THE FEDERATION OF INFECTIOUS DISEASES SOCIETIES OF SOUTHERN AFRICA

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16th ICID, 2-5 April 2014. 1800 delegates, 120 countries and many happy memories. Thanks Team FIDSSA!

Points of interest

Feedback from 16th ICID

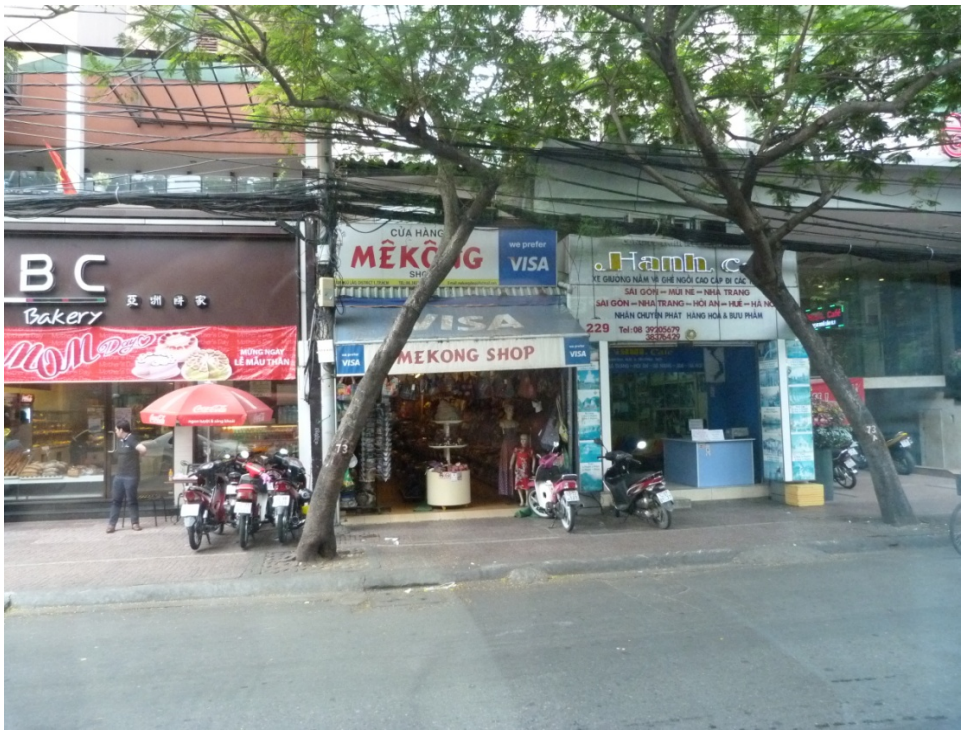
Paediatric TB

National AMR Strategy on its way

News from Ho Chi Minh City and the Asia Pacific Travel Health Conference

South African Society of Travel Medicine

From polio to yellow fever, from trichinella to rickettsial infections and, of course, malaria. The changing scene of infectious diseases, the impact of vaccination (or the lack thereof) was discussed, debated and argued at the Asia Pacific Travel Health Conference held in Ho Chi Minh City recently.



Yellow fever

The WHO has updated its information relating to yellow fever country requirements (http://www.who.int/ith/ITH_country_list.pdf?ua=1) and a few additional countries now require proof of yellow fever vaccination upon entry. Interestingly, in a presentation given by Dr David Freedman, it appears that the determining factor in yellow fever vaccine response in HIV individuals is viral load dependant and not the CD4 Count.

Polio

The importance of ongoing surveillance was demonstrated in a report on the finding of polio virus in the sewage system in Israel. Stool samples, mostly in children who had only received IPV, were positive. It is thought that the resurgence of polio was due to the fact that Israel had changed its policy from using OPV in the EPI programme to IPV. It is considered important therefore to use OPV in the EPI rather than IPV. If the surveillance was not in place an outbreak of polio could have resulted which would have taken considerable time and effort to control. The WHO has advised that all countries using only OPV should add one IPV in the schedule. Recently three countries have been exporting polio virus being Syria, Cameroon and Pakistan. Travellers to countries should be fully immunised against polio prior to travel. If there is a history of prior immunisation of three or four doses, a booster dose must be administered if the last dose was more than twelve months prior to travel. If only IPV was given, the booster must then be OPV.

Pertussis

Pertussis has once again reared its head. The whole cell vaccine was introduced in the 1940s, and was replaced with the acellular vaccine which is less effective – six years at best. There has been increase in the number of cases and it is estimated that the incidence is in excess of 50 million cases per year, particularly in Asia, Africa and South America. Death occurs in children who are usually less than six months old. This stresses the importance of immunising adolescents and adults so as to ensure longer protection. Treatment, to interrupt household transmission, must be started early and the antibiotic of choice is azithromycin.

Dengue fever

Dengue fever is a hot topic at the moment with predictions of dengue outbreaks during the World Cup in Brazil. Annelies Wilder-Smith reported in detail on the global burden of dengue. The incidence of Dengue in Africa is unknown but ten cases of Dengue fever were reported in travellers returning from Angola in 2013. Dengue is spreading, the reasons for which are complex; the greatest problem being that of uncontrolled rapid urbanisation with little or no vector control.

Travel Health Africa: Quo Vadis?

SASTM will be hosting Annelies Wilder-Smith at its Congress to be held in Durban from 18 – 21 September and she will provide an update on the dengue situation and vaccine development. Included in the programme are presentations on sexually transmitted infections in travellers (Prof A Hoosen), trypanosomiais, enteric infections in travellers and meningitis.
The programme is downloadable at http://www.sastm.org.za/Academic%20programme%20Nov%2013%20Website.pdf

The keynote address will be delivered by the President of FIDSSA, Professor Marc Mendelson. Registration and other details are available at www.sastm.org

Update from 9th International Conference on *Cryptococcus* and Cryptococcosis

sascm
South African Society for Clinical Microbiology

The Royal Institute for Tropical Diseases (KIT) in Amsterdam hosted the 9th International Conference on *Cryptococcus* and Cryptococcosis (ICCC-9) from 15 to 19 May 2014. The conference attracted approximately 250 clinicians, epidemiologists and basic scientists from resource-limited and resource-rich countries to discuss new trends in clinical disease management, antifungal treatment strategies, prevention and control of disease, immunology, pathophysiology and molecular biology. All sessions were held as plenaries. Short master classes on genomics and clinical management were held immediately after the formal close of the conference.

Public health highlights: Revised estimates of global burden of HIV-associated cryptococcal meningitis were presented based on newer data on cryptococcal antigenaemia prevalence and the impact of ART programmes. The earlier published estimate for sub-Saharan Africa of 720 000 cases per annum was revised downwards to 205 000 cases per annum, with a global estimate of 300 000 cases per annum. South Africa's burden of disease was estimated as the second highest in Africa (25 000 cases per annum) following Nigeria (56 000 cases per annum).

The estimated case fatality ratio remained 70% at 90 days post-diagnosis. Cryptococcal screen-and-treat remains an attractive strategy that is now being implemented in 12 countries globally with South Africa leading the way. Approx. 16 000 persons with a CD4+ T-cell count <100 were reflexively screened for cryptococcal antigenaemia in the Gauteng phase 1 programme with 5% being CrAg-positive (up to 30 April 2014). Preliminary data from the ORCAS trial in Uganda (a stepped wedge randomised cluster trial looking at effectiveness of screen-and-treat) showing that the intervention was associated with a survival benefit.

Clinical research highlights: Five multicentre randomised control trials are currently underway to look at shorter, cheaper, less toxic and more efficacious regimens. These include the phase III ACTA trial (including arms with shorter courses of conventional amphotericin B and combination oral fluconazole and flucytosine regimens) the phase II AMBITION trial (short-course liposomal amphotericin B), a phase II ACTG trial (fluconazole dose escalation), the ORCAS trial (shorter course fluconazole for antigenaemia) and a smaller phase 2 trial looking at sertraline. Access to essential medicines and diagnostics was also explored as a theme at the meeting. There is a great deal of interest in the underpinning of disease among non-HIV, non-transplant patients, in part because this a very-difficult-to-manage entity.

Basic science highlights: With the cost spiralling down to $300 per genome, there has been a shift towards whole genome sequencing to explore the molecular epidemiology of *Cryptococcus*. There is also a great deal of work at the host-pathogen interface including the pathophysiology, mechanisms and clinical management of IRIS.

ICCC-9 highlighted the significant progress made across all spheres of cryptococcal research and this can only translate into benefits of patients at risk of this devastating fungal disease.

Detection of HIV-specific T and B cell immunity in highly exposed HIV seronegative individuals

Sexually Transmitted Diseases Society of Southern Africa

Recent evidence suggests that not all individuals are equally susceptible to HIV infection despite multiple high-risk exposures, and that some individuals appear to have a natural resistance to HIV infection. Highly exposed, persistently seronegative (HEPS) individuals have been reported amongst several cohorts such as commercial sex workers, intravenous drug users (IDU), and serodiscordant couples. The correlates of protection that confer this unique “resistance” remains controversial, as no single factor has been identified consistently throughout the different groups. However, there is general consensus that studying these individuals may provide a better understanding of HIV acquisition and progression. The overall goal of this project is to establish an association between NK cell activity and T cell activation and in so doing establish whether specific KIR/HLA allele combinations play a role in increasing or lowering the potential for HIV acquisition.

Ninety six patients were recruited into a 2 year follow-up study where a standard interview was conducted by the study nurse. Ethics approval was granted from University of Witwatersrand ethics committee. Peripheral blood mononuclear cells (PBMCs) was isolated from whole blood and plasma stored . KIR genotyping was determined by real-time PCR while HLA-class 1 typing while HLA-class 1

typing was performed by an in-house assay sequence-specific primer (SSP)- PCR . Luminex assay was used to determine plasma cytokines and 12-color flow cytometry to determine T cell and NK cell function.

The key results of this study were:
KIR genotyping:
a. Most common KIR alleles were 2SDL1, 3DL1, 2DS4 and 2 DP1. Least common KIR allele was 3DS1. No significant difference were observed between HIV-negative participants
b.Expression of IP-10 was significantly different ($p< 0.001$) within the HIV-positive group as compared to the HIV-negative group.
c.Expression of IL-7 were low and not significantly different ($p=0.6506$) between the HIV-negative and HIV-negative individuals.
T and NK cell function testing and evaluation is still ongoing.

Certain individuals remain seronegative despite repeated exposure to HIV. It was found in this study that this "resistant" individuals have KIR genotype profiles that do not differ significantly between the HIV-negative and HIV-positive but significantly differ between the two groups when comparing the IP-10 cytokine expression. Since HIV-negative HEPS had a level of IP-10 that was not previously reported in healthy uninfected individuals, the speculation is that this low levels of IP-10 could reflect a profile associated with resistance to HIV infection.

ICSSA News

The ICSSA webpage has undergone some changes and the chapter committee details have been up-dated as far as possible. Members from Limpopo and the Western Cape are requested to check to see if your chapter details are correct and to contact us with any changes.

All chapters are requested to submit a quarterly report detailing their programmes and news.

North West and Kwazulu Natal don't have active societies (that we are aware of) and new committee members are needed to set up Chapters. Any nominations to take the lead in creating an Infection Prevention and Control 'conscience' in these areas will be most welcome!

Free State: MICI (Multi-disciplinary Infection Control Indaba) has responded to our request to re-energize the Chapter and I am happy to announce that their first study day for 2014 is scheduled for the 14th June. We wish them every success!
Johannesburg: GICS (Gauteng Infection Control Society) continue to run quarterly study days with the next one scheduled for 26th June.
Pretoria: PIF (Infection Control Forum) continue to run quarterly study days. Next one scheduled in July.
Western Cape: Infection Control Society also continue to run quarterly study days with the next one scheduled for June. They have also just elected a new committee with Yolanda van Zyl as Chairperson, Vida Morris as secretary and Michelle Osborne as secretary.
Eastern Cape: Ibhayi Infection Control Society has a committee in place, hold meetings and host talks. They are however, resource strained and need support.

Going forward, society study day programmes can be submitted to me and they will be made available on our webpage under 'News'.

We look forward to feedback from the Limpopo Infection Control Society as well as the Namibia Infection Control Society.

Competencies and a motivation for a formal standardized course in Infection Prevention and Control that is recognized by the South African Nursing Council is in draft and will be taken forward during this quarter.

Thanks to all for the tremendous amount of support for the ICAN 'Colour Africa Orange' drive, but.... the map on the WHO site is now green and South Africa doesn't seem to be represented! This is disappointing, but I am sure, just a temporary glitch and we will be able to see our impact when this is rectified. Professor Mehtar will take this up and give us feedback.

An executive member will represent ICSSA at ICAN in Zimbabwe during November. There are also 2 bursaries and the conference link will be placed onto our webpage.

If you would like to share anything or have comments or suggestions, please contact either myself (joy.cleghorn@lifehealthcare.co.za); Lesley Devenish (Lesley.Devenish@netcare.co.za) or Briette du Toit (briette.dutoit@mediclinic.co.za)

Highlights from the 16th ICID

The 16th ICID was held in Cape Town in April this year. This is the second time it has been held in Africa, and was a first for South Africa. It was hosted locally by FIDSSA and was very well attended by delegates, who enjoyed a wide array of topics from a distinguished faculty. With a programme such as this, it was inevitable that delegates would miss parallel sessions with great topics. It also gave local researchers an opportunity to showcase their research and present issues pertinent to ID in Africa.

There were some broad themes that were echoed across sessions that tied in with recent outbreaks. There was a strong emphasis on the concept of "One Health", which is the philosophy that the healthcare of humans, animals and the environment are all linked. The relationship of pathogen, human, vector and reservoir does not fully allow the prediction of the emergence of disease, and one health looks at addressing how disease emergence, transmission and spread are also linked to human behaviours, sociocultural and political systems, human-animal interactions and environmental changes.

This was seen in the session on the Surveillance of Zoonotic Diseases, when William Karesh described how 60% of all human pathogens are shared with wild or domestic animals. He outlined how the Emerging Pandemic Threats (EPT) Programme was working to identify ways to predict and preempt the next pandemic zoonosis at its source through identifying high risk species such as non-human primates, rodents and bats, and high risk geographic areas in Latin America, Africa and South east Asia and conduct surveillance to identify circulating and emerging pathogens. Over 35 000 animals have been tested and 200 new viruses have been described. Local partnerships have been developed to build laboratory capacity and outbreak readiness, with a focus on maintaining animal, human and

environmental health. As a practical example he described how the EPT was involved in the MERS CoV outbreak in helping identifying the camel reservoir.

Similar surveillance work was described by Didier Raoult who discussed Rickettsioses in Africa. He challenged the traditional geographic distribution patterns of the Rickettsial species and how, in West Africa, Rickettsioses are a common cause of febrile illness in the indigenous populations. He also showed how Rickettsia felis infection and Malaria share common epidemiological patterns regarding geographic distribution, seasonality, asymptomatic infections and a potential vector, with Rickettsia species having been found in Anopheles and Aedes mosquitoes.

Larry Madoff took the theme further by explaining how different surveillance systems worked, and how ProMED and other systems differed from the traditional notification systems to provide a real time ability to track diseases in animals and humans and allow early information dissemination and interventions. The human sociocultural and political systems and surveillance were further explored in sessions on "ID in refugees and migrants" as well as in "Travelling bugs, far and wide", where Sachit Basari described the incredible event of the 2013 Kumbh Mela in Allahabad where 100 million Hindu pilgrims gather to bathe in the sacred river over 55 days. This is the largest peaceful human gathering and an entire city with amenities and clinics are temporarily constructed and the flow of the river is adjusted to ensure it is not too fast to be unsafe, but enough to flush the river. Real time digital surveillance was used to monitor trends in symptoms and scripts to identify outbreaks. Measles and drug resistant TB were found and he further discussed how this sort of gathering could also be used for screening and interventions like vaccinations.

Ziad Memish bought the concepts together in his plenary on the MERS-CoV outbreak. He worked back from the original clinical description of the outbreak in which males with comorbidities suffered more severe disease, with early mild non-specific symptoms followed by severe pneumonia with an overall case fatality rate of 39%. The initial cases tended to suffer more severe disease, whilst secondary cases had more attenuated disease, with more cases of asymptomatic or mild disease subsequently being described with less mortality. The route of transmission was not yet evident, but transmission occurred in family and nosocomial clusters, however the Ro was felt to be well below pre-pandemic SARS levels and unlikely to be as serious a threat. The source was likely to be related to bats or camels, with a single specimen from a bat showing 100% nucleotide identity from a human index case and epidemiological links between a camel and human infection. Of concern, even with a lower Ro, was the potential for an outbreak at the Hajj, with strict guidelines and conditions being put in place. Travelers with comorbidities, immune deficiencies, terminal illness or malignancies, as well as pregnant women and young children are to postpone the performance of the Hajj and Umrah for the year. There have been no reports of MERS-CoV at the Hajj in 2 years and surveillance is carried out through active screening in hospitals and extra laboratory capacity in put in place over Hajj season.

Another strong theme was that of antimicrobial resistance. Again the role of humans, animals and the environment was explored. Ursula Theuretzbacher discussed global resistance hotspots and the role of low and middle income countries in the problem. Antibiotic use in animal farming and antibiotic contaminated water from waste water treatment plants and antibiotic manufacturing factories are present in manure rich soils and surface water allowing genetic exchange of resistance genes with human gut commensals as well as direct low level human exposure to environmental antibiotics. This is common in China and India and Ramanan Laxminarayan further described how in low income countries antibiotics are not only freely available without a script, but even with a doctor, prescriptions are

no more appropriate than when no doctor is consulted. Satisfying patient needs are the main driver to prescriptions and may also be used to compensate for failures in public health systems that are more difficult to rectify like improved sanitation, hand washing and safe water. India was highlighted as a hotspot both in terms of environmental contamination and inappropriate prescribing, which together with global travel spreads resistant organisms to and from these countries. In addition, the economic impact of even 10% resistance to simple affordable antibiotics would make much of modern medicine financially unaffordable, such as surgery and transplants

Ross Davidson in "20 years of antibiotic prescribing" outlined the drying up pipeline of antimicrobials and the disproportionate increasing antimicrobial resistance with the implications of treatment failure, expensive agents, longer hospital stays and no alternative agents. He echoed the drivers of resistance with inappropriate use, no prescriptions, sub-therapeutic exposure, low potency and frequent exposure to the same class as contributors. Macrolide exposure within 3 months significantly increased the chance of infection with an invasive macrolide-resistant streptococcus pneumoniae. The resistance rate increases proportionately (and significantly) with increasing macrolide half-lives e.g. Azithromycin > Clarithromycin > Erythromycin. Thus antibiotics with a long half-life may preferentially select resistant organisms due to exposure of colonizing bacteria to sub-therapeutic antimicrobial levels for a sustained period of time e.g. Azithromycin. Also, fluoroquinolone use within 3 months increased the chance of infection with resistant Strep. Pneumoniae. To reduce resistance he suggested the use of Clinical guidelines, patient / physician education, appropriate vaccination and regulating antimicrobial use in agriculture. He strongly supported guidelines with the caveat that they have to be updated and published at regular intervals and should address issues of appropriate use, discouraging antibiotics for viral illness, considerations around potency/best in class and that they should be prescribed at a maximum dose. There were many other sessions dealing with the practical issues around how to implement Antibiotic Stewardship and manage the current therapeutic problems of drug resistant organisms.

Management of invasive fungal infections (Dr Sean Wasserman)

There was a symposium dedicated to the controversial topic of intervention or prevention of invasive fungal infection in high-risk patient populations.

There is growing resistance to antifungals, and risk factors include prolonged use of fluconazole and voriconazole, as well as possibly echinocandins. CLSI susceptibility breakpoints have been updated and are now more conservative and similar to those published by EUCAST. Major updates in the two guidelines are as follows:

C glabrata and fluconazole: CLSI does not provide a breakpoint value, EUCAST reports susceptibility at MICs ≤ 0.002

C glabrata and caspofungin: CLSI has lowered the susceptibility breakpoint to isolates with MICs ≤ 0.25. No EUCAST criteria exist, and it is recommended that breakpoints for other echinocandins be used as surrogates to determine susceptibility.

C albicans is still the most common cause of invasive fungal infection and remains reliably susceptible to triazoles and echinocandins. *C parapsilosis* is becoming increasingly prevalent and has reduced susceptibility to triazoles, and should be taken into consideration when prescribing empiric antifungal therapy. *C glabrata* is more common in older patients, and therefore fluconazole should be avoided as empiric therapy in this population. There is a concerning signal of emerging resistance to caspofungin (but not to other echinocandins). This is more frequent in fluconazole resistant isolates, is associated with *FKS1* and *FKS2* gene mutations and may lead to clinical failures.

In an observational study of over 2000 episodes of candidemia in North America, the incidence of non-albicans species was 54%. The highest 12 week mortality rate was associated with *C krusei*, at 53%, although this only represented 2.5% of isolates. The most common non-albicans species was *C glabrata*, at 26%, highlighting the need to understand local epidemiology when using empiric antifungal therapy [Horn CID 2013].

The presenter listed some clinically important characteristics of non-albicans candida:

C tropicalis: high virulence, colonisation possibly an indication for pre-emptive therapy.

C parapsilosis: associated with CVC-related infections & contamination of hyperalimentation solutions.

C lusitaniae: inherent resistance to amphotericin

There was a strong emphasis on the use of echinocandins to treat invasive candida infections. This recommendation is supported by their broad spectrum of activity against candida and non-candida species, fungicidal activity, penetration of biofilms, low potential for drug-drug interactions, and consistent clinical evidence of efficacy as shown in randomised trials.

The presenter recommended against treating candida recovered from tracheal aspirates or sputum, urine cultures and asymptomatic peritoneal drain cultures in medical patients.

In the ICU about 20% of patients are colonised with candida. The rate of colonisation of tracheal aspirates is lower for aspergillus, however half of all positive cultures represent invasive disease and thus should always be treated. The risk factors for intra-abdominal infections with candida include recurrent surgery, particularly with upper GIT surgery, and anastomosis leakage.

Key concepts in the management of invasive fungal infection:
Remove foreign material
Start antifungal therapy early
Using an empiric echinocandin improves survival by > 10%
Definitive therapy with an echinocandin for late onset candidemia reduces mortality by > 60%

Inadequate therapy is the main risk factor for death, but the presence of liver disease is another important prognostic factor. It was suggested that initial therapy can be deescalated to fluconazole only after 10 days of intravenous administration, and if there is confirmed susceptibility and if the patient is able to tolerate oral treatment.

Paediatric TB: always something new from Africa - James Nuttall

Improved diagnosis and management of paediatric TB are major priorities. Although up to a million new cases of childhood TB are diagnosed globally each year, the true incidence of TB in children is unknown as a result of inability or unavailability of microbiological confirmation. Both over diagnosis and underdiagnosis are common partly because there is considerable overlap between the clinical presentation of TB and other diseases. In many clinical settings, the diagnosis of TB in young children still relies on suggestive clinical features, history of a close contact with another individual with TB with or without evidence of latent TB infection indicated by tuberculin skin testing (or interferon gamma release assay (IGRA) on blood) and radiological features. Microbiological confirmation using culture or polymerase chain reaction (PCR) is not routine. There have however been a number of recent developments in relation to paediatric TB diagnosis and management.

Despite its well-known limitations in the diagnosis of TB infection and disease, the recent nationwide shortage of Mantoux skin tests (after it was noted in 2013 that there were some batches of Tuberculin PPD RT23 that failed to meet the required potency specification at the end of their shelf life) highlighted our limited diagnostic armamentarium and the risks associated with a sole registered supplier. Following a temporary hold placed on the distribution of batches in August 2013, bottlenecks at the manufacturer exacerbated dwindling supplies. There are no locally produced TB skin tests available, and alternative international suppliers are currently unregistered in South Africa. The Tine test has been unavailable on the local market for the last few years. It is hoped that availability of the Mantoux test will be restored by the end of June 2014.

Recently published research [N Engl J Med 2014;370:1712-23] investigated the use of genome wide RNA expression in host blood to distinguish TB from other diseases that are prevalent among African children with and without HIV infection. Researchers explored the use of a score for disease risk derived from the transcriptional signature as the basis for a possible diagnostic test.

Children (n=2955) undergoing evaluation for suspected TB were recruited from three high burden African countries: South Africa, Malawi and Kenya. A complex study design enrolled children into a discovery cohort (South Africa and Malawi) and a validation cohort (Kenya). A systematic diagnostic evaluation was performed in children younger than 15 years of age who had a cough, fever, or weight loss of more than 2 weeks' duration; pneumonia that was unresponsive to antibiotics; any other clinical findings that were suggestive of TB; or a history of close contact with an adult who had TB. Investigations included chest radiography, C-reactive protein level, a serologic test or PCR assay for HIV, and a tuberculin skin test, with or without an IGRA. Two spontaneous or induced sputum samples and a specimen of tissue or cerebrospinal fluid (if clinically indicated) were examined for acid-fast bacilli and cultured for mycobacteria. The Xpert MTB/RIF21 real-time PCR assay was performed on respiratory samples in the Kenyan cohort. Bacterial cultures, histologic examination of tissue-biopsy specimens, and analysis of blood films for the presence of malaria were performed as clinically indicated. Clinical follow-up was undertaken at 3 months to confirm that children with latent TB infection remained free of active TB and other diseases and to determine whether there had been a response to treatment in children with confirmed or suspected TB.

Children were allocated to one of 4 pre-defined groups: culture-confirmed TB, culture-negative TB, other diagnosis (TB excluded), and latent TB. Culture-negative cases were further categorised into one of the following categories: highly probable TB, probable TB and possible TB.

The study was able to identify a 51-transcript signature from microarray analysis of blood RNA expression that could distinguish TB from other diseases. A risk score based on the signature for TB and for diseases other than TB showed a sensitivity of 82.9% (95% confidence interval [CI], 68.6 to 94.3) and a specificity of 83.6% (95% CI, 74.6 to 92.7) for the diagnosis of culture-confirmed TB. Among patients with culture-negative TB who were treated for TB (those with highly probable, probable, or possible TB), the estimated sensitivity was 62.5 to 82.3%, 42.1 to 80.8%, and 35.3 to 79.6%, respectively, for different estimates of actual TB in the groups.

In comparison, the sensitivity of the Xpert MTB/RIF assay for molecular detection of *M. tb* DNA in cases of culture-confirmed TB was 54.3% (95% CI, 37.1 to 68.6), and the sensitivity in highly probable, probable, or possible cases was an estimated 25.0 to 35.7%, 5.3 to 13.3%, and 0%, respectively; the specificity of the assay was 100%.

This is a very significant result and it is hoped that this line of investigation will ultimately culminate in the availability of improved diagnostic tests for childhood TB.

Tuberculous meningitis (TBM), recently identified as the most common form of bacterial meningitis in the Western Cape province of South Africa, presents both diagnostic and therapeutic challenges and is associated with significant morbidity and mortality. World Health Organization (WHO) guidelines (2010) recommend treatment with 2 months of isoniazid (INH), rifampicin (RMP), pyrazinamide (PZA) and ethambutol followed by 10 months of INH and RMP. Following research by Donald et al. published in 1998, local practice has been to treat TBM with a short, intensive 4-drug regimen consisting of daily INH 20 mg/kg (maximum 400 mg daily), RMP 20 mg/kg (maximum 600 mg daily), PZA 40 mg/kg (maximum 2 g daily) and ethionamide (ETH) 20 mg/kg (maximum 750 mg daily), all given in a single daily dose, for 6 months duration. HIV-infected children, however, are treated for 9 months because of perceived slower response to treatment. Prednisone 2 mg/kg/d (maximum 60 mg/d) is given for the first month of treatment and gradually discontinued over the next 2 weeks.

A review of evidence behind the WHO guidelines for TBM treatment in children [*J Trop Pediatr*. 2008;54:220–224] found that all existing trials assessing anti-TB treatment for TBM had limited power, poor methodology and used varying treatment regimens with conflicting results. The studies reviewed reported similar completion and relapse rates when 6 months therapy with at least INH, RMP and PZA was compared with longer treatment regimens, suggesting that 6-month therapy for TBM may be sufficient. Shorter treatment regimens are cheaper, less labour-intensive and may improve patient compliance.

A recently published prospective study [*Pediatr Infect Dis J* 2014;33:248–252] from Tygerberg Children's Hospital described local experience with short-course intensified TBM treatment (mostly 6 months of RMP/INH/PZA/ETH for HIV-uninfected and 9 RMP/INH/PZA/ETH for HIV-infected). Amongst 184 children with TBM with median age 58 months and HIV prevalence of 14% (22/155 children tested), 90 (49%) children were treated at home after the first month of therapy while all others received their full treatment in hospital. Anti-TB drug-induced hepatotoxicity occurred in 5% (8 of 143 children tested) and in all 8 cases, the original regimen was restarted without recurrence.

After treatment completion, 147 (80%) children had a good outcome, 7 (3.8%) died. There was no difference in outcome between HIV-infected and HIV-uninfected children who completed treatment (*P* = 0.986). The authors concluded that short intensified treatment is safe and effective in both HIV-infected and HIV-uninfected children with drug-susceptible TBM.

The Hospital Level Paediatrics Standard Treatment Guidelines and Essential Medicines List for South Africa (2013) and the National Department of Health Tuberculosis Guidelines (2013) recommend a TBM regimen comprising RMP (20mg/kg/day, maximum daily dose 600mg), INH (20mg/kg/day, maximum daily dose 400mg), PZA 40mg/kg/day, maximum daily dose 2000mg, and ETH (20mg/kg/day, maximum daily dose 1000mg. The recommended treatment duration is 6 months but if there are concerns about clinical progress, the treatment can be prolonged by another 3 months to 9 months in total and a paediatrician should be consulted.

The National AMR Strategy

A number of factors have come together to ignite work towards a national strategy for antimicrobial resistance (AMR) in South Africa. Following GARP-SA's situational analysis in 2011 and SAASP's dual approach of introducing stewardship programmes in our hospitals, and advocacy, a meeting with the National Minister of Health enabled us to highlight the crisis. This bottom-up approach complimented the international drive from WHO, resulting in the adoption of resolution WHA 67.25 'Combating antimicrobial resistance, including antibiotic resistance' on 17th May 2014. This global call to action urges member states to develop or strengthen national plans, strategies and international collaboration for the containment of antimicrobial resistance.

A working group was formed by the NDoH to begin drafting South Africa's strategy. The first draft was reviewed by a large stakeholders meeting in early April and with the resultant feedback, a second draft is now in circulation for comment. Lea will be circulating it to all FIDSSA members via our email database (good time to update your details!). The 4 pillars of the strategy will be governance, surveillance & reporting, stewardship, and prevention. An intesectoral ministerial advisory committee is envisaged to bring together the departments of Health, Agriculture, Forestry and Fisheries, Science and Technology, Education, Trade and Industry, as well as public and private health providers, academia, infection societies and other relevant stakeholders. The work of the committee will cover all forms of antimicrobial resistance, with input form already established programmes in HIV, TB and Malaria.

Please give your input to the strategy document. If your email isn't on file, then please contact Lea, our FIDSSA administrator, at info@fidssa.co.za.