biopsy (p=0.45) as well as the presence of comorbidities and severity of renal failure at presentation (p=0.10)

Interpretation: Recovery was incomplete in a substantial number of patients. Anti-tuberculous drugs are the leading cause of AIN in our setting. Acute interstitial nephritis should reasonably be suspected as a cause of renal failure in this era of multiple comorbidities requiring an array of medications.

Prevalence of *FAM111B* gene mutations in systemic sclerosis

Gcelu A*, Deshpande G, Kalla A, Shaboodien G, Tikly M, Mayosi BM, Hodkinson B

Background: Systemic sclerosis (SSc) is a prototypic systemic fibrotic disease with unclearly characterized genetic basis. Implicated genes have been associated with autoimmune dysregulation with relatively few variants associated with fibrosis. We have discovered that mutations in *FAM111B* gene cause hereditary fibrosing poikiloderma with tendon contractures, myopathy, and pulmonary fibrosis (POIKTMP), a multisystem fibrotic condition with clinical aspects of SSc. This observation has established *FAM111B* as a candidate gene for SSc.

Subjects and Methods:
Patients with a definite diagnosis of SSc attending the Rheumatology outpatient departments at Groote Schuur Hospital, Cape Town, and Chris Hani Baragwanath Hospital, Johannesburg, were enrolled into the study. Physical examination assessing the extent of disease was done in all patients and the modified Rodnan skin score (mRSS) was used to determine the extent of the skin involvement. Blood samples were collected for DNA extraction and mutation screening using the high-resolution melt technique. Samples with abnormal electropherograms were selected for Sanger sequencing to identify mutations. Public databases were used to verify the frequency of variants in *FAM111B*.

Results: 131 patients were genotyped, 13 men and 118 women, with a mean age of 26.6 years and mean age of symptom onset at 25.3 years. The majority of patients were black (59.5%). 72% of patients had diffuse systemic sclerosis (DSSc) with a median mRSS of 11. Genetic analysis revealed seven rare genetic variants (C832G>A; C855G>T; C917A>G; C937G>A; C988C>T; C995A>C and C1006G>C) in eight patients (five patients from Johannesburg and three patients from Cape Town). These variants were missense mutations of unknown significance with a minor allele frequency <0.01. No *FAM111B* mutations that cause POIKMT were found in patients with SSc.

Interpretation
Rare genetic variants of unknown significance (GVUS) in *FAM111B* gene were found in patients with SSc. It is possible that the GVUS may modify the function of *FAM111B*, and influence the pathogenesis of SSc or are rare polymorphisms with no functional impact.

A "RACY" screening tool for delirium in general medical in-patients

C Day,* F Abdullah, C April, N Vorajee, L Grace, K James, K Manning, G Calligaro, S Pandie, A Stanley, R Homan, H Hutton, L Bertels, Z Kerbelker, S Naidoo, R Sher, S Baboolal, J Seggie, M Combrinck, P Raubenheimer and J Peter

---

Introduction: Delirium is common in general medical in-patients and is known to associate with poor short-, medium-, and long-term outcomes. A number of standardised bedside instruments are available for delirium testing in different settings, but routine clinical use and suitability to busy general medical wards is variable.

Subjects and Methods: The development study (n=356) was conducted amongst general medical admissions to Groote Schuur Hospital (GSH), with the validation study (n=851) including both GSH (n=484) and Victoria Hospital (n=367) in Cape Town, South Africa. Patients were excluded if they had a GCS≤12/15, aphasia, or required ICU admission. RACY and delirium testing were performed between 6-48 hours after admission. The 4-question "RACY" tool was developed from the validated 10-question abbreviated mental test using stepwise regression modeling. Delirium reference testing used the validated confusion assessment method or DSM-IV criteria, evaluated during mini-mental state formal cognitive testing by neuropsychologists. Interobserver agreement was assessed using two trained physicians.

Results: The prevalence of delirium and median (IQR) age in the development and validation cohorts were 19.1% (68/356) and 45 (32-59) years, and 12.1% (103/851) and 51 (36-65) respectively. The AUROC for RACY was 0.88 and 0.86 in the development and validation cohorts respectively. A RACY score greater than or equal to 2/4 correctly classified 90% of patients, with sensitivity, specificity, PPV, NPV (95% CI) of 93.7 (91.7-95.2), 62.1 (52.5-70.9), 94.7 (92.9-96.1), and 57.7 (48.4-66.4). Interobserver agreement was 93% overall with a very good kappa of 0.80.

Interpretation:
The novel RACY delirum screening tool is a simple and effective bedside delirium diagnostic instrument for use in non-geriatric general medical in-patient settings. Performance is not affected by patient education level and/or the use of a translator, making it ideal for developing country settings.

Characterization of efavirenz-associated cutaneous adverse drug reactions

Thuraya Isaacs*, Sipho Dlamini, Jonny Peter, Rannakoe Lehloenya

---

Introduction: Non-nucleotide reverse transcriptase inhibitors (NNRTIs), are a major cause of cutaneous adverse drug reactions (CADRs), and reactions can range from mild to life-threatening. There is limited data on efavirenz-associated (EFZ-CADR) and in particular reactions types and severity warranting treatment termination. The aim of this study was to better describe the reactions that can be treated through and the clinical and laboratory features necessitating discontinuation of therapy.

Subjects and methods: All patients admitted to the Groote Schuur Hospital Dermatology service diagnosed with EFZ-CADR between 5 July 2004 to 31 December 2015 were included. Key factors included age; sex; CD4 count; drugs used in the preceding 8 weeks; duration of ART exposure; clinical features, ALT, AST and eosinophil counts; management, including whether treatment discontinued or rechallenged; and outcomes. Patients were phoned if there was missing data on whether ART was withdrawn or continued. Verbal consent was obtained from all the participants phoned.

Results: Thirty-five**,** predominantly female patients (80%) with EFZ-CADR were included with a median (IQR) age and CD4 count of 35 (27-41) years and 244 (126-395) cells/mm^3 respectively. Clinical presentation included: 43% (15/35) morbilliform eruptions, 49% (17/35) indurated erythema; and 6% (2/35) both; in 43% (15/35) the eruption was photo-distributed, and 83% (29/35) were Grade 1. The median (IQR) time from starting EFZ to a reaction was 11 (7-20) days. Overall, in 50% (16/32) EFZ was either continued through the CADR or successfully rechallenged after brief cessation of therapy, with the presents of fever being the most important features associated with drug cessation (p=0.026).

Interpretation: In the majority of EFZ-CADR, reactions are mild with the absence of systemic features, and treatment can either be continued or briefly interrupted and reintroduced. The main risk factor for termination of therapy is systemic illness.

SESSION 2

Chairperson:

Prof Mpiko Ntsekhe

10:20am - 10:40am

Stevens Johnson syndrome and toxic epidermal necrolysis: maternal and foetal outcomes in twenty-two consecutive pregnant women.

Lauren Knight*, Gail Todd, Rudzani Muloiwa, Mushi Matjila and Rannakoe J Lehloenya

---

Introduction: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) form a spectrum of one rare and life-threatening cutaneous drug reaction. SJS/TEN in pregnancy poses largely unknown risk factors and outcomes for both the mother and foetus compared to the general population.

Methods: We conducted a retrospective study of consecutive pregnant women admitted to single tertiary referral centre in South Africa with SJS/TEN over a 3 year period. They were all managed by the same group of physicians using the same protocols. We evaluated their underlying illnesses, offending drugs and the course of pregnancy and outcomes to determine factors influencing maternal and fetal outcomes.

Results: We identified twenty-two women who developed SJS/TEN while pregnant, all of them HIV-infected. Their median age was 29 years. The majority 16/22 (73%) had SJS, the milder variant of the disease affecting < 10% body surface area. Nevirapine was the offending drug in 21/22 (95%) cases. All 22 of the mothers survived with 3/22 (14%) developing postpartum sepsis. Pregnancy outcomes were known in 18/22 women and 9/18 (50%) babies were delivered by caesarean section. There were 2 fetal deaths at 21 and 31 weeks respectively and both were associated with post-partum sepsis. Postnatal complications occurred in 5 cases, 3 involving the respiratory system and the other two being low birth weight deliveries. Eight placentae and one fetus were sent for examination and none showed macroscopic or microscopic features of SJS/TEN. On follow-up, only 12/20 children were tested for HIV at 6 weeks post-delivery and none of them were HIV-infected.

Conclusions: TEN, the severe form of the disease, seems to be associated with poorer fetal outcomes. SJS/TEN-associated mortality is not increased in HIV-infected pregnant women. Maternal SJS/TEN does not seem to commonly manifest in the foetus.

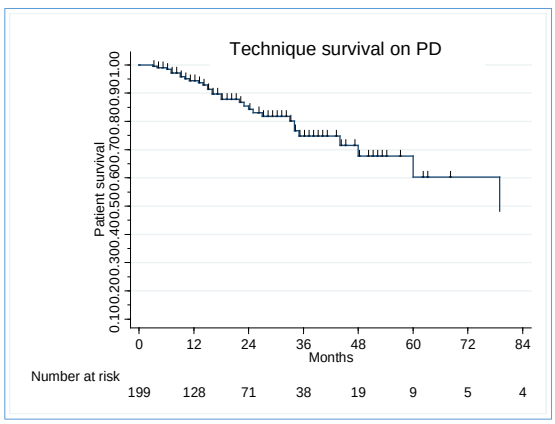
Patient outcomes in a peritoneal dialysis first program in Cape Town South Africa

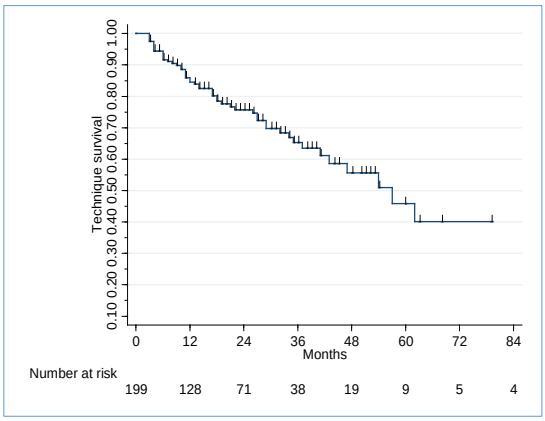
B. Davidson*, K. Manning, N. Wearne

Background: South Africa [SA] currently does the most peritoneal dialysis in Africa. Yet, outcome data is limited. With the collision of epidemics of communicable and non-communicable diseases in Africa the need for effective dialysis is escalating. Peritoneal dialysis [PD] remains a life-saving modality especially as haemodialysis is limited in the state sector.

Methods: We retrospectively analyzed all patients undergoing PD at Groote Schuur Hospital from January 2008 until June 2014 and thereafter prospectively until June 2015. Variables included demographics [age, sex and race], yearly adequacy scores, modality, fluid, cardiovascular risk and diabetes. The influence of these variables on peritonitis rate, catheter malfunction, technique and patient survival were assessed.

Results: 230 patients were initiated on PD, 31 were excluded as they were on PD for < 90 days. The mean age was 39.7 +/- 10.4 years [SD], 49,8% were male, and ethnicity (32.2% African, 63.8% mixed ancestry and 4% white). Hypertension (33%) was the most common causes of end stage renal disease. 11.6% were diabetic at dialysis initiation. Our average length of time on PD was 17 months (IQR 8 – 32). The peritonitis rate was 0.87 events per patient years (declining from the previous reported rate of 1.7(2010). 1, 2 and 5 year patient and technique survival was 94.4%, 84.3% and 60.2% and 84.6%, 75.7% and 45.9% respectively. Diabetes (HR 2.94, 95% CI 1.17-7.37; p=0.015) was the only significant predictor of patient survival. African race (p = 0.0087) and albumin < 30 (p=0.052) were both predictors of technique failure.





Conclusions: In our PD first program the results are encouraging, despite lack of home visits due to safety, resource limitations and a high disease burden. Technique failure in African race needs further evaluation. However, we truly believe that peritoneal dialysis remains a viable, life-saving alternative in an African setting.

Risk factors for incident diabetes in a chort taking first-line nonnucleoside reverse transcriptase inhibitor-based antiretroviral therapy

Sumanth Karamchand*, Rory Leisegang, Michael Schomaker, Gary Maartens, Lourens Walters, Michael Hislop, Joel A. Dave, Naomi S. Levitt, and Karen Cohen.

Introduction: Efavirenz is the preferred nonnucleoside reverse transcriptase inhibitor (NNRTI) in first-line antiretroviral therapy (ART) regimens in low- and middle-income countries, where the prevalence of diabetes is increasing. Randomized control trials have shown mild increases in plasma glucose in participants in the efavirenz arms, but no association has been reported with overt diabetes. We explored the association between efavirenz exposure and incident diabetes in a large Southern African cohort commencing NNRTI-based first-line ART.

Subjects and Methods: Our cohort included HIV-infected adults commencing NNRTI-based ART in a private sector HIV disease management programme from January 2002 to December 2011. Incident diabetes was identified by the initiation of diabetes treatment. Patients with prevalent diabetes were excluded. We compared the incidence of diabetes in patients receiving efavirenz versus nevirapine containing regimens with a Kaplan-Meier plot and a log-rank test. We modelled the association of efavirenz exposure with the hazard of developing diabetes using a multivariate Cox-proportional hazards model. We adjusted for the following variables: age, sex, baseline BMI, baseline CD4, baseline viral load, exposure to diabetogenic drugs, nucleoside reverse transcriptase inhibitor (NRTI) exposure.

Results: We included 56,298 patients with 113,297 patient-years of follow-up (PYFU) on first line ART. The crude incidence of diabetes was 13.24 per 1000 PYFU. In the multivariate analysis treatment with efavirenz rather than nevirapine was associated with increased risk of developing diabetes (hazard ratio 1.27 (95% confidence interval 1.10 - 1.46). Zidovudine and stavudine exposure, older baseline age, elevated baseline BMI, and exposure to diabetogenic medication were also associated with increased risk of diabetes.

Interpretation: We found that treatment with efavirenz, as well as stavudine and zidovudine, increased the risk of incident diabetes. Interventions to detect and prevent diabetes should be implemented in ART programmes, and use of antiretrovirals with lower risk of metabolic complications should be encouraged.

A Clinical Prediction Rule for the Diagnosis of Tuberculosis in Seriously Ill HIV-Infected Adults

Rulan Griesel*, Annemie Stewart, Helen van der Plas, Welile Sikhondze, Molebogeng Rangaka, Mark Nicol, Marc Mendelson and Gary Maartens

---

Introduction: The World Health Organization (WHO) algorithm for diagnosis of tuberculosis in seriously ill HIV-infected patients with danger signs (any one of respiratory rate >30/min; heart rate >120/min; temperature >39^{o}C; unable to walk unaided) and cough for ≥14 days uses chest x-ray (CXR) and sputum smear results to start empiric tuberculosis therapy. We aimed to develop a clinical prediction rule (CPR) for the diagnosis of tuberculosis by determining an evidence base for the duration of cough, the role of other tuberculosis symptoms, and simple laboratory tests. In addition, we determined the diagnostic performance of the Xpert MTB/RIF assay.

Subjects and Methods: A cross-sectional diagnostic study was conducted at 2 secondary level hospitals in Cape Town. Inclusion criteria were: HIV-infection, cough (any duration), WHO danger signs, age ≥18 years, and able to produce sputum. CXRs were assessed by a specialist radiologist and categorised as unlikely, possibly or likely tuberculosis. The reference standard was culture of *M. tuberculosis* from blood or sputum. In a multivariate logistic regression model we assessed the ability of the following *a priori* chosen variables to predict the diagnosis of tuberculosis: WHO danger signs; duration of cough; tuberculosis symptoms; CXR assessment; haemoglobin; and white cell count (WCC). The most predictive variables were used to establish a CPR for the diagnosis of tuberculosis.

Results: 484 participants were enrolled into the study: median age 36 years; 317 (66%) female; median CD4 count was 89 cells/µL (IQR 34-210); and 171 were on ART. A total of 256 participants were culture-positive for tuberculosis. Xpert MTB/RIF had a sensitivity of 86.3% and a specificity of 96.1%. The final model included the following variables: cough ≥14 days, being unable to walk unaided, temperature >39^{o}C, CXR assessment, haemoglobin, and WCC. CXR assessment of "likely tuberculosis" and anaemia were the strongest predictors of tuberculosis. The ROC AUC for the CPR was 0.81 (95% CI 0.80-0.82).

Interpretation: The CPR could facilitate rapid initiation of empiric tuberculosis therapy in seriously ill patients using simple measures. Xpert MTB/RIF performed well in this population.

We acknowledge the National Institute of Health (USA) for the funding opportunity that made this study possible. Grant number: R01 AI 96735-01 IRIDA

Differentiating Crohn's disease (CD) and Intestinal Tuberculosis (ITB) at presentation in patients with tissue granulomas

Gill Watermeyer, **Sandie Thomson***

Introduction: Overlap of clinical, endoscopic, radiographic and histological features, coupled with a poor microbiological yield makes differentiating CD from ITB challenging. Granulomas are present in both diseases; in CD they predict the need for immunosuppressive therapy which before initiation requires ITB to be excluded. The aim of this study is thus to compare patients with granuloma-positive CD or ITB, in order to identify factors that may aid in differentiating them.

Methods: a retrospective cohort study evaluating patients with granuloma-positive CD or ITB. Subjects were identified from a pathology database and information extracted from patient folders, laboratory and radiology records.

Results: Sixty-eight ITB and 48 CD cases were identified. Patients with ITB were more likely to be male, of black ethnicity, have HIV infection, isolated colonic involvement, night sweats and tachycardia at presentation. ITB was also associated with lower serum albumin and haemoglobin concentrations, higher CRP values, X-ray features suggesting active TB and lymphnodes >1cm on cross-sectional imaging. Extra-intestinal manifestations (EIMS) were predictive of CD. There were no significant differences in age at diagnosis, smoking status, symptom du- ration, or perianal disease. On multivariate analysis HIV positivity (OR 29.72, 95% CI 2.15- 410.96, p=0.01), isolated colonic disease (OR 6.17, 95% CI 1.17- 32.52, p=0.03) and the absence of EIMs (0.09, 95% CI 0.01-0.65, p=0.02) remained as significant risk factors for ITB. The presence of these 3 risk factors yielded 93% specificity for the diagnosis of ITB.

Conclusion: Excluding ITB is essential when considering potent immunosuppressive therapies for CD. This study focused on subjects with tissue granulomas at diagnosis as this predicts a severe course of CD. Several clinical and biochemical factors were identified which will aid in making the correct diagnosis, notably HIV infection which is the strongest risk factor for ITB in this study.

Preliminary genealogical evidence for the Plakophilin-2 gene, *PKP2* c.1162C>T founder mutation in South Africans with Arrhythmogenic Right Ventricular Cardiomyopathy

Tafadzwa Machipisa*, Gasnat Shaboodien, Gerhard Geldenhuys and Bongani M Mayosi

---

Introduction: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a progressive form of inherited heart muscle disease characterized by ventricular arrhythmias and sudden cardiac death. Often pathogenesis is linked to deleterious mutations in the desmosomal gene plakophilin-2 (*PKP2*). Prior investigations of the pathogenic *PKP2* c.1162C>T mutation showed a common haplotype carried by four 'unrelated' probands self-identified as Afrikaners. Genetic genealogy suggests common haplotypes are linked to common founder(s) in homogenous populations. This study aimed to employ genealogical methods to identify common founder(s) for the *PKP2* c.1162C>T mutation in ARVC families of Afrikaner descent.

Subjects and Methods: Forty-six participants (7 probands and 39 relatives) from the ARVC Registry of South Africa were screened for the *PKP2* c.1162C>T mutation using High Resolution Melt analysis and Sanger sequencing. Microsatellite typing was also performed using three markers to construct haplotypes spanning the *PKP2* gene. Subsequently, genealogical tracing to identify common progenitors went back through multiple generations into the implicated ancestral lines of the present day Afrikaner families.

Results: We observed that 65.2% (30/46) of the family members harboured the mutation of interest and carried a common haplotype in the seven Afrikaner families. A common haplotype emerged that segregated with all the mutation carriers. Four of the seven families had 17th century progenitors, and five candidate founder couples were identified all of whom were linked to the families whose ancestors could be traced to the 17th century.

Interpretation: Preliminary genetic and genealogical data suggest that the *PKP2* c.1162C>T mutation segregates in Afrikaner families due to a founder effect. The genealogical record supports the hypothesis that the *PKP2* c.1162C>T mutation is a founder mutation, and that descendants of the five candidate common founder couples are at risk of developing ARVC. Further genealogical analysis is underway in the other three families in order to establish one common founder for the *PKP2* c.1162C>T mutation.

The impact of new TB diagnostic technologies on community-based intensified case-finding: a multi-centre randomised controlled trial

Gregory L. Calligaro, Lynn S. Zijenah, Jonathan G. Peter, Grant Theron, Virginia Buser, Ruth McNerney, Wilbert Bara, Tsitsi Bandason, Ureshnie Govender, Michele Tomasicchio, Liezel Smith, Bongani M. Mayosi and Keertan Dheda.

Presenter: Phindile Gina

Introduction: Inadequate case detection results in high levels of undiagnosed TB in sub-Saharan Africa. Data on the impact of new diagnostic tools when used for community-based intensified case finding are lacking.

Subjects and Methods: In a randomized controlled trial we compared on-the-spot diagnosis using Xpert-MTB/RIF, and if HIV-infected the Determine TB LAM urine test, to standard laboratory-based sputum smear-microscopy in congregate community settings in Cape Town and Harare. Participants were randomized following screening at sputum induction-equipped mobile clinics. Culture was the reference standard. The primary endpoint was the time-specific proportion of patients initiating treatment. This study was registered at ClinicalTrials.gov (NCT01990274).

Results: Of 2261 persons screened, 875 (39%) met the criteria for diagnostic testing, and 74/875 (9%) had confirmed tuberculosis. The proportion of patients receiving same-day treatment (intervention test positive or empiric) was higher in the novel arm (57% vs. 31%, p=0·0268) and median time-to-treatment (IQR) was shorter [1·0 (0·1-4) vs. 4·5 (0·1-31) days, p=0·0407]. This incremental difference was significant at all time-points up to 60 days when, if additional cases diagnosed by culture were included, the proportion initiating treatment in either arm was similar (93% vs. 81%, p=0·1302). Xpert-MTB/RIF testing by minimally trained healthcare workers was feasible in a mobile van with equivalent accuracy to laboratory-based testing.

Interpretation: Compared to traditional tools, Xpert-MTB/RIF for community-based case detection in HIV and TB-endemic settings is feasible, shortens time-to-treatment initiation, and increases the time-specific proportion of patients initiating treatment.

SESSION 3

Chairperson:

Prof Nonhlanhla Khumalo

13:55am – 16:03am

Genomics in the South African research context: human rights and the Discovery Genomics Initiative

Marlyn Faure* and Dr Jantina de Vries

The primary reference to science in the 1948 Universal Declaration of Human Rights is in Article 27, which stipulates the right of people "to share in scientific advancement and its benefits". This right includes the right to freely engage in responsible scientific enquiry. Although infrequently applied to scientific research, several authors have applied this clause, and a subsequent clause in the same article, to genomics research.[1-3] Amongst others, such an approach can inform the development of international codes of conduct for genomics research, for instance in terms of ensuring fair and equal access to genomic research methods and data. In this paper, we will explore how the Discovery Health Genomics Initiative (DHGI) relates to this human right. Taking place at the intersection of healthcare and research, the DHGI has already been accused of potentially misleading private health insurance customers [4] and being a form of bioexploitation [5]. A critical feature of the DHGI is that it proposes to employ the services of a US company to conduct sequencing. This company will not only retain clients' individual genetic data, but will also be given copies of all relevant data that Discovery Health holds of those individuals – including for instance medical claims information and nutritional and behavioural data. The US Company will possess and commercialise this data to other private entities for research and development. In this paper, we will evaluate the merits of this kind of privatisation of genomic research as counter to scientific research being for the common good. We argue that such a neo-liberal approach to research creates a double barrier given that it excludes those who are not able to afford private health care and has the potential to perpetuate unequal global power relationships by privileging research and development in the US and not South Africa.

Development of a Th1-polarising dendritic cell vaccine driving cytotoxic T-lymphocyte-mediated killing of primary breast cancer cells *in vitro*

Michele Tomasicchio*, Lynn Semple, Richard Maldau, Phillippa Randall, Malika Davids, Anil Pooran, Ali Esmail, Suzette Oelofse, Lydia Carncross, Jennifer Downs, David Anderson, Francois Malherbe, Nickolas Novitsky, Eugene Panieri, Thuran Naiker, Keertan Dheda

---

Introduction: Breast cancer remains one of the leading causes of death worldwide. Traditional treatment of stage 3 and 4 cancers are associated with substantial toxicity and suboptimal efficacy. We therefore investigated the utility of a dendritic cell (DC) vaccine as a potential immunotherapeutic intervention against breast cancer, and to inform the rationale for a phase I/IIA clinical trial.

Subjects and methods: We recruited 11 female participants with stage 1, 2 and 3 breast cancer and matured their DCs post-phlebotomy, *ex vivo*, using a maturation cocktail and tumour-specific lysate. The efficacy of the vaccine was evaluated by its ability to elicit a cytotoxic T-lymphocyte response to autologous primary breast cancer cells *in vitro*. Methods were developed to sustain *in vitro* survival of breast cancer cells obtained from tissue biopsies, and to cryopreserve DCs for re-infusion post-chemotherapy.

Results: We were able to optimally mature breast cancer-driven DCs *ex vivo* as assessed by the upregulation of CD80 (74%; $p < 0.05$), CD86 (82%; $p < 0.005$), CCR7 (50%; $p < 0.05$) and CD83 (77%; $p < 0.005$) compared to the immature DCs. The mature DCs produced high levels of the Th1 effector cytokine, IL12p70 (1.2 ng/ml; $p < 0.0001$) compared to DCs matured with tumour lysate or maturation cocktail alone. We further show that the mature DCs were able to elicit an antigen-specific robust and dose-dependent cytotoxic T-lymphocyte response, which was tumoricidal to autologous primary breast cancer cells. Lastly, we showed that the mature DCs post-cryopreservation maintained high viability, preserved their mature phenotype, and remained sterile and free of endotoxins or mycoplasma.

Interpretation: We have developed a DC vaccine that is cytotoxic to autologous breast cancer cells *in vitro*. The tools and technology generated here will now be evaluated in a phase I/IIA clinical trial.

The phenotype and natural history of ketosis-onset diabetes in Cape Town, South Africa

Peya B*, Skelton J, **Seedahmed K***, Mampane R, Levitt NS and Raubenheimer PJ

Introduction: Many adults presenting with diabetic ketoacidosis (DKA) in South Africa do not have the classical clinical features of type 1 diabetes (T1DM). Elsewhere, studies have shown that patients with the phenotype of type 2 diabetes (T2DM), may not require long term insulin therapy. This study describes the phenotype of patients presenting with a first episode of DKA in Cape Town and aims to assess incidence and predictors of "insulin remission".

Subjects and Methods: Patients > 18 years old, presenting with a first episode of DKA to 4 hospitals in the UCT/Groote Schuur Academic Health complex were prospectively enrolled. Patients were reviewed 1-3 weeks post discharge for clinical, biochemical and immunological phenotyping, and were then followed up closely for the next year. If possible, patients were weaned from insulin according to a standard protocol.

Results: 116 patients were enrolled; in 94 (78%) there was no prior diagnosis of diabetes ("Ketosis-onset diabetes"). 56% were men, the mean age was 32 years. Median BMI was 29kg/m2; 46% had a BMI of > 30. 30% were antibody +ve (anti GAD or anti-IA2) and 46.8% had a fasting c-peptide > 0.9ng/ml. The commonest phenotype based on the AB classification was antibody –ve, c-peptide preserved. (47%). In 58% of patients (42/72) with 6 months follow-up, insulin has been stopped. On initial presentation, patients in whom insulin could be stopped were clinically assessed as type 2 diabetes and were of a higher BMI. Antibody status was largely negative and c-peptide status positive in 69%, with AB classification the most significant predictor of insulin remisin on multivariate analysis.

Interpretation: In Cape Town, South Africa, the most common phenotype of adults presenting with 1st onset DKA is that of T2DM. 76% of newly diagnosed patients classified as T2DM could be completely weaned off insulin by 6 months.

Changes in estimated glomerular filtration rate over time in HIV-1-infected patients receiving Tenofovir

Reneé de Waal*, Karen Cohen, Matthew P Fox, Kathryn Stinson, Gary Maartens, Andrew Boulle1, Ehimario U Igumbor6, Mary-Ann Davies

---

Introduction: Tenofovir has been associated with decline in kidney function over time, but in patients with baseline kidney impairment, improvements over time have been reported. There are limited data from Africa regarding the effect of tenofovir on kidney function. We described changes in estimated glomerular filtration rate (eGFR) over time, and the incidence and risk factors for kidney toxicity, in a South African cohort.

Subjects and Methods: We included antiretroviral-naïve patients ≥16 years old who started tenofovir-containing antiretroviral therapy (ART) at two clinics. We calculated eGFR using the Modification of Diet in Renal Disease formula. We described changes in eGFR from ART initiation using linear mixed effects regression. We described the proportion of patients with eGFR <30 mL/min and <60 mL/min on treatment, and identified associations with decreased eGFR using Cox regression.

Results: We included 15156 patients. At ART initiation median age was 35.4 years (IQR 29.9–42.0), median CD4 cell count was 168 cells/µL (IQR 83–243), and median eGFR was 98.6 mL/min (IQR 84.4–115.6). Median duration of follow up on tenofovir was 12.9 months (IQR 5.1–23.3).

Mean eGFR change from baseline at 12 months was -4.4 mL/min (95% CI -4.9 to -4.0) and 11.9 mL/min (95%CI 11.0–12.7) in those with baseline eGFR ≥90 and <90 mL/min respectively.

Overall 292 (1.9%) patients developed eGFR <30 mL/min and 1 085 (7.2%) developed eGFR <60 mL/min. Significant associations with decreased eGFR included older age, baseline eGFR <60 mL/min, CD4 count <200 cells/µL, body weight <60 kg, and concomitant protease inhibitor use.

Interpretation: Patients on tenofovir with baseline eGFR ≥90 mL/min experienced small but significant declines in eGFR over time, while those with eGFR<90 mL/min at baseline experienced improvements over time. Decreases to below 30 mL/min were uncommon. In settings with limited access to laboratory testing, monitoring guidelines should consider focusing on higher risk patients.

Validation of the *PARVA* c.392A>T variant in a South African family with severe Arrhythmogenic Right Ventricular Cardiomyopathy.

Stephen Kamuli*, Gasnat Shaboodien and Bongani Mayosi.

Introduction: Cardiomyopathy is an endemic disease in Africa that is a major contributor to heart failure. Various genetic abnormalities associated with cardiomyopathy have been unraveled. A previous whole exome sequencing project conducted in the United Kingdom (UK) had identified the parvin alpha (*PARVA*) c.392A>T variant as a as a possible cause of arrhythmogenic right ventricular cardiomyopathy (ARVC) in a South African family.

Subjects and Methods: We investigated the ACM 8 family with three affected individuals in whom whole exome sequencing was previously performed using the Illumina platform. We expanded on this work by using high resolution melt (HRM) analysis and Sanger sequencing to screen all the available ACM 8 family members to determine segregation of the *PARVA* c.392A>T variant within this family. We also screened a cohort of 180 probands diagnosed with ARVC and other cardiomyopathies for any variants in *PARVA*

Results: No pathogenic *PARVA* variants were found in any of the cardiomyopathy probands screened. We subsequently performed whole exome sequencing on this family to validate the UK findings using the Ion Torrent platform. We found that both affected individuals were homozygous for the *PKP2* c.1162C>T mutation.

Interpretation: We found no definitive evidence of *PARVA* as a causal gene for ARVC. While this study set out to validate the whole exome sequencing experiments conducted in family ACM 8 in the UK, we instead found the causal variant to be the previously reported *PKP2* c.1162C>T mutation. *PKP2* is a gene known to cause ARVC, and the c.1162C>T mutation has been described as a founder mutation for autosomal dominant ARVC families of Afrikaner decent in South Africa.

A Comparison of Adolescent Sexual Reproductive Healthcare Utilization at the DTHF Youth Centre vs an Adolescent-friendly City Clinic

Andrea Mendelsohn*, Katherine Gill, Rebecca Marcus, Landisiwe Mzukwa, Eve Mendel, Dante Robbertze and Linda-Gail Bekker

---

Introduction: Despite the increasing HIV incidence among young South African women, HIV counselling and testing (HCT) rates remain unacceptably low. One in three young women has a pregnancy by age 20. Alternative strategies need to be explored in order to increase prevention and screening among high-risk adolescents.

Methods: The Desmond Tutu HIV Foundation (DTHF) Youth Centre (YC) in Masiphumelele offers integrated health, educational and recreational programs in order to increase adolescent access to comprehensive sexual and reproductive health services (SRH). Participation is incentivized and clinic statistics tracked with a biometric data system. We compared HIV testing and contraception rates with data from a public clinic in Imizamo Yethu (IY), a community of similar demographics, to ascertain the impact of the YC on SRH and HCT utilisation rates for adolescents.

Results: In 2015, adolescent females under 18 had 3.74 times more contraception visits at the YC than adolescents at IY clinic. There was no difference in the type of contraception used, with both populations favouring injectable methods. Adherence to contraception was sub-optimal, with the average YC female using contraception for 6.1 months/year. Masiphumelele youth were 1.85 times more likely to have HCT at the YC than youth in IY. This difference was greater in boys, with those aged between 15-24, 3.83 times more likely to test. Masiphumelele YC attendees were a third less likely to test HIV positive than their Imizamo Yethu counterparts.

Interpretation: Adolescents from Masiphumelele were significantly more likely to access SRH and HCT services at the YC in comparison to the city clinic in Imizamo Yethu that has made adolescent friendly accommodations. The differences were most dramatic in contraception coverage for females under 18 and HIV testing rates in males. Lessons from the DTHF YC may be applied to clinics in order to increase adolescent healthcare utilisation rates.

The Liver Clinic experience with Direct Acting Antiviral Therapy for Hepatitis C - the first year

Mark W. Sonderup*, Neliswa Gogela, Wendy Spearman

Introduction: All oral DAA therapies have revolutionized hepatitis C management. In the pre-DAA era, cure rates ranged between 40-60%. Through access programs, DAAs are increasingly affordable and accessible in South Africa. We review our experience in the first year of DAA use.

Subjects and methods: Patients sequentially treated with all oral DAA therapy were included in a registry. A variety of DAA combinations were used as per availability, cost and genotype (GT). Patient data and virological outcomes were documented.

Results: 50 patients were evaluated, 32 men, 18 women; men significantly younger than women; median age 51 [IQR 44-58], 59 [52-66]; p=0.05, respectively. GT distribution included 19 GT 1a, 13 GT 1b, 1 GT 2, 6 GT 3, 9 GT 4 and 2 GT 5a. 14% were HIV co-infected, 28% were treatment experienced. Baseline fibrosis scores were 24% F1; 22% F2; 20% F3 and 34% F4. Baseline median HCV viral load was log 6.1 [IQR 5.5-6.6]. Treatment regimens included Paritaprevir(PTV)/Ombitasvir(OMB)/Dasabuvir(DSV) n=15; PTV/OMB n=7; Sofosbuvir(SOF)/Ledipasvir(LDV) n=15; SOF/Daclatasvir(DCL) n=6; SOF/Ribavirin n=5; SOF/Simeprevir(SIM) n=2. Baseline, week 4 and end of treatment (EOT) median ALT was 103 [65-145]; 26 [19-31] and 2 2[17-30], respectively. HCV RNA was undetectable/LLOQ in 82% at week 4; in all at EOT. One patient died whilst on therapy. Of those with end of follow up results available to date (n=42), sustained virological response (SVR) rates for regimens include 100% for PTV/OMB/±DSV; 93% for SOF/LDV; 83% SOF/DCL; 60% SOF/RBV; 100% SOF/SIM

Interpretations: In our initial first year experience, DAA therapy was highly effective in our setting in achieving SVR in a diverse pangenotypic population with advanced fibrosis. Treatment availability should be expanded.

Comparison of Full-spectrum endoscopy, magnetic endoscopic imaging and standard forward viewing colonoscopy

Robert Nel*, SR Thomson

Introduction: Equipment may be a key variable influencing the efficacy of colonoscopy. We compared two devices, namely the Full-spectrum endoscopy (FUSE) and magnetic endoscopic imaging (MEI) to the standard forward-viewing endoscopy (FVE).

Methods: For the primary aim of caecal intubation time, a significant difference was considered to be 20% and the power calculation intimated a number of 96 per device. 292 patients between the ages of 18-70 years with no prior abdominal surgery were recruited from the colonoscopy lists at Groote Schuur Hospital (FUSE n=105, MEI n=83, FVE n=94). The FUSE cases were collected during an initial three week period when the device was available to our unit. Thereafter the recruited cases were randomized to either the MEI or FVE group. Two experienced (over 1000 prior colonoscopies) and three trainees (150-500 prior colonoscopies) endoscopists participated. Key performance indicators of caecal intubation rate, caecal intubation time, polyp detection rate and ileal intubation rate were calculated. Caecal intubation times longer than 30min and ileal intubation times longer than 5min were considered as failed.

Results: Median caecal intubation times were 9:58 min for the FUSE, 11:21 min for MEI and 12:33 min for FVE (p=0.07). The caecal intubation rates were 93.3% for FUSE, 87.2% for MEI and 95.2% for FVE (p = 0.13). The ileal intubation rates were as follows: 58.1% for FUSE, 68% for MEI and 50.6% for FVE (p = 0.06). Polyp detection rates were 21.9% for FUSE, 24.5% for MEI and 22.9% for FVE (p = 0.91).

Conclusion: Caecal intubation times for both the FUSE and MEI were shorter than with FVE, with a 20.6% improvement in the FUSE over FVE, which trended towards significance. No statistically significant benefit was demonstrated between the three modalities for CIR, ileal intubation and polyp detection.