Issue 9 - November 2018

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.

Prof Cheryl Cohen

Prof Anne von Gottberg

Editorial Commentary: Hib combination vaccines: efficient and effective

Cohen C, von Gottberg A.

The Lancet Infectious Diseases
Impact Factor: 25.148

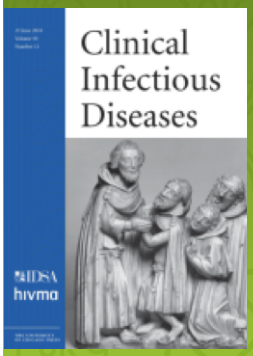
Combination vaccines have advantages compared with single-antigen formulations—for instance, they require fewer injections and patient visits and potentially lower costs. As many countries begin to include inactivated polio vaccine (IPV) in routine vaccination programmes, the use of high-valency combination vaccines is increasing (including the hexavalent diphtheria, tetanus, and acellular pertussis–hepatitis B virus–IPV/ *Haemophilus influenzae* type b disease vaccine [DTPa-HBV-IPV/Hib]). Combination vaccines are generally licensed on the basis of immunogenicity data, but these data can be inconclusive, and the interpretation of differing antibody titre responses to different products can be challenging. A resurgence of Hib in the UK between 1999 and 2002 was partly attributed to the use of poorly immunogenic combination vaccines, including an acellular pertussis component with no booster dose. In their article in The Lancet Infectious Diseases, Susana Monge and colleagues assess the effectiveness of the hexavalent DTPa-HBV-IPV/ Hib vaccine in the routine immunisation programme in the Netherlands, to determine whether reduced vaccine effectiveness is contributing to an increase in the incidence of Hib. Reassuringly, the authors found that vaccine effectiveness against invasive Hib disease was high and did not differ by vaccine. The authors did, however, find that vaccine effectiveness waned with increasing age.

Prof Cheryl Cohen

The role of HIV in influenza- and respiratory syncytial virus-associated hospitalisations in South African children, 2011-2016

McMorrow ML, Tempia S, Walaza S, Treurnicht FK, Moyes J, Cohen AL, Pretorius M, Hellferscee O, Wolter N, von Gottberg A, Nguweneza A, McAnerney JM, Naby F, Mekgoe O, Venter M, Madhi SA, ***Cohen C.***

Clinical Infectious Diseases
Impact Factor: 9.117



Data describing influenza– or respiratory syncytial virus (RSV)–associated hospitalised illness in children aged <5 years in Africa are limited. During 2011–2016, we conducted surveillance for severe respiratory illness (SRI) in children aged <5 years in three South African hospitals. Nasopharyngeal aspirates were tested for influenza and RSV using real-time reverse transcription polymerase chain reaction. We estimated rates of influenza- and RSV-associated hospitalised SRI by human immunodeficiency virus (HIV) status and compared children who tested positive for influenza vs RSV using multivariable penalized logistic regression. Among 3650 hospitalised children, 203 (5.6%) tested positive for influenza viruses, 874 (23.9%) for RSV, and 19 (0.5%) for both. The median age of children hospitalised with influenza was 13.9 months vs 4.4 months for RSV ($P < .01$). Annual influenza-associated hospitalisation rates per 100 000 were highest among infants aged six–11 months (545; 95% confidence interval [CI], 409–703), while RSV-associated hospitalisation rates were highest in infants aged zero–two months (6593; 95% CI, 5947–7217). HIV exposure was associated with increased incidence of influenza- and RSV-associated hospitalisation in infants aged zero–five months, with relative risk (RR) 2.2 (95% CI, 1.4–3.4) and 1.4 (95% CI, 1.3–1.6), respectively. HIV infection was associated with increased incidence of influenza- and RSV-associated hospitalisation in all age groups; RR 2.7 (95% CI, 2.0–3.5) and 3.8 (95% CI, 3.1–4.8), respectively. Influenza- and RSV-associated hospitalisations are common among South African infants. HIV infection and HIV exposure in infants increase risk of influenza- and RSV-associated hospitalisation.

Dr Villyen Motaze

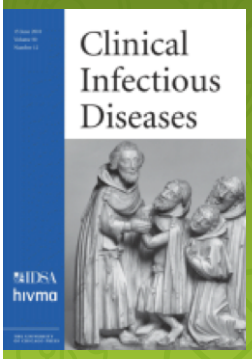
Dr Melinda Suchard

Congenital rubella syndrome surveillance in South Africa using a sentinel site approach: A cross-sectional study

Motaze NV, *Manamela J, Smit S, Rabie H, Harper K, duPlessis N, Reubenson G, Coetzee M, Ballot D, Moore D, Nuttall J, Linley L, Tooke L, Kriel J, Hallbauer U, Sutton C, Moodley P, Hardie D, Mazanderani AH, Goosen F, Kyaw T, Leroux D, Hussain A, Singh R, Kelly C, Ducasse G, Muller M, Blaauw M, Hamese M, Leeuw T, Mekgoe O, Rakgole P, Dungwa N, Maphosa T, Sanyane K, Preiser W, Cohen C,* ***Suchard M.***

Clinical Infectious Diseases
Impact Factor: 9.117

Congenital rubella syndrome (CRS) includes disorders associated with intrauterine rubella infection. Incidence of CRS is higher in countries with no rubella-containing vaccines (RCV) in their immunisation schedules. In the World Health Organization African region, RCVs are being introduced as part of the 2012-2020 global measles and rubella strategic plan. This study aimed to describe the epidemiology of confirmed CRS in South Africa prior to introduction of RCVs in the immunisation schedule. This was a descriptive study with 28 sentinel sites reporting laboratory-confirmed CRS cases in all nine provinces of South Africa. In the retrospective phase (2010 to 2014), CRS cases were retrieved from medical records and in the prospective phase (2015 to 2017) clinicians at study sites reported CRS cases monthly. There were 42 confirmed CRS cases in the retrospective phase and 53 confirmed CRS cases in the prospective phase. Most frequently reported birth defects were congenital heart disease and cataracts. The median age of mothers of CRS cases was 21 years in the retrospective phase (range: 11 to 38 years) and 22 years in the prospective phase (range: 15 to 38 years). Baseline data on laboratory-confirmed CRS will enable planning and monitoring of RCV implementation in the South African EPI programme. Ninety-eight percent of mothers of infants with CRS were young women 14 to 30 years old, indicating a potential immunity gap in this age group for consideration during introduction of RCV.



Prof Nazir Ismail

Prevalence of drug-resistant tuberculosis in South Africa – Authors' reply

Ismail NA, *Omar SV, Mvusi L, Madhi SA.*

Lancet Infectious Diseases
Impact Factor: 9.117

Unlike in southeast Asian countries where the private sector is substantially involved in the care of individuals with tuberculosis, in South Africa the majority of individuals (84%) do not have private medical insurance and use public health facilities, including 91% of black Africans who are also disproportionately affected by tuberculosis. Furthermore, even among those with private medical insurance, the management of tuberculosis is generally undertaken in public health facilities in South Africa and funded by the government at no cost to the patients. Thus, although Ranjeet Singh Mahla's concern is that the absence of including sampling from the private sector might have biased in our results, we believe that our sampling is representative of tuberculosis cases in South Africa. We, however, concur that WHO's End TB strategy and the UN's Sustainable Development Goals have ambitious targets and reaching these would be hampered if high burden countries do not improve the effectiveness of their national policies for tuberculosis control, which should be based on robust epidemiological data.

In addition to the doubling in prevalence of rifampicin resistance observed, equally important was the increase thereof among new cases implying primary transmission of rifampicin-resistant strains. This highlights the importance of applying the Xpert MTB/RIF assay as the primary diagnostic tool for tuberculosis, irrespective of treatment history.

Although our study does illustrate the value of repeat surveys to monitor for the prevalence of drug-resistant tuberculosis, such surveys are complex, costly, and the data generally only available 2–3 years after the survey is done. Future surveys should also, probably, make use of next generation molecular tools instead of culture. Furthermore, if programmes are to be agile in their response to drug-resistant tuberculosis, structured routine surveillance is preferred, allowing trend analysis, mapping geographical burden of the disease, and achieving granularity at low levels to inform a response; all of which are now being implemented in South Africa.

Although we note the suggestion by Emmanuel André that the absence of investigation for the Ile491Phe rpoB mutation in isoniazid-resistant isolates from our survey could have under-represented whether these isolates were in fact multi-drug resistant tuberculosis, we believe that such under-representation is unlikely, as the prevalence of isoniazid mono-resistant tuberculosis observed was similar to that reported elsewhere globally. Furthermore, the high prevalence (30%) of the Ile491Phe mutation observed in the 2009 drug resistance survey in Swaziland, has not been observed elsewhere.

Also, as part of a separate WHO multi-country study using isolates from the survey, whole-genome sequencing was done on 1535 isolates from two provinces in South Africa (KwaZulu-Natal, which neighbours Swaziland, and Gauteng) and there were minimal differences in the prevalence of rifampicin resistance based on phenotypic (5·7%) and sequencing data (5·5%), and the prevalence of Ile491Phe mutation was less than 0·1% (one out of 1535), and identified phenotypically. Since the publication of our results, we have further analysed 92 of the isoniazid mono-resistant isolates that had whole-genome sequencing, and sequenced another 48 isoniazid mono-resistant survey strains from the Mpumalanga and North-West province, none of which had the Ile491Phe mutation.

We declare no competing interests.

Prof Nelesh Govender

Brief Report: Point of care cryptococcal antigen screening: Pipetting finger-prick blood improves performance of immunomycologics lateral flow assay

Wake RM, Jarvis JN, Harrison TS, ***Govender NP.***

Journal of Acquired Immune Deficiency Syndromes
Impact Factor: 4.556

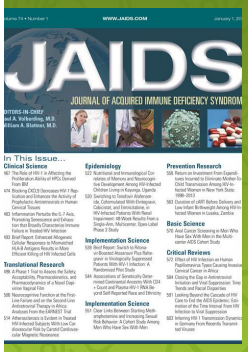
Background: Cryptococcal antigen (CrAg) screening at the point of care could improve cryptococcal meningitis prevention where laboratory resources are limited. We evaluated the accuracy of Immunomycologics (IMMY, Norman, OK) CrAg lateral flow assay (LFA) using different techniques at point of care.

Setting: Two tertiary-level hospitals in Johannesburg and a community health clinic in Soweto, South Africa.

Methods: A case-control diagnostic validation study and a prospective clinic-based implementation study using the IMMY CrAg LFA on finger-prick blood. Accuracy, using direct application of LFA to sample, or pipette to transfer sample to diluent, and reading after 10 and 20 minutes, was compared with laboratory-based plasma testing.

Results: The validation study tested 64 CrAg-positive and 152 CrAg-negative patients with no symptoms or signs of meningitis, identified by routine laboratory screening, recruited by convenience sampling. Consecutively diagnosed HIV-infected adults (n = 654) were included in the implementation study. Sensitivity was 82% and 20% when the LFA was read 10 minutes after direct application to finger-prick blood in the validation and implementation studies, respectively. Using a pipette to transfer blood and reading after 20 minutes improved sensitivity to 100%, while retaining 100% specificity, in both studies.

Conclusion: Although the IMMY CrAg LFA performs well when applied directly to finger-prick blood for diagnosing cryptococcal meningitis, this technique may not provide adequate volume to detect low concentrations of CrAg when screening asymptomatic patients. Using a pipette to transfer larger volumes of blood to diluent before CrAg LFA testing and reading results after 20 minutes is a more reliable point-of-care method.



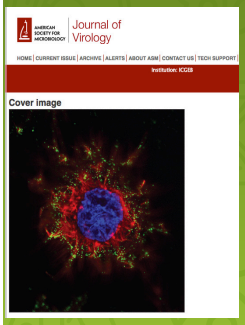
Dr Zanele Ditse

Prof Lynn Morris

HIV-1 subtype C-Infected children with exceptional neutralisation breadth exhibit polyclonal responses targeting known epitopes

Ditse Z, *Meunchhoff M, Adland E, Jooste P, Goulder G, Moore PL,* ***Morris L.***

Journal of Virology
Impact Factor: 4.368



We have previously shown that HIV-1-infected children develop broader and more potent neutralising antibody responses than adults. This study aimed to determine the antibody specificities in 16 HIV-1 subtype C-infected children who displayed exceptional neutralisation breadth on a 22-multisubtype virus panel. All children were antiretroviral treatment (ART) naive with normal CD4 counts despite being infected for a median of 10.1 years with high viral loads. The specificity of broadly neutralising antibodies (bNAbs) was determined using epitope-ablating mutants, chimeric constructs, and depletion or inhibition of activity with peptides and glycoproteins. We found that bNAbs in children largely targeted previously defined epitopes, including the V2-glycan, V3-glycan, CD4bs, and gp120-gp41 interface. Remarkably, 63% of children had antibodies targeting two or three and, in one case, four of these bNAb epitopes. Longitudinal analysis of plasma from a mother-child pair over nine years showed that while they both had similar neutralisation profiles, the antibody specificities differed. The mother developed antibodies targeting the V2-glycan and CD4bs, whereas bNAb specificities in the child could not be mapped until six years, when a minor V2-glycan response appeared. The child also developed high-titer membrane-proximal external region (MPER) binding antibodies not seen in the mother, although these were not a major bNAb specificity. Overall, exceptional neutralisation breadth in this group of children may be the result of extended exposure to high antigenic load in the context of an intact immune system, which allowed for the activation of multiple B cell lineages and the generation of polyclonal responses targeting several bNAb epitopes.

Prof Penny Moore

Development of broadly neutralising antibodies in HIV-1 infected elite neutralisers

Landais E, ***Moore PL.***

Retrovirology
Impact Factor: 3.417

Broadly neutralising antibodies (bNAbs), able to prevent viral entry by diverse global viruses, are a major focus of HIV vaccine design, with data from animal studies confirming their ability to prevent HIV infection. However, traditional vaccine approaches have failed to elicit these types of antibodies. During chronic HIV infection, a subset of individuals develops bNAbs, some of which are extremely broad and potent. This review describes the immunological and virological factors leading to the development of bNAbs in such "elite neutralisers." The features, targets and developmental pathways of bNAbs from their precursors have been defined through extraordinarily detailed within-donor studies. These have enabled the identification of epitope-specific commonalities in bNAb precursors, their intermediates and Env escape patterns, providing a template for vaccine discovery. The unusual features of bNAbs, such as high levels of somatic hypermutation, and precursors with unusually short or long antigen-binding loops, present significant challenges in vaccine design. However, the use of new technologies has led to the isolation of more than 200 bNAbs, including some with genetic profiles more representative of the normal immunoglobulin repertoire, suggesting alternate and shorter pathways to breadth. The insights from these studies have been harnessed for the development of optimized immunogens, novel vaccine regimens and improved delivery schedules, which are providing encouraging data that an HIV vaccine may soon be a realistic possibility.

Prof John Frean

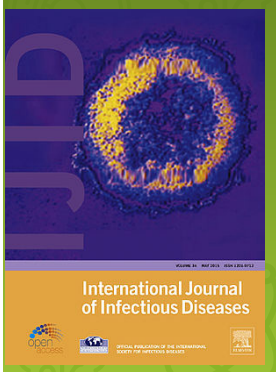
Prof Lucille Blumberg

Clinical management of East African trypanosomiasis in South Africa: Lessons learned

Frean J, *Sieling W, Pahad H, Shoul E,* ***Blumberg L.***

International Journal of Infectious Diseases
Impact Factor: 3.202

East African trypanosomiasis is an uncommon, potentially lethal disease if not diagnosed and treated in a timely manner. South Africa, as a centre for emergency medical evacuations from much of sub-Saharan Africa, receives a high proportion of these patients, mostly tourists and expatriate residents. The cases of East African trypanosomiasis patients evacuated to South Africa, for whom diagnostic and clinical management advice was provided over the years 2004–2018, were reviewed, using the authors' own records and those of collaborating clinicians. Twenty-one cases were identified. These originated in Zambia, Malawi, Zimbabwe, Tanzania, and Uganda. Nineteen cases (90%) had stage 1 (haemolymphatic) disease; one of these patients had fatal myocarditis. Of the two patients with stage 2 (meningoencephalitic) disease, one died of melarsoprol encephalopathy. Common problems were delayed diagnosis, erroneous assessment of severity, and limited access to treatment. The key to early diagnosis is recognition of the triad of geographic exposure, tsetse fly bites, and trypanosomal chancre, plus good microscopy. Elements for successful management are rapid access to specific drug treatment, skilled intensive care, and good laboratory facilities. Clinical experience and the local stock of antitrypanosomal drugs from the World Health Organization have improved the chance of a successful outcome in the management of East African trypanosomiasis in South Africa; the survival rate over the period was 90.5%.

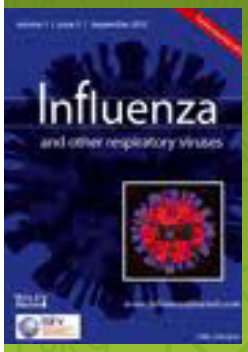


Dr Florette Treurnicht

Replacement of neuraminidase inhibitor susceptible influenza A(H1N1) with resistant phenotype in 2008 and circulation of susceptible influenza A and B viruses during 2009-2013, South Africa

Treurnicht FK, *Buys A, Tempia S, Seleka M, Cohen AL, Walaza S, Glass AJ, Rossouw I, McAnerney J, Blumberg L, Cohen C, Venter M.*

Influenza and other Respiratory Viruses
Impact Factor: 2.954



Background: Data on the susceptibility of influenza viruses from South Africa to neuraminidase inhibitors (NAIs) is scarce, and no extensive analysis was done.

Objectives: We aimed to determine oseltamivir and zanamivir susceptibility of influenza A and B virus neuraminidases (NAs), 2007-2013, South Africa.

Patients/Methods: We enrolled participants through national influenza-like illness surveillance, 2007-2013. Influenza diagnosis was by virus isolation and real-time polymerase chain reaction (qPCR). Drug susceptibility was determined by chemilluminescence-based NA-STAR/NA-XTD assay. Sanger sequencing was used to determine molecular markers of NAI resistance.

Results: Forty percent (6,341/15,985) of participants were positive for influenza viruses using virus isolation (2007-2009) and qPCR (2009-2013) methods. 1,236/6,341 (19.5%) virus isolates were generated of which 307/1,236 (25%) were tested for drug susceptibility. During 2007-2008 the median 50% inhibitory concentration (IC50) of oseltamivir for seasonal influenza A(H1N1) increased from of 0.08 nM (range 0.01-3.60) in 2007 to 73 nM (range 1.56-305 nM) in 2008. Influenza A isolates from 2009-2013 were susceptible to oseltamivir [A(H3N2) median IC50 = 0.05 nM (range 0.01-0.08); A(H1N1)pdm09= 0.11 nM (range 0.01-0.78)] and zanamivir [A(H3N2) median IC50 = 0.56 nM (range 0.47-0.66); A(H1N1)pdm09= 0.35 nM (range 0.27-0.533)]. Influenza B viruses were susceptible to both NAIs. NAI resistance-associated substitutions H275Y, E119V, and R150K (N1 numbering) were not detected in influenza A viruses that circulated in 2009-2013.

Conclusions: We confirm replacement of NAI susceptible by resistant phenotype influenza A(H1N1) in 2008. Influenza A and B viruses (2009-2013) remained susceptible to NAIs; therefore these drugs are useful for treating influenza-infected patients.

Dr Kerrigan McCarthy

Using mHealth to improve tuberculosis case identification and treatment initiation in South Africa: Results from a pilot study

Maraba N, Hoffmann CJ, Chihota VN, Chang LW, Ismail N, Candy S, Madibogo E, Katzwinkel M, Churchyard GJ, ***McCarthy K.***

PLoS ONE
Impact Factor: 2.766

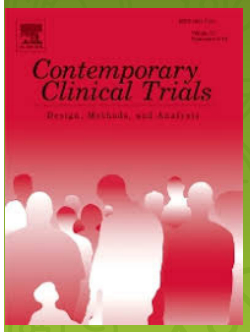
Tuberculosis (TB) incidence in South Africa is among the highest globally. Initial loss to follow-up (ILFU), defined as not starting on TB treatment within 28 days of testing positive, is undermining control efforts. We assessed the feasibility, acceptability, and potential of a mHealth application to reduce ILFU. An mHealth application was developed to capture patients TB investigation data, provide results and monitor treatment initiation. This was implemented in two primary health clinics (PHC) in inner-city Johannesburg. Feasibility was assessed by comparing documentation of personal details, specimen results for same individuals during implementation period (paper register and mHealth application). Effectiveness was assessed by comparing proportion of patients with results within 48 hours, and proportion started on treatment within 28 days of testing TB positive during pre- implementation (paper register) and implementation (mHealth application) periods. In-depth interviews with patients and providers were conducted to assess acceptability of application. Pre-implementation, 457 patients were recorded in paper registers [195 (42.7%) male, median age 34 years (interquartile range IQR (28–40), 45 (10.5%) sputum Xpert positive]. During implementation, 319 patients were recorded in paper register and the mHealth application [131 (41.1%) male, median age 32 years (IQR 27–38), 33 (10.3%) sputum Xpert positive]. The proportion with complete personal details: [mHealth 95.0% versus paper register 94.0%, (p = 0.54)] and proportion with documented results: [mHealth 97.4% versus paper register 97.8%, (p = 0.79)] were not different in the two methods. The proportion of results available within 48 hours: [mHealth 96.8% versus paper register 68.6%), (p <0.001)], and the proportion on treatment within 28 days [mHealth 28/33 (84.8%) versus paper register 30/44 (68.2%), (p = 0.08)] increased during implementation but was not statistically significant. In-depth interviews showed that providers easily integrated the mHealth application into routine TB investigation and patients positively received the delivery of results via text message. Time from sputum collection to TB treatment initiation decreased from four days (pre-implementation) to three days but was not statistically significant. We demonstrated that implementation of the mHealth application was feasible, acceptable to health care providers and patients, and has potential to reduce the time to TB treatment initiation and ILFU in PHC settings.

Dr Tendesayi Kufa

An intervention to optimise the delivery of integrated tuberculosis and HIV services at primary care clinics: Results of the MERGE cluster randomised trial

Kufa T, *Fielding KL, Hippner P, Kielmann K, Vassall A, Churchyard GJ, Grant AD, Charalambous S.*

Contemporary Clinical Trials
Impact Factor: 2.658



To evaluate the effect of an intervention to optimise TB/HIV integration on patient outcomes. Cluster randomised control trial at 18 primary care clinics in South Africa. The intervention was placed on a nurse (TB/HIV integration officer) to facilitate the provision of integrated TB/HIV services, and a lay health worker (TB screening officer) to facilitate TB screening for 24 months. Primary outcomes were (i) incidence of hospitalisation/death among individuals newly diagnosed with HIV, (ii) incidence of hospitalisation/death among individuals newly diagnosed with TB and (iii) proportion of HIV-positive individuals newly diagnosed with TB who were retained in HIV care 12 months after enrolment. Of the 3328 individuals enrolled, 3024 were in the HIV cohort, 731 in TB cohort and 427 in TB-HIV cohort. For the HIV cohort, the hospitalisation/death rate was 12.5 per 100 person-years (py) (182/1459py) in the intervention arm vs 10.4/100py (147/1408 py) in the control arms respectively (Relative Risk (RR) 1.17 [95% CI 0.92–1.49]). For the TB cohort, hospitalisation/ death rate was 17.1/100 py (67/ 392py) vs 11.1 /100py (32/289py) in intervention and control arms respectively (RR 1.37 [95% CI 0.78–2.43]). For the TB-HIV cohort, retention in care at 12 months was 63.0% (213/338) and 55.9% (143/256) in intervention and control arms (RR 1.11 [95% 0.89–1.38]). The intervention as implemented failed to improve patient outcomes beyond levels at control clinics. Effective strategies are needed to achieve better TB/HIV service integration and improve TB and HIV outcomes in primary care clinics.

Prof Cheryl Cohen

Responses to hypothetical health scenarios overestimate healthcare utilisation for common infectious syndromes: A cross-sectional survey, South Africa, 2012

Wong KK, Cohen AL, Martinson NA, Norris SA, Tempia S, von Mollendorf C, Walaza S, Madhi SA, McMorrow ML, ***Cohen C.***

BMC Infectious Diseases
Impact Factor: 2.620

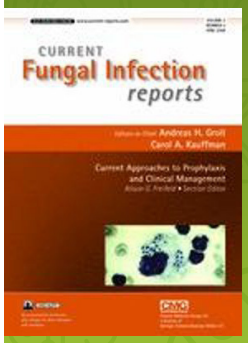
Asking people how they would seek healthcare in a hypothetical situation can be an efficient way to estimate healthcare utilisation, but it is unclear how intended healthcare use corresponds to actual healthcare use. We performed a cross-sectional survey between August and September 2012, among households in Soweto and Klerksdorp, South Africa, to compare healthcare seeking behaviors intended for hypothetical common infectious syndromes (pneumonia, influenza-like illness [ILI], chronic respiratory illness, meningitis in persons of any age, and diarrhea in a child <5 years old) with the self-reported healthcare use among patients with those syndromes. For most syndromes, the proportion of respondents who intended to seek healthcare at any facility or provider (99-100%) in a hypothetical scenario exceeded the proportion that did seek care (78-100%). More people intended to seek care for a child <5 years old with diarrhea (186/188 [99%]) than actually did seek care (32/41 [78%], P<0.01). Although most people faced with hypothetical scenarios intended to seek care with licensed medical providers such as hospitals and clinics (97-100%), patients who were ill reported lower use of licensed medical providers (55-95%). People overestimated their intended healthcare utilisation, especially with licensed medical providers, compared with reported healthcare utilisation among patients with these illnesses. Studies that measure intended healthcare utilisation should consider that actual use of healthcare facilities may be lower than intended use.

Prof Nelesh Govender

Emergomyces: A new genus of dimorphic fungal pathogens causing disseminated disease among immunocompromised persons globally

Schwartz I, Maphanga TG, ***Govender NP.***

Current Fungal Infection Reports
Impact Factor: 2.58



The emergence of a group of previously unknown or unrecognized dimorphic fungal species causing systemic human disease resulted in taxonomic shifts and the creation of a new genus, *Emergomyces*, within Onygenales. We review the morphology, taxonomy, physiology, and ecology of *Emergomyces spp*., and the epidemiology, clinicopathology, diagnosis, and management of disease. *Emergomyces* species have been reported as causes of human disease in Europe, Asia, Africa, and North America. *Es. pasteurianus* is most cosmopolitan, and *Es. africanus*, in southern Africa, causes the largest reported disease burden; in fact, emergomycosis is the most common endemic mycosis diagnosed in South Africa. The classic clinical picture is of disseminated disease, often with cutaneous involvement, in immunocompromised individuals. Members of the genus *Emergomyces* are uncommon but important agents of systemic disease in immunocompromised hosts worldwide. Knowledge gaps include the biology of the fungus, and the pathophysiology and management of disease.

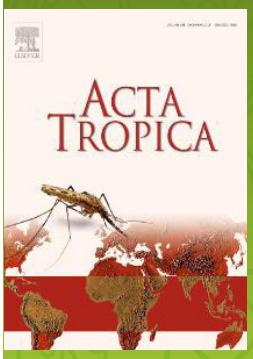
Dr Shune Oliver

Prof Basil Brooke

The effect of commercial herbicide exposure on the life history and insecticide resistance phenotypes of the major malaria vector *Anopheles arabiensis* (Diptera: culicudae)

Oliver SV, Brooke BD.

Acta Tropica
Impact Factor: 2.509



Herbicides, such as atrazine and glyphosate, are common agrochemicals known to pollute surface ground water. As such, aquatic invertebrates associated with agricultural activities can be exposed to varying doses of these xenobiotics. *Anopheles arabiensis*, a major malaria vector species in southern Africa, is often closely associated with agricultural activities. This study aimed to examine the effects of larval atrazine or glyphosate exposure on larval and adult life history traits on two laboratory strains of *An. arabiensis;* one insecticide susceptible (SENN), the other selected for resistance (SENN DDT). Atrazine delayed time to pupation in both strains, but markedly more so in SENN DDT. Glyphosate treatment reduced time to pupation in SENN DDT. Larval atrazine exposure decreased adult longevity in SENN, while both herbicide treatments significantly increased adult longevity in SENN DDT. Larval glyphosate exposure was the more potent enhancer of insecticide tolerance in adult mosquitoes. In SENN DDT, it reduced deltamethrin and malathion-induced mortality, and the LT50 s for these insecticides were increased in association with herbicide exposure. Glyphosate exposure also increased the LT50 s for malathion and deltamethrin in SENN. Exposure to both herbicides had contrasting effects on detoxification enzyme activities. Although both increased cytochrome P450 activity, they had opposite effects on those enzymes involved in reactive oxygen species detoxification. Glyphosate decreased glutathione S-transferase activity, but increased catalase activity with atrazine having the opposite effect. This study demonstrates that larval exposure to the herbicides atrazine and glyphosate can affect the insecticide susceptibilities and life history traits of epidemiological importance in *An. arabiensis*, with glyphosate being the more potent effector of insecticide resistance.

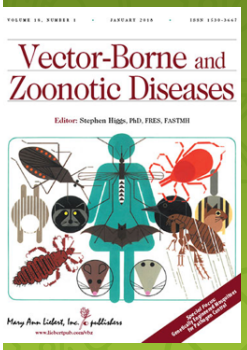
Dr Petrus Jansen van Vuren

Prof Janusz Paweska

Human cases of Rift Valley fever in South Africa, 2018

Jansen van Vuren P, *Kgaladi J, Patharoo V, Ohaebosim P, Msimang V, Nyokong B,* ***Paweska JT.***

Vector-Borne and Zoonotic Diseases
Impact Factor: 2.171



Major Rift Valley fever (RVF) epidemics in South Africa occur at irregular intervals, usually spanning several decades, with human cases rarely reported in the absence of widespread outbreaks in livestock. This report describes four cases of RVF in farm workers associated with an isolated outbreak on a sheep farm in the Free State Province of South Africa, in 2018. In contrast to the last major RVF epidemic in South Africa in 2010–2011, where detection of human cases served as an alert for an ongoing outbreak in livestock, the current isolated outbreak was first detected in livestock, and human cases recognised following subsequent epidemiological investigation. This highlights the importance of early recognition of livestock cases in reducing risk and impact of a subsequent RVF epidemic in humans. People working with animals should be aware of transmission routes and take precautions to minimise risk of infection.

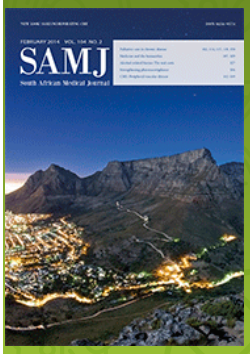
Dr Ahmad Mazanderani

Leveraging the Road to Health booklet as a unique patient identifier to monitor the prevention of mother-to-child transmission programme

Mazanderani AH, *Sherman GG, Moyo F, Goga AE, Feucht U.*

South African Medical Journal
Impact Factor: 2.163

Currently there is no unique patient identification system in the South African public health sector. Therefore, routine laboratory data cannot effectively be de-duplicated, thereby hampering surveillance of laboratory-diagnosed diseases such as mother-to-child transmission of HIV. To determine the uptake of Road to Health booklet (RTHB) identifiers at HIV polymerase chain reaction (PCR) birth test and describe their performance in linking follow-up test results in the early infant diagnosis programme. Between May 2016 and May 2017, Tshwane District Clinical Services implemented a unique patient identifier pilot project in which a sticker-page of unique, readable, barcoded patient identifiers was incorporated in the patient-retained immunisation record (the RTHB) before distribution. Uptake of RTHB identifiers at birth was calculated as the proportion of HIV PCR tests in infants aged <6 days registered with an RTHB identifier over the total number of registered HIV PCR tests. Descriptive analysis of demographic details was performed among infants with two registered HIV PCR tests linked by the RTHB identifier, and performance of the National Health Laboratory Service Corporate Data Warehouse (NHLS CDW)-linking algorithm in matching RTHB-linked results was calculated using a 2 × 2 table. A total of 5 309 HIV PCR birth tests registered with an RTHB identifier were extracted from the NHLS CDW over the 13-month period of the pilot project. The number of registered RTHB identifiers increased from 24 (2% of birth PCR tests) in May 2016, peaking at 728 (56% of birth PCR tests) in May 2017. Among infants with a registered RTHB identifier at birth, 635 (12%) had a subsequent linked HIV PCR test, as indicated by the same RTHB number registered for a later specimen. Demographic details at the time of birth and subsequent PCR test were compared, demonstrating that <4% of infants had exact matches for name, surname, date of birth and sex; 74% of birth tests had variations such as 'born to' or 'baby of ' in place of a first name; surnames matched exactly in 61% of cases; 18% (n=116) of infants had both tests performed at the same facility, of which only 27% (n=31) had the same patient folder number on both test results. Leveraging RTHBs as unique patient identifiers, even if used temporarily until linkage to other future national unique identifiers, promises to be an effective scalable approach to laboratory-based surveillance, facilitating healthcare provider access to all test results from birth.



Dr Tendesayi Kufa

Knowledge of HIV status and antiretroviral therapy use among sexually transmitted infections service attendees and the case for improving the integration of services in South Africa: A cross sectional study

Kufa T, *Maseko VD, Nhlapo D, Radebe F, Puren A, Kularatne RS.*

Medicine
Impact Factor: 2.133

We describe knowledge of human immunodeficiency virus (HIV) status, correct report of HIV status and antiretroviral therapy (ART) use among sexually transmitted infection (STI) service attendees in South Africa. An anonymous questionnaire was administered and serological HIV testing done. Proportions of attendees reporting knowledge of HIV status and HIV status consistent with laboratory results and ART use (among HIV positives) were determined as were factors associated with knowledge and inconsistent report of HIV status. Of 1054 attendees, 288 (27.3%) were HIV positive and 830 (78.8%) self-reported knowledge of HIV status. Not knowing one's HIV status was associated with male gender [adjusted Odds Ratio (aOR) 2.66 (95% confidence interval (CI) 1.70-4.18] medical circumcision [aOR 0.48 (95% CI 0.24-0.95)] and site [Gauteng Province (GP)-aOR 6.20 (95% CI 3.51-10.95), Eastern Cape (EC)-aOR 17.29 (95% CI 10.08- 29.66) versus Free State (FS)/ Western Cape (WC) sites]. Of 219 HIV positive attendees with knowledge of HIV status, 136 (62.1%) self-reported being HIV positive, of whom 80 (58.8%) reported taking ARVs in the preceding 3 days. Inconsistent report of status was associated with males [aOR 2.26 (95%CI 1.05-4.87)], prior STI treatment [aOR 0.33 (95% CI 0.16-0.69)], recent HIV testing (6months) [aOR 3.20 (95% CI 1.62-6.36)] and site [GP-aOR 6.89 (95% 3.21-14.82), EC-aOR 5.08 (95% CI 2.15-11.64) versus FS/WC sites]. Knowledge of HIV status was lower than targeted. HIV testing and linkage to care services are essential in STI-related care and validation of self-reported indicators in this population maybe necessary.

Dr Ranmini Kularatne

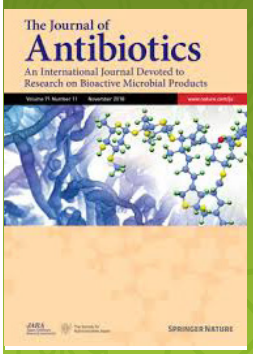
Dr Tendesayi Kufa

Trends in *Neisseria gonorrhoeae* antimicrobial resistance over a ten-year surveillance period, Johannesburg, South Africa, 2008-2017

Kularatne R, *Maseko V, Gumede G,* ***Kufa T.***

The Journal of Antibiotics
Impact Factor: 2.033

In South Africa, sexually transmitted infections (STIs) are managed through a syndromic approach at primary healthcare centres (PHCs). *Neisseria gonorrhoeae* is the predominant cause of male urethritis syndrome. We describe antimicrobial resistance patterns and trends in *Neisseria gonorrhoeae* during a ten-year surveillance period at a large PHC in Johannesburg. *Neisseria gonorrhoeae* was cultured from genital discharge swab specimens obtained from consenting adult patients presenting at the Alexandra Health Centre in Johannesburg between 2008 and 2017. Isolates were tested for antimicrobial susceptibility by Etest™ (cefixime, ceftriaxone, ciprofloxacin) or agar dilution (penicillin, tetracycline, azithromycin). Results: During the period of surveillance, high-level resistance prevalence increased from 30% to 51% for penicillin (p-value for trend < 0.001), 75% to 83% for tetracycline (p-value for trend = 0.008), and 25% to 69% for ciprofloxacin (p-value for trend < 0.001). Analysis did not reveal high-level resistance to spectinomycin or a minimum inhibitory concentration (MIC) creep for extended-spectrum cephalosporins, and the prevalence of intermediate-resistance to azithromycin was less than 5%. High prevalence resistance to penicillin, tetracycline, and ciprofloxacin in *N. gonorrhoeae* obviates their use in future national treatment algorithms for genital discharge. It is essential to continue monitoring for emerging resistance to currently recommended antimicrobial therapy in this rapidly evolving pathogen.



Prof Nazir Ismail

In vitro approaches for generation of *Mycobacterium tuberculosis* mutants resistant to bedaquiline, clofazimine or linezolid and identification of associated genetic variants

Ismail NA, *Omar SV, Peters RPH.*

Journal of Microbiological Methods
Impact Factor: 1.701

Bedaquiline, clofazimine and linezolid are pertinent drugs for drug-resistant tuberculosis. Drug-resistant mutants provide insight into important resistance acquisition mechanisms. Methods for in vitro *Mycobacterium tuberculosis* mutant generation are poorly described. Induction (serial passaging) and spontaneous (adapted Luria-Delbrück assay) approaches using *M. tuberculosis* ATCC reference strains (one fully-susceptible, four unique mono-resistant) were performed. Mutant MIC values were confirmed (MGIT960) and resultant RAVs compared between approaches and to a catalog of previously published RAVs. Mutant MIC values showed a 3-4-fold (induced) and a 1-4-fold (spontaneous) increase compared to baseline. The pyrazinamide-resistant strain had higher baseline MIC values and acquired resistance (≥4-fold) in fewer passages than other strains (induction approach) for bedaquiline. Previously described and novel RAVs in atpE (8 vs. 1) and rv0678 (4 vs 12) genes were identified in bedaquiline- and clofazimine-resistant mutants. No rv1979c and rv2535c RAVs were identified. Previously described RAVs were identified in rplC and rrl genes for linezolid-resistant mutants. Both approaches successfully led to in vitro mutants with novel RAVs being described in atpE and rv0678 genes. It was observed that pre-existing resistance may influence mutant phenotypic and genotypic characteristics and warrants further attention.

Dr Ashika Singh-Moodley

Prof Olga Perovic

Laboratory based antimicrobial resistance surveillance for *Pseudomonas aeruginosa* blood isolates from South Africa

Singh-Moodley A, *Duse A, Naicker P, Kularatne R, Nana T, Lekalakala R, Mbelle N, Dawood H, Han KSS, Ramjathan P, Bhola P, Whitelaw A,* ***Perovic O.***

Journal of Infection in Developing Countries
Impact Factor: 1.330

Antimicrobial resistant bacterial infections are widespread globally and increases in antimicrobial resistance presents a major threat to public health. *Pseudomonas aeruginosa* is an opportunistic healthcare-associated pathogen with high rates of morbidity and mortality and an extensive range of resistance mechanisms. This study describes the antibiotic susceptibility profiles of *P. aeruginosa* isolates from patients with bacteraemia submitted by sentinel laboratories in South Africa from 2014 to 2015. Organism identification and antimicrobial susceptibility testing were done using automated systems. Molecular methods were used to detect common resistance genes and mechanisms. Overall the susceptibility was high for all antibiotics tested with a decrease over the two-year period. There was no change in the MIC50 and MIC90 breakpoints for all antibiotics from 2014 to 2015. The MIC50 was within the susceptible breakpoint range for most antibiotics and the MIC90 was within the susceptible breakpoint range for colistin only. Phenotypically carbapenem non-susceptible isolates harboured the following plasmid-mediated genes: blaVIM (n = 81, 12%) and blaGES (n = 6, 0.9%); blaNDM (n = 4, 0.6%) and blaOXA-48 and variants (n = 3, 0.45%). Porin deletions were observed in one meropenem non-susceptible isolate only, and multi-drug resistance efflux pumps were expressed in the majority of the non-susceptible isolates investigated. BlaVEB-1, blaIMP and blaKPC were not detected. The prevalence of resistance to commonly used antibacterial agents was low for *P. aeruginosa* isolates and similarly, tested resistance mechanisms were detected in a relatively small proportion of isolates. Findings in this study represent baseline information for understanding antimicrobial susceptibility patterns in *P. aeruginosa* isolates from blood. Our surveillance report may assist in contributing to hospital treatment guidelines.

Dr Kathleen Subramoney

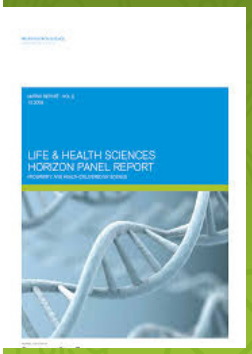
Dr Florette Treurnicht

Human bocavirus, coronavirus and polyomavirus detected among patients hospitalised with severe acute respiratory illness in South Africa, 2012-2013

Subramoney K, *Hellferscee O, Pretorius M, Tempia S, McMorrow M, von Gottberg A, Wolter N, Variava E, Dawood H, Kahn K, Walaza S, Madhi SA, Cohen C, Venter M,* ***Treurnicht F.***

Health Science Reports
Impact Factor: 0.71

To investigate the prevalence of human bocavirus (hBoV), human coronaviruses (hCoV), and human polyomaviruses (hPyV) among patients with severe acute respiratory illness (SARI), in South Africa. The study included 680 South African patients randomly selected in age defined categories from hospitalised patients enrolled through SARI surveillance during 2012 to 2013. A multiplex reverse transcription real-time polymerase chain reaction assay was used to detect hBoV; hCoV-OC43, hCoV-229E, hCoV-NL63, and hCoV-HKU1; and Washington University hPyV (hPyV-WU) and Karolinska Insitute hPyV (hPyV-KI), in respiratory tract specimens collected from patients with SARI. All respiratory specimens from patients enrolled through SARI surveillance were also routinely tested by multiplex reverse transcription real-time polymerase chain reaction for adenovirus; enterovirus; human metapneumovirus; parainfluenza virus types 1, 2, and 3; respiratory syncytial virus; rhinovirus; influenza A, and influenza B. Human bocavirus, hCoV-229E, and hPyV-WU were detected in 3.7% (25/680), 4.1%(28/680), and 4.1%(28/680) of respiratory specimens, respectively. All other viruses were detected in <2% of specimens. Rhinovirus was the most common coinfecting virus (21.4%-60.7%), followed by adenovirus (21.4%-39.3%), and respiratory syncytial virus (10.7%-24.0%). Testing for the additional viruses (hBoV, hCoV, and hPyV) decreased the number of specimens that initially tested negative by 2.9% (20/680). Inclusion of laboratory tests for hBoV, hCoV-229E, and hPyV-WU in differential testing algorithms for surveillance and diagnostics for suspected cases of respiratory illness of unknown cause may improve our understanding of the etiology of SARI, especially in a country like South Africa with a high number of immune compromised persons.



Prof Nelesh Govender

Initiatives from the Federation of Infectious Diseases Societies of Southern Africa (FIDSSA) to tackle infectious diseases in South Africa and the region

Govender NP, *Reubenson G.*

South African Journal of Infectious Diseases
Impact Factor: 0.39

Infectious diseases continue to contribute to suffering and death in southern Africa. In the second South African national burden of disease study, 33.6% of more than half a million deaths in 2012 were attributed to HIV or TB and 13.5% deaths were attributed to other communicable diseases, maternal/perinatal conditions or nutritional deficiencies. While the study's authors reported a substantial decline in HIV- and TB-associated mortality since 2006 associated with the expanded antiretroviral treatment programme, mortality associated with communicable diseases other than HIV and TB has not declined. This unchanged mortality may reflect South Africa's limited progress in combating preventable or treatable infectious causes of death such as pneumonia, diarrhoeal diseases and sepsis in children and adults. The relentless emergence of antimicrobial resistance (AMR) in bacterial, fungal, viral and parasitic pathogens globally compounds this issue and may ultimately result in untreatable infections in the community and healthcare settings. Delivery of high-quality patient care and public health interventions to prevent infectious diseases in southern Africa are also compromised by 'silos' in the healthcare system, poor up- and down-referral systems and an inability to link patients who repeatedly seek care for chronic infectious diseases at different levels in the system. Conversely, novel diagnostics and treatments as well as strategic information from national laboratory record linkage offer opportunities to turn this infectious diseases tide.

Prof Olga Perovic

Dr Erika van Schalkwyk

Antimicrobial resistance surveillance in the South African public sector

Perovic O, *Ismail NA,* ***Van Schalkwyk E.***

South African Journal of Infectious Diseases
Impact Factor: 0.39

Colonisation and infection due to multidrug-resistant (MDR) bacteria has become a significant public health concern with both clinical and economic consequences. Surveillance for antimicrobial resistance (AMR) is conducted not only to detect changes or variation in AMR either geographically or over time, but is a vital component of any antimicrobial stewardship programme. Integrated health data on bacterial AMR were obtained from an electronic database of antimicrobial susceptibility testing (AST) results generated by public health laboratories in South Africa. This report was designed to provide information on AMR rates in bacterial pathogens causing both community-associated and healthcare-associated infections and was prepared by the Centre for HAIs, AMR and Mycoses (CHARM) and Surveillance Information Management Unit (SIMU) at the National Institute for Communicable Diseases (NICD) and Corporate Data Warehouse (CDW) at the National Health Laboratory Service (NHLS).

Prof Nazir Ismail

Collated data of mutation frequencies and associated genetic variants of bedaquiline, clofazimine and linezolid resistance in *Mycobacterium tuberculosis*

Ismail NA, *Omar SV, Peters RPH.*

Data Brief

Impact Factor: Score unavailable

A comprehensive literature search was conducted to obtain previously published resistance associated mutations for bedaquiline, clofazimine and linezolid for *Mycobacterium tuberculosis*. Where possible, mutation frequencies for these three drugs were also identified. This catalog of previously published mutations could serve as a reference for comparing mutations associated with either in vitro or clinical resistant mutants. The usage of these data was seen in our study relating to approaches for resistance mutant creation (in vitro approaches for generation of *Mycobacterium tuberculosis* mutants resistant to bedaquiline, clofazimine or linezolid and identification of associated genetic variants (Ismail et al., 2018 in press). Previously published mutations for clofazimine were described in the rv0678 and rv1979c genes, for bedaquiline in atpE, rv0678 and rv2535c (pepQ) genes and for linezolid in the rplC and rrl genes.

All Impact Factors were sourced from Web of Science

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