Issue 12 - August 2019

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

SCIENCE FOCUS

Science Focus acknowledges NICD members of staff who have published in peer-reviewed journals. The Science Focus is a compilation of scientific publications included in the quarterly reports submitted to the National Department of Health. It includes only publications where an NICD staff member is either the first or last author.

Editor's Note

It is my pleasure to introduce the first editorial treatise of the Science Focus; by this, we seek to offer a summarised discussion of the various research topics that are covered in this publication.

In this issue, we report on the previous financial year's (2018/19) performance indicators concerning research. An increase in the number of peer-reviewed articles produced, totalling 196 compared to 184 of 2017/18 is noted. The indicators look at the quantity and quality of research within the institution.

This 12th issue of the Science Focus aims to profile research excellence within the NICD. In the first quarter of the Fiscal Year 2019/20, 55 peer-reviewed journal articles were produced; this issue features 27 of those articles for which the first and the last authors are from the NICD.

In an effort to continuously profile research output of the NICD, scientific articles are also featured on the homepage of the NICD website. We urge all members of staff to continue sending their contributions to the Communications Unit.

I salute you all for your incredible work and hope that you will enjoy the read.

On behalf of the team.

Sinenhlanhla Jimoh
Senior Communications Manager

EXCEPTIONAL RESEARCH OF THE NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

NUMBER OF PEER REVIEWED ARTICLES PRODUCED

184 2017/18

196 2018/19

TOP 5

MOST PUBLISHED AUTHORS

Data was sourced from **PubMed**, totalling the number of **articles an author published** during the financial year 2018/19, as of 13 August 2019.

PROF LYNN MORRIS

PROF CHERYL COHEN

PROF JANUSZ PAWESKA

PROF NAZIR ISMAIL

PROF ANNE VON GOTTBERG

Prof Lynn Morris was among the most **highly cited international researchers in 2018**, according to the Web of Science's Clarivate Analytics. She is the highly cited researcher in the field of microbiology.

TOP 5
MOST CITED ARTICLES

1. **Journal Name:** Archives of Virology
   Citation: 40
   Title: Taxonomy of order Mononegavirales: Update 2018
   NICD Author: Janusz Paweska

2. **Journal Name:** Archives of Virology
   Citation: 32
   Title: Taxonomy of the family Arenaviridae and the order Bunyavirales: Update 2018
   NICD Authors: Monica Birkhead, Petrus Jansen van Vuren, Alan Kemp, et al

3. **Journal Name:** The Lancet Respiratory Medicine
   Citation: 29
   Title: Effect of bedaquiline on mortality in South African patients with drug-resistant tuberculosis: A retrospective cohort study
   NICD Author: Nazir Ismail

4. **Journal Name:** The New England Journal of Medicine
   Citation: 27
   Title: Prediction of susceptibility to first-line tuberculosis drugs by DNA sequencing
   NICD Authors: Nazir Ismail and Shaheed Vally Omar

5. **Journal Name:** The Lancet Infectious Diseases
   Citation: 21
   Title: Genetic sequencing for surveillance of drug resistance in tuberculosis in highly endemic countries: A multi-country population-based surveillance study
   NICD Authors: Nazir Ismail and Shaheed Vally Omar

PUBLICATIONS WITH ≥10 CITATION

1. **Journal Name:** Archives of Virology
   Citation: 15
   Title: Taxonomy of the order Bunyavirales: Second update 2018
   NICD Author: Janusz Paweska

2. **Journal Name:** PLOS Pathogens
   Citation: 11
   Title: HIV-specific Fc effector function early in infection predicts the development of broadly neutralising antibodies
   NICD Authors: Simone Richardson, Penny Moore and Lynn Moris

3. **Journal Name:** The Lancet Infectious Diseases
   Citation: 10
   Title: Prevalence of drug-resistant tuberculosis and imputed burden in South Africa: A national and sub-national cross-sectional survey
   NICD Authors: Nazir Ismail, Anata Nanoo, Andries Dreyer, et al

4. **Journal Name:** The Lancet Global Health
   Citation: 10
   Title: Use of quantitative molecular diagnostic methods to investigate the effect of enteropathogen infections on linear growth in children in low-resource settings: Longitudinal analysis of results from the MAL-ED cohort study
   NICD Author: Nicola Page

HIGH

IMPACT FACTOR ARTICLES

Journal Name	Title	NICD Authors	Score
The New England Journal of Medicine	Prediction of susceptibility to first-line tuberculosis drugs by DNA sequencing	Nazir Ismail and Shaheed Vally Omar	79.260
The Lancet Infectious Diseases	Leave no one behind: Response to new evidence and guidelines for the management of cryptococcal meningitis in low-income and middle income countries	Nelesh Govender	25.148
The Lancet Infectious Diseases	Multidrug-resistant tuberculosis outbreak in South Africa	Nazir Ismail and Kerrigan McCarthy	25.148
The Lancet Infectious Diseases	Tenofovir 1% vaginal gel for prevention of HIV-1 infection: A phase 3, randomised, double-blind, placebo-controlled trial	Lynn Morris	25.148
The Lancet Infectious Diseases	Prevalence of drug-resistant tuberculosis in South Africa – Authors' reply	Nazir Ismail	25.148
The Lancet Infectious Diseases	Prevalence of drug-resistant tuberculosis and imputed burden in South Africa: A national and sub-national cross-sectional survey	Nazir Ismail	25.148
BMJ Global Health	Performance of verbal autopsy methods in estimating HIV-associated mortality among adults in South Africa	Kerrigan McCarthy	23.562
The Lancet Respiratory Medicine	Effect of bedaquiline on mortality in South African patients with drug-resistant tuberculosis: a retrospective cohort study	Nazir Ismail	21.466
The Lancet Global Health	Use of quantitative molecular diagnostic methods to investigate the effect of enteropathogen infections on linear growth in children in low-resource settings: Longitudinal analysis of results from the MAL-ED cohort study	Nicola Page	18.705
The Lancet Global Health	Effect of Xpert MTB/RIF on clinical outcomes in routine care settings: Individual patient data meta-analysis	Kerrigan McCarthy	18.705

NRF RATED RESEARCHERS

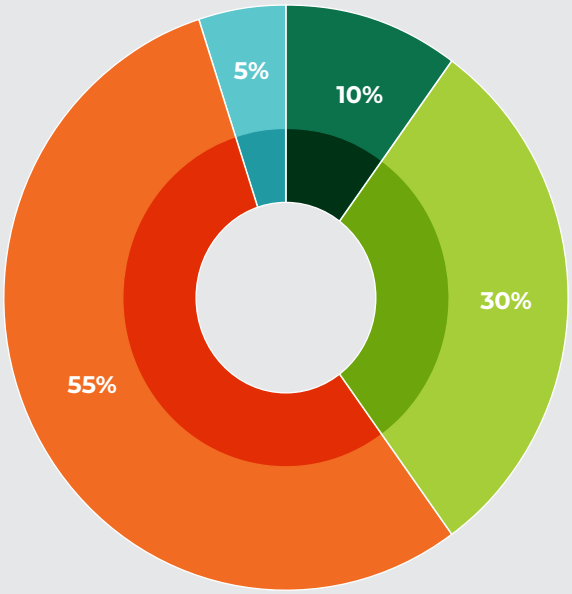
The National Research Foundation (NRF) rating system is a key driver in the NRF's aim to build a globally competitive science system in South Africa. It is a valuable tool for benchmarking the quality of our researchers against the best in the world. NRF ratings are allocated based on a researcher's recent research outputs and impact as perceived by international peer reviewers.

A – LEADING INTERNATIONAL RESEARCHERS

PROF MAUREEN COETZEE

PROF LYNN MORRIS

Name	Surname	Centre	Rating
Maureen	Coetzee	CEZP	A
Lynn	Morris	CHIVSTI/ Executive	A
Janusz	Paweska	CEZP	B
Basil	Brooke	CEZP	B
Anne	von Gottberg	CRDM	B
Cheryl	Cohen	CRDM	B
Penny	Moore	CHIVSTI	B
Caroline	Tiemessen	CHIVSTI	B
John	Frean	CEZP	C
Jackie	Weyer	CEZP	C
Petrus	Jansen van Vuren	CEZP	C
Givemore	Munhenga	CEZP	C
Nelesh	Govender	CHARM	C
Olga	Perovic	CHARM	C
Anthony	Smith	CED	C
Nicola	Page	CED	C
Mignon	du Plessis	CRDM	C
Nicole	Wolter	CRDM	C
Etienne	Muller	CHIVSTI	C
Nazir	Ismail	CTB	C
Ashika	Singh-Moodley	CHARM	Y



The rating process is coordinated by members of academia who are represented in the following committees:

- 27 Specialist Committees coordinated by a Convener
- The Executive Evaluation Committee
- The Appeals Committee

The ratings that are awarded fall within the following categories:

- A – Leading international researchers
- B – Internationally acclaimed researchers
- C – Established researchers
- P – Prestigious Awards
- Y – Promising young researchers

FEATURED RESEARCH ABSTRACTS FOR FIRST QUARTER 2019/20

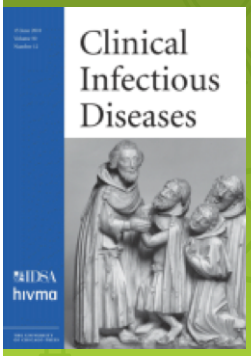
Dr Sabelle Jallow

Dr Melinda Suchard

Accelerated immunodeficiency-associated vaccine derived poliovirus serotype 3 (iVDPV3) sequence evolution rate in a 3-monthold boy with X-linked agammaglobulinemia and perinatal HIV

Jallow S, *Wilmshurst JM, Howard W, Copelyn J, Seakamela L, Chan KW, Sebunya R, Sibiya R, du Plessis H, Jacobs C, Berkowitz N, Blumberg L, McCarthy K, Maseti E, Kamupira M, Dlamini N, Gumede N, Diop OM, Lau YL, Moonsamy S, Eley B,* ***Suchard MS.***

Clinical Infectious Diseases
Impact Factor: 9.055



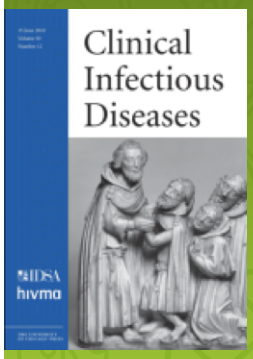
Primary B-cell immunodeficiencies are risk factors for the generation of vaccine-derived polioviruses. We report immunodeficiency-associated vaccine-derived poliovirus serotype 3 in an 11-week old boy with X-linked agammaglobulinemia. Unique characteristics of this case include early age of presentation, high viral evolutionary rate and that the child was perinatally exposed to HIV.

Dr Sabelle Jallow

Impaired transplacental transfer of respiratory syncytial virus-neutralising antibodies in human immunodeficiency virus-infected versus -uninfected pregnant women

Jallow S, *Agosti Y, Kgagudi P, Vandecar M, Cutland CL, Simões EAF, Nunes MC, Suchard MS, Madhi SA.*

Clinical Infectious Diseases
Impact Factor: 9.055



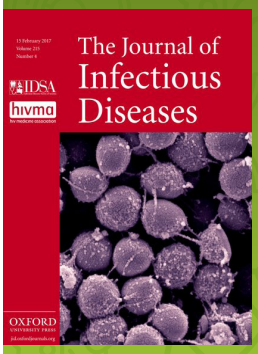
Respiratory syncytial virus is one of the major causes of respiratory tract infections during infancy with high rates of hospitalisation and mortality during the first years of life. It is the most common cause of acute bronchiolitis and viral pneumonia in children below two years of age and second most common cause of postneonatal infant mortality all around the world following malaria. In addition, the virus has been causally linked to recurrent wheezing and associated with pediatric asthma. The respiratory syncytial virus infections tend to be severe in high risk patients such as patients below six months of age, with prematurity, congenital heart diseases, neuromuscular diseases and immune deficiencies. No specific treatment is available for respiratory syncytial virus infections to date. Severe cases require supportive therapy, mainly oxygen supplementation and hydration, and less frequently, ventilatory support. Because there is no vaccine to prevent respiratory syncytial virus infections or clinically effective treatment to administer to children with respiratory syncytial virus infection, immunoprophylaxis with palivizumab is currently the only method for reducing morbidity associated with severe respiratory syncytial virus in high-risk infants.

Prof Cheryl Cohen

Household transmission of seasonal influenza from HIV-infected and HIV-uninfected individuals in South Africa, 2013-2014

Cohen C, *Tshangela A, Valley-Omar Z, Iyengar P, von Mollendorf C, Walaza S, Hellferscee O, Venter M, Martinson N, Mahlase G, McMorrow M, Cowling BJ, Treurnicht FK, Cohen AL, Tempia S.*

The Journal of Infectious Diseases
Impact Factor: 5.045



Background: We estimated the household secondary infection risk (SIR) and serial interval (SI) for influenza transmission from HIV-infected and HIV-uninfected index cases.

Methods: Index cases were the first symptomatic person in a household with influenza-like illness, testing influenza positive on real-time reverse transcription polymerase chain reaction (rRT-PCR). Nasopharyngeal swabs collected from household contacts every 4 days were tested by rRT-PCR. Factors associated with SIR were evaluated using logistic regression.

Results: We enrolled 28 HIV-infected and 57 HIV-uninfected index cases. On multivariable analysis, HIV-infected index cases were less likely to transmit influenza to household contacts (odds ratio [OR] 0.2; 95% confidence interval [CI], 0.1-0.6; SIR 16%, 18/113 vs 27%, 59/220). Factors associated with increased SIR included index age group 1-4 years (OR 3.6; 95% CI, 1.2-11.3) and 25-44 years (OR 8.0; 95% CI, 1.8-36.7), and contact age group 1-4 years (OR 3.5; 95% CI, 1.2-10.3) compared to 5-14 years, and sleeping with index case (OR 2.7; 95% CI, 1.3-5.5). HIV infection of index case was not associated with SI.

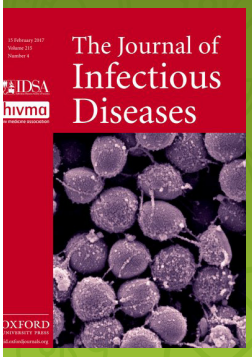
Conclusions: HIV-infection was not associated with SI. Increased infectiousness of HIV-infected individuals is likely not an important driver of community influenza transmission.

Ms Orienka Hellferscee

The fraction of rhinovirus detections attributable to mild and severe respiratory illness in a setting of high human immunodeficiency virus prevalence, South Africa, 2013-2015

Hellferscee O, *Treurnicht FK, Walaza S, du Plessis M, von Gottberg A, Wolter N, Moyes J, Dawood H, Variava E, Pretorius M, Venter M, Cohen C, Tempia S.*

The Journal of Infectious Diseases
Impact Factor: 5.045



Background: The association of rhinovirus (RV) detection to illness is poorly understood.

Methods: We enrolled case patients hospitalised with severe respiratory illness (SRI) at 2 hospitals and outpatients with influenza-like illness (ILI) and asymptomatic individuals (controls) from 2 affiliated clinics during 2013–2015. We compared the RV prevalence among ILI and SRI cases to those of controls stratified by human immunodeficiency virus (HIV) serostatus using penalised logistic regression. The attributable fraction (AF) was calculated.

Results: During 2013–2015, RV was detected in 17.4% (368/2120), 26.8% (979/3654), and 23.0% (1003/4360) of controls, ILI cases, and SRI cases, respectively. The RV AF (95% confidence interval) was statistically significant among children aged <5 years (ILI: 44.6% [30.7%–55.7%] and SRI: 50.3% [38.6%–59.9%]; P <.001), individuals aged ≥5 years (ILI: 62.9% [54.4%–69.8%] and SRI: 51.3% [38.7%–61.3%]; P <.001) as well as among HIV-infected (ILI: 59.9% [45.8%–70.3%], SRI: 39.8% [22.3%–53.3%]; P <.001), HIV-uninfected (ILI: 53.6% [44.7%–61.1%] and SRI: 55.3% [45.6%–63.2%]; P <.001) individuals.

Conclusions: Although RV detection was common among controls, it was also associated with a substantial proportion of clinical illness across age groups, irrespective of HIV status.

Ms Ntando Phaahla

Prof Caroline Tiemessen

Chronic HIV-1 infection alters the cellullar distribution of FCyIIIa and the functional consequence of the FCyIIIa-F158V variant

Phaahla GN, *Lassauniere R, Da Costa Dias B, Waja Z, Martinson NA,* ***Tiemessen CT.***

Frontiers in Immunology
Impact Factor: 4.716

Chronic HIV-infection modulates the expression of Fc gamma receptors (FcγRs) on immune cells and their antibody-dependent effector function capability. Given the increasingly recognised importance of antibody-dependent cellular cytotoxicity (ADCC) in HIV-specific immunity, we investigated the cellular distribution of FcγRIIIa on cytotoxic lymphocytes—natural killer cells and CD8+ T cells—and the effect of the FcγRIIIa-F158V variant on ADCC capacity in HIV-infected individuals (n = 23) and healthy controls (n = 23). Study participants were matched for F158V genotypes, carried two copies of the FCGR3A gene and were negative for FcγRIIb expression on NK cells. The distribution of CD56dimFcγRIIIabright and CD56negFcγRIIIabright NK cell subsets, but not FcγRIIIa surface expression, differed significantly between HIV-1 negative and HIV-1 positive donors. NK cell-mediated ADCC responses negatively correlated with the proportion of the immunoregulatory CD56brightFcγRIIIadim/neg cells and were lower in the HIV-1 positive group. Intriguingly, the FcγRIIIa-F158V variant differentially affected the NK-mediated ADCC responses for HIV-1 negative and HIV-1 positive donors. Healthy donors bearing at least one 158V allele had higher ADCC responses compared to those homozygous for the 158F allele (48.1 vs. 34.1%), whereas the opposite was observed for the HIV-infected group (26.4 vs. 34.6%), although not statistically significantly different. Furthermore, FcγRIIIa+CD8bright and FcγRIIIa+CD8dim T cell subsets were observed in both HIV-1 negative and HIV-1 positive donors, with median proportions that were significantly higher in HIV-1 positive donors compared to healthy controls (15.7 vs. 8.3%; P = 0.016 and 18.2 vs. 14.1%; P = 0.038, respectively). Using an HIV-1-specific GranToxiLux assay, we demonstrate that CD8+ T cells mediate ADCC through the delivery of granzyme B, which was overall lower compared to that of autologous NK cells. In conclusion, our findings demonstrate that in the presence of an HIV-1 infection, the cellular distribution of FcγRIIIa is altered and that the functional consequence of FcγRIIIa variant is affected. Importantly, it underscores the need to characterise FcγR expression, cellular distribution and functional consequences of FcγR genetic variants within a specific environment or disease state.

Mrs Shelina Moonsamy

Immunogenicity of a combined schedule of trivalent oral and inactivated polio vaccines in South African infants

Moonsamy S, *Suchard MS, Madhi SA*

Expert Review of Vaccines
Impact Factor: 4.531

Background: South Africa transitioned from using live-attenuated trivalent oral polio vaccine (tOPV), to a combination of tOPV and inactivated polio vaccine (IPV) in April 2009. We evaluated the immunogenicity of the South African combined tOPV-IPV schedule versus the tOPV-only schedule in South African infants.

Methods: Serum samples of HIV-unexposed infants were analysed retrospectively from two cohorts; infants enrolled from April 2005 through June 2006 and infants enrolled from December 2009 to April 2010. The primary vaccination series of the tOPV-only schedule included doses at birth, 6, 10 and 14 weeks, and the tOPV-IPV schedule included tOPV at birth and 6 weeks and IPV at 6, 10 and 14 weeks. Serum polio neutralising antibody titres to serotype-1, serotype-2 and serotype-3 were evaluated in infants at 18 weeks of age.

Results: Infants who received the tOPV-IPV schedule had higher GMTs than infants who received tOPV-only for serotype-2 (9.63 vs. 8.80, P <0.001) and serotype-3 (10.01 vs. 8.53, P <0.001), as well as higher sero-protective titres for serotype-1 (100% vs. 96%, P = 0.014).

Conclusion: Our data support the option of the South African combined polio vaccination schedule as an immunogenic option for a combined schedule.

Dr Batsirai Mabvakure

Prof Lynn Morris

Evidence for both intermittent and persistent compartmentalisation of HIV-1 in the female genital tract

Mabvakure BM, *Lambson BE, Ramdayal K, Masson L, Kitchin D, Allam M, Karim SA, Williamson C, Passmore JA, Martin DP, Scheepers C, Moore PL, Harkins GW,* ***Morris L.***

Journal of Virology
Impact Factor: 4.324

HIV-1 has been shown to evolve independently in different anatomical compartments, but studies in the female genital tract have been inconclusive. Here, we examined evidence of compartmentalisation using HIV-1 subtype C envelope (Env) glycoprotein genes (gp160) obtained from matched cervicovaginal lavage (CVL) and plasma samples over 2 to 3 years of infection. HIV-1 gp160 amplification from CVL was achieved for only 4 of 18 acutely infected women, and this was associated with the presence of proinflammatory cytokines and/or measurable viremia in the CVL. Maximum likelihood trees and divergence analyses showed that all four individuals had monophyletic compartment-specific clusters of CVL- and/or plasma-derived gp160 sequences at all or some time points. However, two participants (CAP177 and CAP217) had CVL gp160 diversity patterns that differed from those in plasma and showed restricted viral flow from the CVL. Statistical tests of compartmentalisation revealed evidence of persistent compartment-specific gp160 evolution in CAP177, while in CAP217 this was intermittent. Lastly, we identified several Env sites that distinguished viruses in these two compartments; for CAP177, amino acid differences arose largely through positive selection, while insertions/deletions were more common in CAP217. In both cases these differences contributed to substantial charge changes spread across the Env. Our data indicate that, in some women, HIV-1 populations within the genital tract can have Env genetic features that differ from those of viruses in plasma, which could impact the sensitivity of viruses in the genital tract to vaccine-elicited antibodies.

Importance: Most HIV-1 infections in sub-Saharan Africa are acquired heterosexually through the genital mucosa. Understanding the properties of viruses replicating in the female genital tract, and whether these properties differ from those of more commonly studied viruses replicating in the blood, is therefore important. Using longitudinal CVL and plasma-derived sequences from four HIV-1 subtype C-infected women, we found fewer viral migrations from the genital tract to plasma than in the opposite direction, suggesting a mucosal sieve effect from the genital tract to the blood compartment. Evidence for both persistent and intermittent compartmentalisation between the genital tract and plasma viruses during chronic infection was detected in two of four individuals, perhaps explaining previously conflicting findings. In cases where compartmentalisation occurred, comparison of CVL- and plasma-derived HIV sequences indicated that distinct features of viral populations in the CVL may affect the efficacy of microbicides and vaccines designed to provide mucosal immunity.

Dr Shune Oliver

The contribution of gut bacteria to insecticide resistance and the life histories of the major malaria vector *Anopheles arabiensis* (Diptera: Culicidae)

Barnard K, Jeanrenaud ACSN, Brooke BD, ***Oliver SV.***

Scientific Reports
Impact Factor: 4.011

The gut microbiota of mosquitoes is a crucial determinant of their fitness. As such, the biology of the gut microbiota of *Anopheles arabiensis*, a major malaria vector of Southern Africa, was investigated. Two laboratory strains of *An. arabiensis* were used; SENN, an insecticide susceptible strain, and SENN-DDT, a resistant strain. The strains were supplemented with either non-commensal bacteria or antibiotics via a sucrose source to sterilise the gut. The strains were fed the broad-spectrum bactericidal antibiotic gentamicin, or a preferentially Gram-positive bactericidal (vancomycin), Gram-negative bactericidal (streptomycin) or broad-spectrum bacteriostatic (erythromycin), either by sugar supplementation or by artificially-spiked blood-meal. The effects on adult mosquito longevity and insecticide resistance phenotype were assessed. Bacteria from the midgut of both strains were characterised by MALDI-TOF mass spectroscopy. Bactericidal antibiotics increased longevity in SENN-DDT. Bacterial supplementation increased insecticide tolerance. Antibiotic supplementation via sugar decreased tolerance to the insecticides deltamethrin and malathion. Blood-supplemented vancomycin decreased insecticide resistance, while gentamicin and streptomycin increased resistance. SENN showed a greater gut bacterial diversity than SENN-DDT, with both strains dominated by Gram-negative bacteria. This study suggests a crucial role for bacteria in *An. arabiensis* life history, and that gut microflora play variable roles in insecticide resistant and susceptible mosquitoes.'

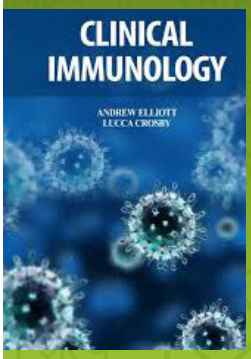
Ms Gemma Koor

Prof Caroline Tiemessen

Cis-regulatory genetic variants in the CCR5 gene and natural HIV – 1 control in black South Africans

Koor GW, *Paximadis M, Picton ACP, Karatas F, Lousber SA, He W, Ahuja SK, Chaisson RE, Martinson N, Ebrahim O,* ***Tiemessen CT.***

Clinical Immunology
Impact Factor: 3.548



Studies have investigated CCR5 haplotypes (HHA, HHB, HHC, HHD, HHE, HHF*1, HHF*2, HHG*1, HHG*2), defined by seven 5'UTR single nucleotide polymorphisms (SNPs), CCR2-V64I and CCR5Δ32, in HIV-1 disease. CCR5 cis-regulatory regions were sequenced, CCR2-V64I and CCR5Δ32 genotyped, and compared in HIV-1-infected black South Africans: 71 HIV-1 controllers (23 elite controllers, 37 viraemic controllers (VCs), 11 high viral load long-term non-progressors) and 74 progressors. The HHE haplotype and 3'UTR +2919 T > G SNP heterozygosity were underrepresented in total controllers and VCs vs. progressors ($p = .004$; $p = .007$ and $p = .002$, pbonferroni = 0.032; $p = .004$, respectively). Possession of the +2919 T > G SNP (dominant mode) was associated with HIV-1 progression (controllers vs. progressors: $p = .001$, pbonferroni = 0.016). The +2919 T > G SNP is in linkage disequilibrium (LD; $r2 = 0.73$) with two 5'UTR SNPs (-2459G > A and -2135 T > C; $r2 = 1$: 5'UTR-2SNP-hap). The 5'UTR-2SNP-hap was lower in total controllers and VCs vs. progressors ($p = .003$, pbonferroni = 0.048; $p = .01$, respectively). Results suggest -2459G > A, -2135 T > C, and + 2919 T > G as key CCR5 variants in HIV-1 control.

Prof Lucille Blumberg

Is the global measles resurgence a "public health emergency international concern?"

Durrheim DN, Crowcroft NS, ***Blumberg LH.***

International Journal of Infectious Diseases
Impact Factor: 3.538

The 2005 revision of the International Health Regulations (IHR) came into force on 15 June 2007 and is legally binding on 196 countries, including all the Member States of World Health Organization (WHO). In the IHR, a public health emergency of international concern (PHEIC) is defined as: "an extraordinary event that may constitute a public health risk to other countries through international spread of disease and may require an international coordinated response." (World Health Organization, 2005). The IHR requires that countries notify the WHO of any public health event that meets any two of the following four criteria: Is the public health impact of this event potentially serious?; Is this event unusual or unexpected?; Is there the potential for international spread?; or Is there the potential for travel and trade restrictions? The purpose of declaring a PHEIC is to focus attention on those acute public health risks that have the potential to cross borders and threaten people worldwide, and "require coordinated mobilisation of extraordinary resources by the international community" for prevention and response. The decision to declare a PHEIC rests with the WHO Director-General. To date four PHEICs have been declared.

Ms Jacoba Kleynhans

Prof Anne von Gottberg

Can pneumococcal meningitis surveillance be used to assess the impact of pneumococcal conjugate vaccine on total invasive pneumococcal disease? A case- study from South Africa, 2005-2016

Kleynhans J, *Cohen C, McMorrow M,Tempia S, Crowther-Gibson P, Quan V, de Gouveia L,* ***von Gottberg A.***

Vaccine
Impact Factor: 3.269

Introduction: South Africa introduced seven-valent pneumococcal conjugate vaccine (PCV7) in 2009 and PCV13 in 2011. We aimed to compare the estimated impact of PCV on pneumococcal meningitis (PM) to impact of PCV on total invasive pneumococcal disease (tIPD) based on risk reduction after PCV introduction.

Methods: We conducted national, laboratory-based surveillance for tIPD during 2005-2016. We estimated and compared rates of PCV13 and non-PCV13 serotype disease among tIPD and PM in individuals aged <5 years and ≥5 years, and compared these rates between the 2005-2008 pre-PCV introduction period and two time points after PCV introduction, 2012 and 2016.

Results: We enrolled 45 853 tIPD cases; 17 251 (38%) were PM. By 2016, IPD caused by all serotypes decreased 55% (95%CI -57% to -53%) for tIPD, and 54% for PM (95%CI -58% to -51%), 0.7% difference between estimates ($p = 0.7$). No significant differences were observed between PCV7-serotype disease reduction in tIPD and PM in both age groups or the additional 6 serotypes included in PCV13 in <5 year olds in 2012 and 2016. In 2012 there was a significant difference between increases in non-PCV13 serotype disease in those ≥5 years for tIPD and PM (32% greater increase in PM, $p < 0.001$), but this difference was absent by 2016. There was a significant difference between the estimated decrease in additional PCV13 type disease in 2016 between tIPD and PM for those aged ≥5 years (28% greater reduction in PM, $p = 0.008$).

Conclusion: PM showed similar reductions to tIPD seven years after PCV introduction in vaccine serotype disease in those <5 years, and increases in non-vaccine serotype disease in all ages.

Prof Cheryl Cohen

Health and economic burden of influenza-associated illness in South Africa, 2013-2015

Tempia S, Moyes J, Cohen A L, Walaza S, Edoka I, McMorrow ML, Treurnicht FK, Hellferscee O, Wolter N, von Gottberg A, Nguweneza A, McAnerney J, Dawood MH, Variava E, ***Cohen C.***

Influenza and Other Respiratory Viruses
Impact Factor: 3.094

Background: Economic burden estimates are essential to guide policy-making for influenza vaccination, especially in resource-limited settings.

Methods: We estimated the cost, absenteeism, and years of life lost (YLL) of medically and non-medically attended influenza-associated mild and severe respiratory, circulatory and non-respiratory/non-circulatory illness in South Africa during 2013-2015 using a modified version of the World Health Organization (WHO) worksheet based tool for estimating the economic burden of seasonal influenza. Additionally, we restricted the analysis to influenza-associated severe acute respiratory illness (SARI) and influenza-like illness (ILI; subsets of all-respiratory illnesses) as suggested in the WHO manual.

Results: The estimated mean annual cost of influenza-associated illness was $270.5 million, of which $111.3 million (41%) were government-incurred costs, 40.7 million (15%) were out-of-pocket expenses, and $118.4 million (44%) were indirect costs. The cost of influenza-associated medically attended mild illness ($107.9 million) was 2.3 times higher than that of severe illness ($47.1 million). Influenza-associated respiratory illness costs ($251.4 million) accounted for 93% of the total cost. Estimated absenteeism and YLL were 13.2 million days and 304 867 years, respectively. Among patients with influenza-associated WHO-defined ILI or SARI, the costs ($95.3 million), absenteeism (4.5 million days), and YLL (65 697) were 35%, 34%, and 21% of the total economic and health burden of influenza.

Conclusion: The economic burden of influenza-associated illness was substantial from both a government and a societal perspective. Models that limit estimates to those obtained from patients with WHO-defined ILI or SARI substantially underestimated the total economic and health burden of influenza-associated illness.

Dr Jaishree Raman

Safety and tolerability of single low-dose primaquine in a low-intensity transmission area in South Africa: An open-label, randomised controlled trial

Raman J, *Allen E, Workman L, Mabuza A, Swanepoel H, Malatje G, Frean J, Wiesner L, Barnes KI.*

Malaria Journal
Impact Factor: 2.798

Background: To reduce onward falciparum malaria transmission, the World Health Organization recommends adding single low-dose (SLD) primaquine to artemisinin-based combination treatment in low transmission areas. However, uptake of this recommendation has been relatively slow given concerns about whether individual risks justify potential community benefit. This study was undertaken to generate comprehensive local data on the risk–benefit profile of SLD primaquine deployment in a pre-elimination area in South Africa.

Methods: This randomised, controlled open-label trial investigated adding a single low primaquine dose on day 3 to standard artemether–lumefantrine treatment for uncomplicated falciparum malaria. Efficacy, safety and tolerability of artemether–lumefantrine and primaquine treatment were assessed on days 3, 7, 14, 28 and 42. Lumefantrine concentrations were assayed from dried blood spot samples collected on day 7.

Results: Of the 217 patients screened, 166 were enrolled with 140 randomized on day 3, 70 to each study arm (primaquine and no primaquine). No gametocytes were detected by either microscopy or PCR in any of the follow-up samples collected after randomization on day 3, precluding assessment of primaquine efficacy. Prevalence of the CYP2D6*4, CYP2D6*10 and CYP2D6*17 mutant alleles was low with allelic frequencies of 0.02, 0.11 and 0.16, respectively; none had the CYP2D6*4/*4 variant associated with null activity. Among 172 RDT-positive patients G6PD-genotyped, 24 (14%) carried the G6PD deficient (A–) variant. Median haemoglobin concentrations were similar between treatment arms throughout follow-up. A third of participants had a haemoglobin drop >2 g/dL; this was not associated with primaquine treatment but may be associated with G6PD genotype [52.9% (9/17) with A– genotype vs. 31% (36/116) with other genotypes (p = 0.075)]. Day 7 lumefantrine concentrations and the number and nature of adverse events were similar between study arms; only one serious adverse event occurred (renal impairment in the no primaquine arm). The artemether–lumefantrine PCR-corrected adequate clinical and parasitological response rate was 100%, with only one re-infection found among the 128 patients who completed 42-day follow-up.

Conclusions: Safety, tolerability, CYP2D6 and G6PD variant data from this study support the deployment of the WHO-recommended SLD primaquine without G6PD testing to advance malaria elimination in South African districts with low-intensity residual transmission.

Dr Shune Oliver

The effects of larval organic fertiliser exposure on the larval development, adult longevity and insecticide tolerance of zoophilic members of the *Anopheles gambiae* complex (Diptera: Culicidae)

Jeanrenaud ACSN, Brooke BD, ***Oliver SV.***

PLOS ONE
Impact Factor: 2.776

Zoophilic members of the *Anopheles gambiae* complex are often associated with cattle. As such, it is likely that the immature aquatic stages will be exposed to cattle faeces as a pollutant. This study aimed to examine the effect of cattle manure on members of the *An. gambiae* complex found in South Africa. In this study, a commercial organic fertiliser originating from cattle manure was used as a proxy for cattle faeces. Laboratory strains of *An. merus*, *An. quadriannulatus* as well as four *An. arabiensis* strains (SENN and MBN: insecticide susceptible, MBN-DDT: insecticide resistant, unselected, SENN-DDT: insecticide resistant: selected for resistance) were used in this study. The effect of larval fertiliser exposure on larval development rate and adult longevity was assessed in all three species. The effect of larval fertiliser exposure on subsequent adult size, insecticide tolerance and detoxification enzyme activity of the four strains of the malaria vector *An. arabiensis* was also assessed. Following fertiliser treatment, all strains and species showed a significantly increased rate of larval development, with insecticide susceptible strains gaining the greatest advantage. The adult longevities of *An. merus*, *An. quadriannulatus*, insecticide susceptible and resistant *An. arabiensis* were significantly increased following fertiliser treatment. Insecticide susceptible and resistant *An. arabiensis* adults were significantly larger after larval organic fertiliser exposure. Larval fertiliser exposure also increased insecticide tolerance in adult *An. arabiensis*, particularly in the insecticide resistant, selected strain. This 4.7 fold increase in deltamethrin tolerance translated to an increase in pyrethroid resistance intensity, which could exert operational effects. In general, larval exposure to cattle faeces significantly affects the life histories of members of the *An. gambiae* complex.

Mrs Shelina Moonsamy

Effect of HIV-exposure and timing of anti-retroviral treatment on immunogenicity of trivalent live-attenuated polio vaccine in infants

Moonsamy S, *Suchard MS, Madhi SA.*

PLOS ONE
Impact Factor: 2.776

Introduction: The prevalence of HIV infection in South African pregnant women has been approximately 30% over the past decade; however, there has been a steady decline in mother-to-child transmission of HIV from 8% in 2008 to <2% in 2015. We evaluated the immunogenicity of live-attenuated trivalent oral polio vaccine (OPV) following the primary vaccination series (doses at birth, 6, 10 and 14 weeks of age) in HIV-exposed uninfected (HEU), HIV-infected infants initiated on early anti-retroviral treatment (HIV+/ART+), HIV-infected infants on deferred ART (HIV+/ART-) and HIV-unexposed infants (HU) as the referent group.

Methods: Serum polio neutralisation antibody titres were evaluated to serotype-1, serotype-2 and serotype-3 at 6, 10 and 18 weeks of age. Antibody titres ≥8 were considered seropositive and sero-protective.

Results: At 18 weeks of age, following the complete primary series of four OPV doses, no differences in GMTs, percentage of infants with sero-protective titres and median fold change in antibody titre (18 weeks vs 6 weeks) were observed in HEU infants (n = 114) and HIV+/ART+ infants (n = 162) compared to HU infants (n = 104) for the three polio serotypes. However, comparing HIV+/ART- infants (n = 70) to HU infants at 18 weeks of age, we observed significantly lower GMTs for serotype-1 ($p = 0.022$), serotype-2 ($p<0.001$) and serotype-3 ($p<0.001$), significantly lower percentages of infants with sero-protective titres for the three serotypes ($p<0.001$), and significantly lower median fold change in antibody titre for serotype-1 ($p = 0.048$), serotype-2 ($p = 0.003$) and serotype-3 ($p = 0.008$).

Conclusion: Delaying initiation of ART in HIV-infected infants was associated with an attenuated immune response to OPV following a four-dose primary series of vaccines, whereas immune responses to OPV in HIV-infected children initiated on ART early in infancy and HEU children were similar to HU infants.

Dr Ahmad Mazanderani

Hepatisis A virus seroprevalence in South Africa – estimated using routine laboratory data, 2005-2015

Mazanderani AH, *Motaze NV, McCarthy K, Suchard MS, du Plessis NM.*

PLOS ONE
Impact Factor: 2.776

Introduction: South Africa is considered highly endemic for hepatitis A virus (HAV) although few seroprevalence studies have been conducted over the past two decades. The World Health Organization recommends integrating HAV vaccination into national childhood immunisation schedules where there is transition from high to intermediate endemicity. As a means of gauging age-specific rates of infection, we report HAV seroprevalence rates among specimens tested for HAV serology within South Africa's public health sector from 2005–2015.

Materials and methods: Hepatitis A serology results (anti-HAV IgM, IgG and total antibody) from 2005–2015 were extracted from South Africa's National Health Laboratory Service's Corporate Data Warehouse, the central data repository of all laboratory test-sets within the public health sector. Results were extracted according to test-set, result, date of testing, health facility, name, surname, age, and sex. Anti-HAV IgG results were merged with total antibody results to reflect anti-HAV seroprevalence. Testing volume, positivity rates and age-specific anti-HAV seroprevalence rates by year and geographic distribution are described.

Results and discussion: A total of 501 083 HAV IgM results were retrieved, of which 16 423 (3.3%) were positive, 484 259 (96.6%) negative and 401 (0.1%) equivocal; and 34 710 HAV total antibody/IgG tests of which 30 675 (88.4%) were positive, 4 020 (11.6%) negative and 15 equivocal. Whereas IgM positivity was highest among the 1–4 year age group (33.5%) and lowest among patients >45 years (<0.5%), total antibody positivity ranged from its lowest level of 52.7% in the 1–4 year age group increasing to levels of >90% only after 25 years of age.

Conclusion: Anti-HAV total antibody testing within the South African public health sector demonstrates seroprevalence rates reach levels >90% only in adulthood, suggesting South Africa could be in transition from high to intermediate endemicity. Prospective studies with geographically representative sampling are required to confirm these findings and evaluate provincial and urban/rural heterogeneity.

Dr Nishi Prabdial-Sing

Dr Melinda Suchard

Hepatitis B sero-prevalence in children under 15 years of age in South Africa using residual samples from community-based febrile rash surveillance

Prabdial-Sing N, *Makhathini L, Smit SB, Manamela MJ, Motaze NV, Cohen C,* ***Suchard MS.***

PLOS ONE
Impact Factor: 2.776

Introduction and methods: Hepatitis B is a vaccine preventable disease and is notifiable in South Africa. Hepatitis B vaccination was incorporated into the Expanded Programme on Immunisation in South Africa in 1995. We used a convenience sample from community-based febrile rash surveillance in 2013 to estimate hepatitis B sero-prevalence. Of samples serologically negative for acute measles infection, 450 samples spanning nine provinces of South Africa were tested for hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs) and hepatitis B core antibody (anti-HBc).

Results: Two children (2/450; 0.4%) tested positive for HBsAg. Three hundred and three children (67.3%) had evidence of vaccine induced immunity. Vaccine induced immunity was present in 80.2% of 1-5 year olds, but only 60.3% of 10-14 year olds. Natural immunity, indicating exposure to circulating hepatitis B, was present in 13/450 (2.9%) children.

Conclusion: Chronic hepatitis B in South African has decreased in prevalence from highly endemic levels prior to vaccine introduction to approximately 0.4% in this sample, demonstrating impact of a successful vaccination programme 18 years after introduction. Decreased vaccine-induced immunity with increasing age may reflect waning antibody titres over time.

Dr Tendesayi Kufa

CD4 count recovery and associated factors among individuals enrolled in the South African antiretroviral therapy programme: an analysis of national laboratory based data

Kufa T, *Shubber Z, MacLeod W, Takuva S, Carmona S, Bor J, Gorgens M, Pillay Y, Puren A, Eaton JW, Fraser-Hurt N.*

PLOS ONE
Impact Factor: 2.776

Background: We describe CD4 count recovery among HIV positive individuals who initiated antiretroviral therapy (ART) with and without severe immune suppression using complete laboratory data from South Africa's national HIV treatment programme between 2010 and 2014 and discuss implications for CD4 count monitoring.

Methods: Retrospective analysis of routinely collected laboratory data from South Africa's National Health Laboratory Service. A probabilistic record linkage algorithm was used to create a cohort of HIV positive individuals who initiated ART between 2010 and 2014 based on timing of CD4 count and viral load measurements. A CD4 count <50 copies/µl at ART initiation was considered severe immunosuppression. A multivariable piecewise mixed-effects linear regression model adjusting for age, gender, year of starting ART, viral suppression in follow up and province was used to predict CD4 counts during follow up.

Results: 1 070 900 individuals had evidence of starting ART during 2010-2014 and met the criteria for inclusion in the cohort -46.6% starting ART with CD4 <200 cells/µl and 10.1% with CD4 <50 cells/ µl. For individuals with CD4 counts <200 cells/µl, predicted CD4 counts >200 cells/µl, >350 cells/µl and >500 cells/µl corresponded with mean follow up durations of 1.5 years (standard deviation [s.d] 1.1), 1.9 years (s.d 1.2) and 2.1 years (s.d 1.3 years). For those with CD4 counts <50 cells/ µl, predicted CD4 count above these threshold corresponded with mean follow up durations of 2.5 years (s.d 0.9 years), 4.4 years (s.d 0.4 years) and 5.0 years (s.d 0.1years) for recovery to the same thresholds. CD4 count recovery varied mostly with duration on ART, CD4 count at the start of ART and gender.

Conclusion: For individuals starting with ART with severe immunosuppression, CD4 recovery to 200 cells/µl did not occur or took longer than 12 month for significant proportions. CD4 monitoring and interventions recommended for advanced HIV disease should continue until full recovery.

Prof Anne von Gottberg

Invasive pneumococcal disease in neonates prior to pneumococcal conjugate vaccine use in South Africa: 2003-2008

Moodley K, Coovadia YM, Cohen C, Meiring S, Lengana S, De Gouveia L, von Mollendorf C, Crowther-Gibson P, Quan V, Eley B, Reubenson G, Nana T, ***von Gottberg A.***

The Pediatric Infectious Disease Journal
Impact Factor: 2.317

Background: Neonatal invasive pneumococcal disease (IPD) in developing countries is poorly described. We provide a baseline description of neonatal IPD in South Africa, before implementation of the 7-valent pneumococcal conjugate vaccine (PCV7) in 2009.

Methods: Data from children (age ≤2 years) with IPD (pneumococcus identified from a normally sterile specimen) from January 2003 to December 2008 were extracted from a national laboratory-based surveillance database. Clinical and laboratory characteristics of IPD among neonates (0-27 days old) was compared with IPD among young children (≥28 days ≤2 years). Early-onset IPD (0-6 days old) was compared with late-onset IPD (≥7-27 days old). Isolates were serotyped using the Quellung reaction.

Results: Overall 27 630 IPD cases were reported. Of the 26 277 (95%) with known ages, 6583 (25%) were ≤2 years of age, of which 4.5% (294/6583) were neonates. The estimated annual incidence of neonatal IPD in 2008 was 5 per 100 000 live births. Fifty-one percent of neonates with IPD presented with early-onset IPD. Case fatality ratios (CFRs) were high in both groups, 31% (28/89) in neonatal IPD versus 26% (614/2383) in non-neonatal IPD (P = 0.18). Among neonates, the meningitis cases (15/37, 41%) were associated with the highest CFR. The 13-valent pneumococcal conjugate vaccine (PCV13) serotypes accounted for 69% (134/194) of neonatal IPD isolates.

Conclusions: Pneumococcal neonatal disease in South Africa was not uncommon before PCV introduction and is associated with a high CFR. The indirect effect on neonatal IPD of PCV rollout requires further evaluation.

Prof Nazir Ismail

Multicentre study to establish interpretive criteria for clofazimine drug susceptibility testing

Ismail NA, *Said HM, Rodrigues C, Omar SV, Ajbani K, Sukhadiad N, Kohl TA, Niemann S, Kranzer K, Diels M, Rigouts I, Rüsch-Gerdes S, Siddiqi S.*

The International Journal of Tuberculosis and Lung Disease
Impact Factor: 2.024

Objective: To conduct a multicentre study to establish the critical concentration (CC) for clofazimine (CFZ) for drug susceptibility testing (DST) of *Mycobacterium tuberculosis* on the MGIT™960™ system using the distribution of minimum inhibitory concentrations (MIC) and genotypic analyses of Rv0678 mutations.

Design: In phase I of the study, the MIC distribution of laboratory strains (H37Rv and in vitro-selected Rv0678 mutants) and clinical pan-susceptible isolates were determined (n = 70). In phase II, a tentative CC for CFZ (n = 55) was proposed. In phase III, the proposed CC was validated using clinical drug-resistant tuberculosis (DR-TB) isolates stratified by Rv0678 mutation (n = 85).

Conclusion: The MIC distribution of CFZ for laboratory and clinical pan-susceptible strains ranged between 0.125 µg/ml and 0.5 µg/ml. As the MIC values of DR-TB isolates used for phase II ranged between 0.25 µg/ml and 1 µg/ml, a CC of 1 µg/ml was proposed. Validation of the CC in phase III showed that probably susceptible and probably resistant Rv0678 mutants overlapped at 1 µg/ml. We therefore recommend a CC of 1 µg/ml, with additional testing at 0.5 µg/ml to define an intermediate category. This was the first comprehensive study to establish a CC for routine phenotypic DST of CFZ using the MGIT960 system to guide therapeutic decisions.

The International Journal of Tuberculosis and Lung Disease

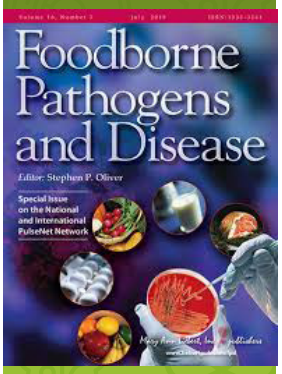
Dr Anthony Smith

Dr Juno Thomas

Outbreak of *Listeria monocytogenes* in South Africa 2017-2018: Laboratory activities and experiences associated with whole-genome sequencing analysis of isolates

Smith AM, *Tau NP, Smouse SL ,Mushal A ,Ismail A, Ramalwa NR, Disenyeng B, Ngomane M,* ***Thomas J.***

Foodborne Pathogens and Disease
Impact Factor: 2.000



In South Africa, a progressive increase in listeriosis cases was noted from mid-June 2017, heralding what was to become the world's largest listeriosis outbreak. A total of 1 060 cases were reported for the period January 1, 2017 to July 17, 2018. We describe laboratory activities, experiences, and results of whole-genome sequencing (WGS) analysis of *Listeria monocytogenes* isolates associated with this outbreak. Bacteria were identified using the VITEK-2 COMPACT 15 microbial identification system. WGS was performed using Illumina MiSeq technology. WGS data were analyzed using CLC Genomics Workbench Software and free-to-use on-line analysis tools/pipelines. Multilocus sequence typing (MLST) showed that 91% of clinical isolates were sequence type 6 (ST6), determining that the outbreak was largely associated with *L. monocytogenes* ST6. Epidemiological and laboratory findings led to investigation of a large ready-to-eat processed meat production facility in South Africa, named Enterprise Foods. *L. monocytogenes* ST6 was found in environmental sampling swabs of the production facility and in ready-to-eat processed meat products (including polony, a product similar to bologna sausage) manufactured at the facility. ST6 isolates, sourced at the Enterprise Foods production facility and from Enterprise food products, were shown by single nucleotide polymorphism (SNP) analysis to be highly related to clinical isolates; these nonclinical ST6 isolates showed <10 SNP differences when compared to clinical ST6 isolates. Core-genome MLST showed that clinical ST6 isolates and Enterprise-related ST6 isolates had no more than 4 allele differences between each other, suggestive of a high probability of epidemiological relatedness. WGS data interpreted together with epidemiological data concluded that the source of the listeriosis outbreak was ready-to-eat processed meat products manufactured by Enterprise Foods. Listeriosis has now been added to the South African list of mandatory notifiable medical conditions. Surveillance systems have been strengthened to facilitate prevention and early detection of listeriosis outbreaks.

Ms Johanna Ledwaba

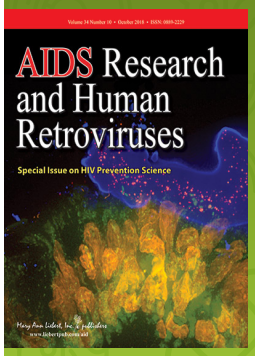
Dr Gillian Hunt

Low frequency protease inhibitor resistance mutation and insertions in HIV -1 subtype C protease inhibitor –naïve sequences

Ledwaba J, *Sayed Y, Pillay V, Morris L,* ***Hunt G.***

AIDS Research and Human Retroviruses
Impact Factor: 1.805

Human immunodeficiency virus-1 (HIV-1) protease sequences from 2 225 protease inhibitor (PI)-naïve HIV-1 subtype C-infected individuals collected over a 14-year period were analysed for polymorphisms. Over 50% of sequences differed from an HIV-1 subtype B consensus sequence at 8 of the 99 amino acids at residues 12, 15, 19, 36, 41, 69, 89, and 93, but not in the functionally important regions. The frequency of primary resistance and accessory mutations occurred in <1% of the sequences. Of note, 11 sequences (0.5%) harbored amino acid insertions between residues 36 and 39, located in the elbow of the flap region. The insertions were found throughout the 13-year period. Occurrence of insertions in subtype C viruses is rare and viruses remain sensitive to currently used PIs (lopinavir/r, atazanavir/r, and darunavir/r). However, ongoing characterisation of isolates is required to identify changes that may impact PI treatment since PIs are part of standard SA regimens.



Dr Petrus Jansen van Vuren

Multiplex real-time RT–PCR for detection and distinction of Spondweni and Zika virus

Rademan R, Markotter W, Paweska JT, ***Jansen van Vuren P.***

Journal of Virological Methods
Impact Factor: 1.746

Zika (ZIKV) and Spondweni viruses (SPOV) are closely related mosquito borne flaviviruses in the Spondweni serogroup. The co-circulation and similar disease presentation following ZIKV and SPOV infection necessitates the development of a diagnostic tool for their simultaneous detection and distinction. We developed a one-step multiplex real-time RT-PCR (ZIKSPOV) to detect and distinguish between SPOV and ZIKV by utilising a single primer set combined with virus specific hydrolysis probes. The ZIKSPOV assay was compared to published virus specific real-time RT-PCR assays and the limit of detection was comparable. The SPOV reference strain AR94 was detectable to 0.001 TCID50 per PCR reaction, while African lineage ZIKV (MR 766) was detectable to 0.002 TCID50 per reaction and Asian lineage ZIKV (H/PF/2013) to 0.05 TCID50 per reaction. The ZIKSPOV assay did not detect other flaviviruses, indicative of its specificity for Spondweni serogroup. The ZIKSPOV assay is a useful addition to arbovirus diagnostic and surveillance tools in areas where ZIKV and SPOV are expected to co-circulate. Further evaluation is required to demonstrate the application of the assay for detection of ZIKV and SPOV in mosquito and human clinical samples.

Ms Anastasia Trataris-Rebisz

Dr Jacqueline Weyer

Spotted fever rickettsiosis in South Africa: Evaluation of laboratory diagnostic capacity and inter-laboratory comparison of serological testing

Trataris-Rebizs AN, *Rossouw J, Markotter W, Frean JA,* ***Weyer J.***

South African Medical Journal
Impact Factor: 1.805

Background: Spotted fever rickettsiosis, also known as tick bite fever (TBF), is a common infectious disease in South Africa (SA). Although the diagnosis of TBF is often based on clinical grounds only, laboratory testing is important to confirm the diagnosis and can contribute to case management in the light of a myriad of differential diagnoses, and in complicated cases.

Objectives: To report on the availability and scope of laboratory tests for investigating suspected cases of TBF in SA, and the outcome of an inter-laboratory comparison (ILC) conducted for serological tests.

Methods: A self-administered questionnaire was circulated to major pathology laboratories in SA to determine what TBF tests they offered for TBF investigation. In addition, a clinical panel was provided to willing laboratories in order to perform an ILC of the serological tests.

Results: Serological tests for TBF were available from five laboratories serving both the private and state medical sectors in SA. There was no standardised testing platform or result interpretation across the different laboratories. Polymerase chain reaction (PCR) tests were less frequently available, and not available to state-operated facilities. The outcome of the ILC indicated varied performance and interpretation of serological results for TBF.

Conclusions: Laboratory investigation for TBF is routinely and widely available in SA. Both serological and PCR-based methods were varied, and the lack of standardisation and interpretation of tests needs to be addressed to improve the overall quality of TBF diagnosis in SA. The utility of ILC to identify problem areas in serological testing for TBF is highlighted, and laboratories in SA are encouraged to use it to improve the quality of testing.

Sr Jo McAnerney

Healthcare utilisation patterns for respiratory and gastrointestinal syndromes and meningitis in Msunduzi municipality, Pietermaritzburg, KwaZulu-Natal Province, South Africa, 2013

McAnerney JM, *Cohen C, Cohen AL, Tempia S, Walaza S, Wong KK, Im J, Marks F, Dawood H, Panzner U, Keddy KH, von Mollendorf C.*

South African Medical Journal
Impact Factor: 1.325

Background: Public health facilities are used by the majority of South Africans, and healthcare utilisation surveys have been a useful tool to estimate the burden of disease in a given area.

Objectives: To describe care-seeking behaviour in a peri-urban site with a high prevalence of HIV infection, as well as barriers to seeking appropriate healthcare.

Methods: We conducted a cross-sectional household survey in 22 wards of the Msunduzi municipality in KwaZulu-Natal Province, South Africa, from October to December 2013 using a simple random sample of households selected from a 2011 census enumeration. A primary caregiver/adult decision-maker was interviewed regarding demographic data as well as health status and recent self-reported episodes of selected illnesses and healthcare utilisation.

Results: Of the 2 238 eligible premises visited, 1 936 households (87%) with a total of 9 733 members were enrolled in the study. Of these, 635 (7%) reported one or more episodes of infectious illness during the study period. Public health clinics were most frequently consulted for all illnesses (361/635, 57%). Private healthcare (general practitioner, private clinic, private hospital) was sought by 90/635 of individuals (14%), only 13/635 (2%) reported seeking care from traditional healers, religious leaders or volunteers, and 71/635 (11%) did not seek any medical care for acute illnesses. Individuals in the lowest income group were more likely to seek care at public health facilities than those in the highest income group (70% v. 32%).

Conclusions: Public health facility-based surveillance may be representative of disease patterns in this community, although surveillance at household level shows that high-income individuals may be excluded because they were more likely to use private healthcare, and the proportion of individuals who died at home would have been missed by facility-based surveillance. Data obtained in such surveys may be useful for public health planning.

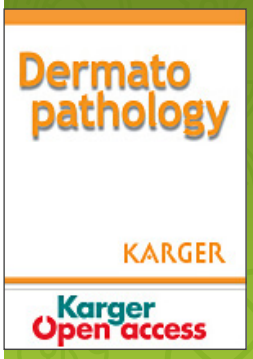
Prof Nelesh Govender

Emergomycosis (*Emergomyces africanus*) in advanced HIV disease

***Govender NP**, Grayson W.*

Dermatopathology
Impact Factor: Score unavailable

In 2013, a novel thermally dimorphic fungal pathogen was described to cause disseminated disease among persons living with advanced HIV/AIDS in South Africa. Although the organism was initially described as an *Emmonsia*-like fungus, it is now known to belong to a new genus of thermally dimorphic fungi and was recently named *Emergomyces africanus*. There is considerable clinical and histopathological overlap between emergomycosis and histoplasmosis. This review addresses taxonomic, clinical, diagnostic, and therapeutic aspects of *Es. africanus* disease, a condition which has, to date, only been reported from southern Africa.



Dr Heather Hong

Dr Melinda Suchard

Measles in South Africa in the era of vaccine hesitancy

Hong H A, Suchard MS.

Paediatric Focus
Impact Factor: Score unavailable

Measles (rubeola) is a highly contagious and serious viral infection caused by a paramyxovirus, genus Morbillivirus. Despite the availability of a safe and effective vaccine, measles remains a leading cause of vaccine-preventable deaths in children under 5 years of age worldwide, especially in developing countries, with up to 20% of these deaths occurring in those under 1 year. Over the past year, cases of measles have been on the rise around the world, with notable outbreaks occurring in the United States and Europe. In 2018, the United States experienced 17 outbreaks with a total of 372 confirmed cases. Furthermore, currently ongoing in 2019, six outbreaks have been reported; many cases largely amongst unvaccinated children with vaccine hesitant parents from Orthodox Jewish communities. This outbreak initiated an official ban on unvaccinated children from public spaces for a period of 30 days. Similarly in Europe in 2018, there were more than 82 000 cases in both adults and children, the highest number in a decade and three times the total reported in 2017. The outbreak prompted Italy to make vaccinations compulsory for all children attending state schools.

Prof John Frean

South African tick bite fever: An overview

Frean JA, *Grayson W.*

Dermatopathology
Impact Factor: Score unavailable

The rickettsiae are a diverse group of vector-borne zoonotic bacterial pathogens. The two common spotted fever diseases in existence in southern Africa are boutonneuse fever-like tick bite fever (TBF), caused by *Rickettsia conorii*, and African TBF, caused by *R. africae*. This review addresses demographic, epidemiological, clinical, diagnostic, therapeutic, and preventive aspects of TBF in the southern African context, including a discussion of the dermatopathological findings and potential diagnostic pitfalls.

Dermato pathology
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