Africa's response to childhood infection

The AfSPID BULLETIN

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EDITOR'S COMMENTARY

Dear Colleagues

Welcome to the seventh edition of our newsletter.

I hope that you have a successful and productive 2018 replete with academic activity.

2017 has come and gone, punctuated by several important infectious diseases developments, including:

- A Lassa fever outbreak in Nigeria causing 501 suspected human cases including 104 deaths between December 2016 and June 2017.
- An Ebola outbreak in Bas Uélé District, Democratic Republic of the Congo in May 2017: This outbreak was fortunately limited to 8 cases (including 5 laboratory-confirmed cases) and 4 deaths. This is in contrast to the largest recorded Ebola epidemic which ravaged West Africa between 2014 and 2016, causing an estimated 28,652 suspected, probable, and confirmed Ebola cases, including 11,325 deaths, and far exceeding the combined total number of Ebola cases reported in approximately 20 previous outbreaks since the 1970s.
- Substantial progress with the Global Polio Eradication Initiative: Thus far there have been only 21 reported cases of wild type polio in just 2 endemic countries reported in 2017 (13 in Afghanistan and 8 in Pakistan). This is the least number of annual cases in history. There have been no new cases of wild type polio in Nigeria or the rest of Africa since the onset of paralysis in the most recent Nigerian case on 21 August 2016. The drive to vaccinate every child continued on the Afghanistan-Pakistan border in 2017, and already in January 2018 new mass immunisation campaigns are planned targeting 5 million children in Afghanistan and 36 million in Pakistan. These interventions will hopefully move the world closer to the ultimate goal of polio eradication.
- An large outbreak of plague in Madagascar: Since the plague outbreak started in that country in August 2017 more than 2400 confirmed, probable or suspected cases have been reported from 57 of the 114 districts (50%), culminating in 209 deaths (case-fatality rate: 9%). 77% of patients experienced pneumonic plague, 15% had bubonic plague, 1 patient experienced *Yersinia pestis* septicaemia and the remaining patients have not yet been classified. The good news is that the shape of epidemic curve indicates that the current outbreak has largely run its course. This large outbreak draws attention to the relation between plague, an ancient disease and the African continent. More than 90% of all cases of human plague are reported in Africa and Madagascar is the most highly endemic country. Madagascar typically experiences a seasonal increase in numbers of human plague between the months of September and April. Thus the current outbreak has occurred in the Madagascar plague season.
- An outbreak of Listeriosis in South Africa: Since January 2017 there has been more than 720 laboratory-confirmed cases reported to the National Institute of Communicable Diseases, including 61 reported deaths (case-fatality rate: 8.4%). Cases have been reported throughout the country 2017 and into 2018. Gauteng, Western Cape and KwaZulu-Natal being the most severely affected provinces. A recent newspaper report described the closure of a poultry processing plant where *Listeria monocytogenes* was isolated. However, investigation is ongoing to identify other food sources for this outbreak.
- A Cholera outbreak declared in Zambia in October 2017, affecting several sub-districts in the capital city, Lusaka: To-date more than 500 cases, including 15 deaths have been reported. This outbreak has been linked to inadequate water supplies, poor sanitation, contaminated food and sub-optimal hygiene practices. This epidemic coincides with the publication by WHO of a global roadmap containing concrete steps for reducing cholera deaths by 90% in 2030. Cholera as we know is a disease of extreme poverty which continues to impact the health and wellbeing of many people on our continent, including communities affected by conflict and famine.

To enrich our understanding of the field of paediatric infectious diseases on the African continent, I encourage and invite you to write regional or local paediatric perspectives on these and other recent / current infectious diseases developments that have occurred on our continent and submit these commentaries to this newsletter for publication.

This edition of the newsletter includes a communiqué from the Nigerian Society for Paediatric Infectious Diseases, reports on recent FIDSSA and WSPID conferences, a

review on solar-powered oxygen therapy and commentary on four publications in our regular journal watch slot.

I hope that you find this edition of the newsletter interesting.

Kind regards, Brian Eley

COMMUNIQUÉ ISSUED BY THE NIGERIAN SOCIETY FOR PAEDIATRIC INFECTIOUS DISEASES (NISPID) AT THE 3rd BIENNIAL GENERAL MEETING AND SCIENTIFIC CONFERENCE, NISPID BGMSC 2017, BENIN CITY, EDO STATE, 21stJune, 2017

Professor Osawaru Oviawe, NISPID National President and Dr Lawal Waisu Umar NISPID Secretary General

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The Nigerian Society for Paediatric Infectious Diseases (NISPID) held its 3rd Biennial General Meeting and Scientific conference at the Doctors House, Benin City, Edo State themed: *"Controlling Paediatric infectious Diseases as a Key to Sustainable Development in a Challenged Economy"*, with subthemes on Epidemic Preparedness, Infections among internally displaced children, Tuberculosis and Antimicrobial resistance. There were 72 participants drawn from academia, research institutes, the private sector, the Ministry of Health, regulatory and donor agencies, the Nigerian Medical Association and the World Health Organization (WHO).

The Edo State Deputy Governor, Rt. Honorable Philip Shaibu chaired the opening ceremony, while the Chief Medical Director, Irrua Specialist Teaching Hospital (ISTH), Edo State, Professor Sylvanus Okugbeni, represented the Guest of Honour, the Honorable Minister of State for Health Dr Osagie Ehanire. The Keynote Address titled, "Rethinking for Success in the Control of Infectious Diseases in Nigeria and Sub-Saharan Africa: it's not about MDGs or SDGs", was delivered by Professor George Akpede, former CMD of ISTH and member, National Lassa Fever Expert Committee. The Vice-Chancellor, University of Benin, the Chief Medical Director, University of Benin Teaching Hospital, the Edo State Chief Judge, Nigerian Medical Association (NMA) and the WHO delivered goodwill messages.

Symposia were held on Antimicrobial Resistance (AMR) and Antibiotic Stewardship; Preparedness and Response for Viral Haemorrhagic Fever (VHF) Outbreaks; Intensified Case Finding and Management of Childhood Tuberculosis (TB); Neglected Tropical Diseases (NTDs) in Nigeria and Problems of Children in Internally Displaced Persons (IDP) camps. The scientific sessions featured presentations on various infections in children, along with product presentations by pharmaceutical companies. The President of NISPID Professor Osawaru Oviawe launched a revised edition of a National job aide titled "Desk Guide on the Management of Childhood TB", on behalf of the National TB, Leprosy and Buruli Control Program.

General Observations:

1. AMR, fueled by inappropriate antibiotic use has become a problem of public health concern
2. There is inadequate epidemic preparedness and response for VHF outbreaks and endemic Lassa fever in the country contributing to devastating effects
3. While NTDs contribute significantly to morbidity and mortality in children, the current efforts at prevention and control have remained donor-driven
4. Childhood TB remains largely neglected resulting in low detection and notification
5. Whereas children in IDP camps face numerous physical, mental and social problems, the existing management efforts are threatened by daunting challenges.

Recommendations

1. Antibiotic stewardship should be ensured at all levels of health care and regulatory bodies should provide leadership and support to expedite a national action plan on antibiotic stewardship
2. There is urgent need for research into indigenous medicinal plant alternatives to replace antibiotic use in animal husbandry
3. There is need to improve on emergency preparedness and response to VHF outbreaks
4. Priority should be accorded to the control and elimination of NTDs in the country through creating awareness and intensified efforts at case detection, treatment and mass prophylaxis
5. Childhood TB case finding and appropriate management require greater priority at all levels of the National Control effort including integration and stronger collaboration with the National Primary Healthcare Development Agency
6. The NTBLCP should facilitate the involvement of relevant stakeholders including private practitioners in policy formulation and implementation to accelerate the achievement of the ambitious goal to End TB in Nigeria by 2035
7. Federal and State Governments should actively engage paediatricians in the provision of care and support for displaced children in IDP camps and within host communities across the country.

REPORT OF THE 7TH FIDSSA CONGRESS

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The Federation of Infectious Diseases Societies of Southern Africa (FIDSSA) held its 7th FIDSSA Congress at the Century City Hotel, Cape Town from the 9th to 11th November, 2017.

The event brought together 530 participants from 25 countries. There was an impressive faculty of both local and international speakers who addressed a large range of topics which included

- Infection Prevention
- Managing infections in adolescents and pregnant women
- Drug-Resistant infections
- Emerging and Re-Emerging Infectious Diseases

For the first time FIDSSA partnered with the International Society for Infectious Diseases (ISID) and the European Society for Clinical Microbiology and Infectious Diseases (ESCMID) in co-sponsored plenary sessions. It was the first time that the Institut Merieux-FIDSSA Young Investigator award was given. It is an award which

recognises outstanding achievement in the field of antimicrobial resistance (AMR).

The 3-day programme was organised into plenary and parallel sessions. During the parallel sessions, participants could choose from an array of topics under the broader headings such as HIV&TB-infants, co-infection and treatment failure; New Directions in Clinical Microbiology; The Alarming Sexually Transmitted Infection epidemic in South Africa; Fungal Infections; Specific Challenges in HIV, and Antimicrobial Research and Development. There were presentations of oral abstracts during the parallel sessions and over 200 poster presentations. The programme commenced with a warm welcome from Professor Marc Mendelson, the President of FIDSSA.

This summary will focus on 3 areas namely; drug-resistant infections and infection prevention, mycotic infections and HIV AIDS among adolescents.

Drug-resistant infections and infection prevention

The worldwide impact of antimicrobials drug resistance is grave. It is estimated that about 700,000 deaths occur in lower middle income countries (LMIC) and 23,000 deaths in the USA.[1] The O'Neill report estimates that almost 700,000 people worldwide, die annually from AMR and there will be about 10 million deaths by 2050 due to AMR.[1]

In a presentation on the management of multi-drug resistance (MDR)-gram negative organisms, **Professor Jesus Rodriguuez-Bano** said it was important for therapy to be individualised in the patient with an infection, through the use of appropriate antimicrobials, source control and resuscitation.

He noted that in choosing the appropriate antimicrobials, the patients' features with regard to the underlying condition e.g. renal failure, age etc. must be considered. Then the bacterial features, which comprise the susceptibility pattern, mechanism of action, species and virulence must be determined. Finally, the source of infection responsible for the inflammatory nature of the condition must be considered.

He said that narrow spectrum antibiotics should be used whenever possible, and to consider the use of the carbapenem sparing agents as well. These include the beta-lactams, aminoglycosides, fluoroquinolones, trimethoprim/sulfamethoxazole and fosfomycin. He said amoxicillin-clavulanic acid or piperacillin-tazobactam if used at adequate dosages, are suitable options for the definitive therapy of susceptible extended spectrum beta-lactamase *E. coli* strains causing bloodstream infections, mainly in the urinary and biliary tracts, and this could help prevent the overuse of carbapenems.[2] He was quick to note however, that patients with high risk of mortality will invariably require combination therapy.

He mentioned that newer drugs like imipenem-relebactam, aztreonam-avibactam and plazomicin, a new generation aminoglycoside, are available for the treatment of multi-drug resistant gram-negative infections.[3,4] However, the cost of these newer antibiotics must be borne in mind and as clinicians we must endeavour to use them judiciously.

Professor Mike Sharland in his presentation on neonatal sepsis and drug resistant infections was concerned that neonatal mortality was not decreasing as fast as child mortality and remained unacceptably high. There is estimated to be 2.9 million deaths in newborns within the first 28 days of life every year.[5] Data from 5 countries with the highest risk of neonatal deaths showed that, AMR is potentially responsible for around 30% of all global neonatal sepsis deaths.[6]

Two main factors underlie this mortality namely; transmission from mothers and nosocomial infections. In the DeNIS study, neonates from 3 tertiary centres in India were followed up from admission till discharge. High rates of MDR were observed in *Acinetobacter spp* (181/222, 82%), *Klebsiella spp* (91/169, 54%), and *Escherichia coli* (52/137, 38%) isolates. Methicillin resistance prevailed in 61% (85/140) of coagulase-negative staphylococci and 38% (43/114) of Staphylococcus aureus isolates. Nearly a 1/4 of the deaths were attributable to sepsis. The population-attributable risks of mortality were 8·6% in culture-negative sepsis, 15·7% in culture-positive sepsis by MDR organisms, and 12·0% in culture-positive sepsis by non-MDR organisms.[7] The high incidence of neonatal sepsis and drug resistance described above is alarming. The study also depicts the changing pattern of organisms isolated in the neonatal period.

To combat the threat of AMR, the one health approach is currently advocated. In her presentation, **Dr Sabiha Essack**, described this as an interaction between humans, animals and the environment. It involves recognising that diseases are transmitted from humans to animals and vice versa, and that both must be tackled together, with the environment serving as a link between both. In that regard the environment also serves as a potential source of MDR organisms. This is depicted in Figure 1.

She noted the fluidity of antibiotic resistant clones, antibiotic resistance genes and mobile genetic elements at the human animal-environmental interface. To this end the Center for Science and Environment in India is already committed to the use of responsible antibiotic use in food animals; surveillance of antibiotic use-residues and resistance; and environmental management to contain AMR.

Figure 1: The One Health Approach (Retrieved from: http://www.climvib.eu/wp-content/uploads/2016/11/One-Health-Approach-WHO.png)

In her discourse she mentioned the objectives of the global action plan on AMR by the WHO namely: Improve awareness and understanding of antimicrobial resistance; strengthen surveillance and research; reduce the incidence of infection; optimize the use of antimicrobial medicines and ensure sustainable investment in countering antimicrobial resistance.[8]

Professor Stephen Harbarth gave a presentation on infection prevention in the hospital. He talked about using a multimodal approach for successful infection control. This he said, involves the use of hand hygiene, antibiotic prophylaxis, prevention of SSI, improved use of devices, vaccines, structural measures (i.e. hospital organisation and management) and surveillance.
He made reference to a study by Pires and Bellissimo-Rodrigues, et al where findings showed that hand-rubbing technique with a fingertips-first emphasis showed greater efficacy than the standard technique in reducing fingertip contamination,

potentially improving hand hygiene-action.[9]This is because hands are implicated in the cross-transmission of microbial pathogens with fingertips as the crux of the problem.
In another recent study the researchers found that all durations of hand-rubbing evaluated, led to significant reductions in bacterial counts. However, reductions achieved after 10, 15, or 20 seconds of hand-rubbing were not significantly different from those obtained after 30 seconds.[10] Thus 15 seconds is probably adequate time to hand rub.

Professor Charles Feldman in his talk on the ethics of antimicrobial use, antimicrobial substances (AMS) and antibiotic resistance raised important ethical issues about the acceleration of antibiotic resistance. He said that the emergence of MDR and extra-drug resistant (XDR) infections accelerate the ethical challenges in treating infectious diseases. This is because isolating a patient with MDR or XDR infection against his or her will, is a trade-off between respect for individual autonomy and public good.

Secondly, the fight with antibiotic resistance raises ethical questions about the fair distribution of resources around the globe. This is because whilst antibiotic use needs to be reduced in some countries around the globe, other countries do not have ready access to effective antibiotics in the first place.

Thirdly, the extensive use of antibiotics in farming and need for AMS raises ethical concerns about the wellbeing and appropriate treatment of farm animals and the way meat is produced. He mentioned that the current farming practices are often lucrative because the use of antibiotics keeps infection rates low. This however comes at the cost of animal welfare and consumer safety when drug resistant infections are transmitted into food.

Fourthly, we have a moral obligation to future generations to protect the effectiveness of antibiotics and not leave a post-antibiotic world behind.[11]

The solution he said would be to: (1) stimulate antibiotic development with incentives by extending patent life, have better approval processes and purchase commitments and tax credits, and (2) use antibiotics more wisely which would have an impact on resistance development, reduce pharmacy costs and toxicity and reduce the acquisition of potentially pathogenic bacteria.[12]

Mycotic infections

The increase in the rate of invasive mycosis results from:

1. The Global AIDS epidemic which has brought with it an increase in the rate of opportunistic infections namely Pneumocystis pneumonia (PCP) and Cryptococcal infections
2. Advances in medical care and treatment such as chemotherapy, transplant and extended critical care which carries with it an increased risk of invasive aspergillosis, PCP, and mucomycosis.
3. Resistance to antifungal agents such as the agricultural-driven, azole resistant *Aspergillus fumigatus*[13], echinocandin resistant *Candida glabrata*[14] and MDR Candida *auris*.

Candida *auris* is an emerging fungus that presents with a serious global health threat.[15] On June 24, 2016, the Center for Disease Control and Prevention (CDC) issued an extraordinary alert, advising US healthcare facilities "to be on the lookout for *Candida auris* in patients". The alert noted that *C. auris* infections had been identified in several countries since 2009.[16] *Candida auris* is often a MDR and virulent organism which causes nosocomial infections, contaminates and persists in the hospital environment.

In an oral abstract presentation, **Erika van Schalwyk** using national laboratory-based surveillance at all public and private-sector hospitals in South Africa, January 2016-June 2017 described the risk factors for candida *auris*. Twenty-nine per cent (12/41) and 85% (35/41) of C. *auris* cases had received prior antifungal/ antibacterial therapy. Being admitted to a private-sector hospital increased the odds of C. *auris* candidemia three-fold (aOR 3.6; 95% CI 1.62-7.77). Other risk factors included older age (aOR 1.01 for every year; 95% CI: 1.01–1.03) and longer hospital stay before first positive blood culture (aOR 1.01 for every day admitted; 95% CI: 1.01–1.03).

Dr Adrian Brink gave a presentation on the prevention and management of antifungal-resistant infections in the Intensive Care Unit (ICU). In his presentation he identified candida species as the predominant agent of fungal sepsis, accounting for 10% to 15% of all health care associated infection (HAIs), and 5% of all cases of severe sepsis and septic shock.
Notably, 1/3 of all episodes of candidemia he said, occurred in the ICU. Invasive candidiasis (IC) is a serious complication in the ICU, with high morbidity and mortality of up to 90% in patients with septic shock. Among patients with IC in the ICU, 2/3 will have candidaemia, and 80% of non-candidaemic patients will have intra-abdominal candidiasis.[17]
However, the epidemiology of Candida infections is continuously changing, with the emergence of new MDR species such as Candida *auris*. There is also in recent times a high prevalence of azole-resistant C. *parapsilosis* causing bloodstream infections in the private sector in SA.[18]

He noted that 70% of critically ill patients receive systemic antifungal (AF) therapy without documented invasive fungal infection, suggesting the need for a paradigm shift in the approach to AF therapy. He noted that, early and appropriate diagnosis and treatment of IC is the key for a significant reduction in mortality due to IC. He suggested three tenets in the approach to AF therapy namely:

***Tenet 1*:** To substitute the concepts of pre-emptive or empiric therapy by ''early'' AF treatment, in which both modalities would be present using biomarkers such as (1,3)-β-D-glucan with associated clinical symptoms and signs.[19]

Tenet 2: Use non-culture based assays to identify patients for initiation of "early" AF therapy in the ICU with biomarkers and predictive rules.[20]

Tenet 3: Use non-culture-based assays concurrently with risk factors for IC to identify patients for discontinuation of "early" AF therapy.[21]

HIV/AIDS in adolescence and youth

Africa is home to 70% of all people living with HIV with South Africa having the majority (19%) of all people living with HIV. This is followed by Nigeria with 6%. More than 1/3 of new infections occur among young

woman globally with over 7000 new HIV infections in women weekly.[22]

Professor Quarisha Karim sought to explain the source of infection in these women and why they were so vulnerable using a study on the Transmission Networks & Risk of HIV Infection in Young Women in KwaZulu-Natal, South Africa.

In a community-wide phylogenetics study,1,589 viruses were sequenced from 9,812 people in Kwazulu-Natal.

In the study findings, young women < 24 years had older male partners 24-40 years, who had a high community HIV prevalence of 40% but low rate of knowledge of their HIV status. The average viral loads for these men were > 50,000 copies/ml. These men were infected by women 25-40 years old with a community HIV prevalence of 59.8%. In these women, 63.3% of them had male partners who were between 25-40 years. Hence most men and women between 25-40 years would acquire HIV from similarly aged partners. In addition, the men would have another female partner less than 25 years, and transmit HIV to them. When these younger women enter age > 25 years they also enter the cycle and a vicious cycle ensues, refer figure 2.[23] For these young women, WHO strongly recommends Truvada as pre-exposure prophylaxis.

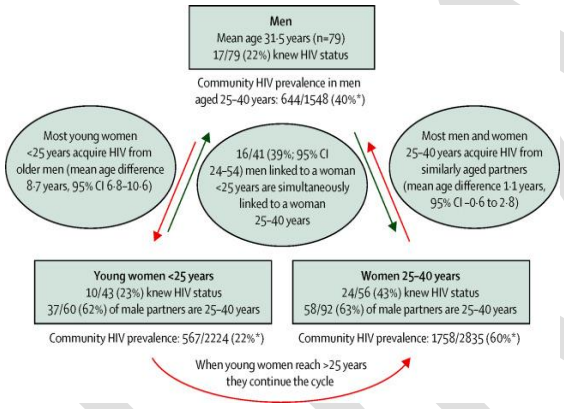

Figure 2: Transmission networks and risk of HIV infection in KwaZulu-Natal, South Africa. (Reference: de Oliveira T, et al. Lancet HIV 2017;4(1): e41-50. [Image retrieved from: http://www.sciencedirect.com/science/article/pii/S2352301816301862)

The call for action against HIV currently is A-abstinence, B-be faithful, C-condom (female, male), C-circumcision, P-PreP.

Dr Kim Anderson shared with us her study findings on treatment outcomes in perinatally infected HIV adolescents and children after 10+ years on antiretroviral therapy. It was a retrospective study involving 127 patients at the Groote Schuur Hospital HIV clinic. After a median follow-up of 12 years on ART, 80% were virally suppressed and 79% had optimal immune status. The long-term virologic and immunologic outcomes were good overall in children remaining in care for ≥10 years. However, there was a worsening trend in adolescence virologic and immunologic parameters.

Conclusion

The 7th FIDSSA congress was hugely successful. Participants were deeply enriched by the wealth of knowledge shared at the congress. Contributions from the various presenters will strengthen the capacity of participants. I look forward to the 8th congress in 2019.

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THE 10th WORLD CONGRESS OF WSPID, SHENZHEN, CHINA, 2nd – 5th DECEMBER 2017

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The 10th World Congress of WSPID was held in Shenzhen, China from the 2nd to the 5th December 2017. It attracted 1745 delegates from 77 countries, an audience record for a WSPID conference. AfSPID was represented by various physicians from more than 14 countries.

The organization of the conference was flawless, enabling the event to fulfill its potential as a platform for the exchange of up-to-date knowledge of care for paediatric infectious diseases. The Shenzhen Children's Hospital, the Chinese Pediatric Society, the Chinese Medical Association and Kenes International partnered with WSPID in organizing the 10th edition of its world congress.

The first day was notable for the PIDS fellows' educational workshop. Participants were given brief and attractive discussions on the conduct of a paediatric ID research project and challenges and opportunities to anticipate. Then fellows presented their research projects following review with their counterparts and an assigned mentor. This activity drove home the lessons on how to successfully convert conceived study projects to practice.

Photograph 1: Participants at the PIDS fellows workshop

The conference addressed a wide spectrum of topics including research methods for paediatric infectious diseases, pneumonia, neonatal infections, viral hepatitis, nosocomial sepsis, antimicrobial resistance, acute infectious diarrhoea, immunization, viral haemorrhagic fevers, Influenza, tuberculosis, adolescent medicine, pertussis, primary immunodeficiencies, paediatric HIV infections, congenital infections, CNS infections, RSV infections, eradication of polio and infection prevention.

Viral hepatitis remains a common paediatric infection. Vaccination against hepatitis B has decreased its incidence in children below 5 years of age by more than three-folds. The 2017 WHO Global Hepatitis Report estimated that 257 million people were infected with hepatitis B virus and 71 million were living with hepatitis C virus; 3.5% & 1% of the world's population respectively. Africa still bears the lion's share of HBV infections, with a 3% HBsAg prevalence.[1]

Dr Giuseppe Indolfi gave an update on the treatment and prevention of chronic hepatitis B and C in children. Administering maternal Tenofovir disoproxil fumarate (TDF) starting from 30 – 32 weeks off gestational age till one month postpartum has been proven to enhance the prevention of mother-to-child transmission of hepatitis B infection.[2]

Concerning developments in therapy of chronic hepatitis B infections, though Tenofovir alafenamide (TAF) has proved to perform better in adults as compared to TDF (higher intra-cellular levels, lower adverse reactions and equal efficacy), similar studies are sparse in children.[3]

Experiences concerning inclusion of Hepatitis A vaccines into national programs were also shared by Professor Carla Vizzotti from Argentina. Various inactivated vaccines (fit for use for children above 1 year of age) have been available for the past 25 years. They have shown high protection rates with mild adverse reactions.[4]

A big focus at the WSPID 2017 convention was anti-microbial resistance and stewardship programs and as such, many sessions were dedicated to these topics.

The observation that Penicillin monotherapy fails in treating high inoculum streptococcal (especially group A streptococcus) infections had been observed as early as 1952 by Eagle et al; hence the nomenclature 'the Eagle effect.[5]

Over the ensuing decades, many authors have advocated the use of protein synthesis inhibitors, especially for toxin-mediated skin and soft-tissue infections.[6] The advantage of initial therapy with protein synthesis inhibitors in pneumococcal meningitis and pneumonia is less clear.[7]

The relevance of this topic in this age of prevalent penicillin-resistant streptococcal infections was not lost at WSPID 2017. And hence, the clinical correlates of the Eagle effect were discussed for the benefit of the audience by Professor B. Keith English.

An unheralded feature of the global threat of antimicrobial resistance is its impact on the biodiversity of microbes in the human gut.[8] Professor Debbie Bogaert outlined these long-term effects of prolonged and unnecessary antibiotic exposure on the gut microbiome at the 2017 WSPID meeting.

Zika virus infections have captured the attention of the public and infectious diseases practitioners alike over the past 3 years. Until March, 2017, there were more than 3600 confirmed cases of congenital Zika virus infections in

26 countries.[9] Dr Kristy Murray and Dr Kleber Luz delivered interesting discussion on the current epidemiology and clinical presentations of Zika virus infections respectively.

A multi-centre case-control study, the PERCH project, performed in seven low and middle-income African and South Asian countries, reported its findings on the aetiology of paediatric pneumonia in those aged 1 – 59 months. Nasopharyngeal, oropharyngeal, induced sputum, blood and urine specimens were used for screening.

It was interesting to note that RSV accounted for 30.7% of all cases with radiologic pneumonia. Close to 56% of cases were accounted by four viruses - RSV, Parainfluenza (commonest cause in the Gambia), HMPV and Rhinovirus (most prominent aetiology in Kenya and Bangladesh). Findings were consistent among the seven countries. Fewer than 10% of cases were attributed to pneumococcal isolates.

RSV infections are important causes of lower respiratory infections in low resource settings, as reaffirmed by findings of the PERCH project. Professor Janet Englund addressed the promising advances in managing RSV infections. Studies (at different stages of application on humans) are ongoing. Research on fusion inhibitors and nucleoside analogues show great promise.[10-13]

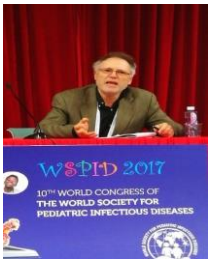
UNAIDS data show that 1.8 million children under the age of 15 years old are living with HIV globally in 2017.

Late presentation during antenatal care and treatment failures for anti-retroviral drugs are common observations in sub-Saharan Africa.[14,15] Professor Mark Cotton reviewed the evidence supporting the antenatal use of Integrase inhibitors in achieving a rapid viral load reduction in the aforementioned settings.[16] Reports of the cohort study IMPAACT P1110 will shed further light on the benefit of raltegravir in HIV-1 exposed full term neonates at high risk of mother-to-child transmission of HIV-1 infection.

Optimizing antiretroviral therapy (including PMTCT practices) using pharmacokinetic peculiarities of newborns, children and adolescents is crucial.[17] Dr Tim Cressey and Professor David Burger discussed these differences in paediatric HIV care.

AfSPID convened its society symposium on day 2 of the conference with presentations on the prevention of adolescent HIV infections by Dr Sabrina Bakeera-Kitaka, pertussis by Dr Nicolette du Plessis and solar-powered oxygen delivery by Professor Amha Mekasha.

AfSPID also hosted an Annual General Meeting (AGM) attended by 18 delegates. The chair of the AGM, Professor Mark Cotton, welcomed participants and gave a brief summary of the activities of AfSPID since its inception. Issues on membership, terms of the executive committee and membership fees were discussed in detail.



Photograph 2: Professor Mark Cotton, Chair of AfSPID

The audience congratulated Prof Mark Cotton and Professor Adegoke G. Falade for their deserved inclusion into the Executive board. Professor Cotton assumes the vice-presidency of WSPID followed by the presidency after 2019.

The meeting also discussed the organization of a first AfSPID conference within the continent by 2021, with the target of 200 – 300 delegates in a convenient city for participants. The theme of the conference will be 'Prevention of antimicrobial resistance and the introduction of antimicrobial stewardship programs in Africa'. Further agenda points were the society bulletin and web page administration.

Photograph 3: Participants of the AfSPID AGM

Conclusion

The WSPID 2017 convention was a successful platform for communicating standards of care, outputs of ongoing research, and overall, advanced the understanding of management of paediatric infectious diseases.

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SOLAR POWERED OXYGEN DELIVERY

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Globally nearly 6 million children under the age of five years die annually and more than half of these early childhood deaths could be prevented or treated with access to simple and affordable interventions. The leading causes of these deaths are preterm birth complications, pneumonia, birth asphyxia, diarrhoea and malaria. Children in sub-Saharan Africa are more than 14 times more likely to die before the age of 5 than children in developed regions.[1]

Hypoxaemia in children with severe pneumonia is a predictor of mortality. It is estimated that, globally, among hospital admitted patients, hypoxaemia accompanies 13% of pneumonia, 20% of sick neonates and 10–15% of children with malaria, meningitis or convulsions.[2]

It is estimated global strengthening of oxygen systems could save lives of up to 122,000 children from pneumonia annually. The median estimate of potential effectiveness of oxygen systems to reduce the overall childhood pneumonia mortality is about 20%.[3] However, supplemental oxygen is not available in most paediatric services in Sub-Saharan African countries.

Oxygen may be delivered from oxygen cylinders, oxygen concentrators and oxygen plants. Mostly oxygen cylinders are only available at central hospitals and operating rooms because they are expensive and difficult to deliver to many health facilities with poor transport facility and system. Experience has shown that it is feasible to implement an oxygen system using concentrators throughout a low-income country.[4] The major disadvantage of a concentrator is that it requires electricity.

Access to electricity is critical to health care delivery. In most African countries electricity failures are very frequent. Only 28% of health care facilities, on average, had reliable electricity in a survey of 8 countries. Among these countries, an average of 7% of facilities relied solely on a generator. In addition the improvement of electricity access in health care facilities is not encouraging; it only increased by 1.5% annually in Kenya between 2004 and 2010, and by 4% annually in Rwanda between 2001 and 2007.[5]

Recently there are attempts to provide electricity for the concentrators using solar powered oxygen concentrators. In solar powered concentrators during the day solar panels supply power to a concentrator and at night charged batteries from the panels supply the power to the concentrator. Studies have shown that solar powered oxygen delivery can run concentrators efficiently. A before-and-after study reported on clinical outcomes in Sierra Leone mean in-patient paediatric mortality across the six-month period prior to solar panel installation was 3.7% (95% CI 2.0–5.3%), which reduced to 1.8% (95% CI 0.5–3.0%) in the six-month period after solar panel installation.[6]

In another study treatment among 28 patients with solar-powered oxygen increased the peripheral saturation to >95% in 25 patients (89%); for the remaining 3 patients, oxygenation improved to >90%, but these patients died before recovery of lung function. Duration of hospitalization was median (range) 3 (1-28) days. The outcomes of the study revealed that 19 patients were discharged without disability, 1 discharged with sequelae (cerebral palsy), 2 transferred to another facility and 6 (23%) died. It was concluded that solar-powered oxygen delivery can be used to concentrate oxygen from ambient air and oxygenate critically ill patients with hypoxemia using unlimited and freely available inputs, the sun and the air.[7]

Currently there are studies in Nigeria, Papua New Guinea and Uganda with the overall objective being to demonstrate the non-inferiority of solar-powered oxygen delivery relative to standard oxygen delivery.[8-10] However, the core issue is cost implication to run solar powered oxygen concentrators. Recent estimates are that the capital cost of solar panels is $25,000, plus the cost of batteries, charger and inverter, merely to run a concentrator which costs less than $1000. It is expected that with increased demand and production the cost will decrease with probably improved batteries.[11]

In conclusion solar powered oxygen delivery system can save lives of millions of children in areas where electricity is not available, especially in the remote areas of Africa.

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JOURNAL WATCH

The timing of antiretroviral initiation in hospitalised children

Review completed by Brian Eley

The timing of antiretroviral therapy (ART) in hospitalised children aged 2-12 years with advanced HIV infection but without suspected or confirmed central nervous system (CNS) co-infection is addressed in the current study. In this randomised controlled clinical trial ART initiation within 48 hours of enrolment (urgent cohort) is compared to ART initiation 7-14 days after enrolment (post-stabilisation cohort). The median age was 1.9 years at baseline and did not differ significantly in the two cohorts. Outcomes were evaluated during the first 6 months post-randomisation. The overall 6-month all-cause mortality was 22% with more than 80% of deaths occurring in the first month. All-cause mortality risk, incidence of immune reconstitution inflammatory syndrome (IRIS) and incidence of drug toxicity (primary outcome measures) were not significantly different in the two study cohorts. Furthermore, there were no statistically significant differences in most of the secondary outcome measures.

Thus, whilst early mortality in these hospitalised children was high, urgent initiation of ART did not improve short-term mortality. Somewhat reassuring is that children in the urgent cohort did not experience more drug toxicity or IRIS than those in the post-stabilisation cohort. Thus undue concerns about drug toxicity and IRIS should not be used to delay the introduction of ART in children without CNS co-infection.

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Effect of community-based support for caregivers on virological failure in children on antiretroviral therapy

Review completed by Brian Eley

Poor adherence and suboptimal retention in care undermine the effectiveness of paediatric antiretroviral therapy (ART) programmes in many low- and middle-income countries. Recent observational studies have shown that community-based adherence support for parents and primary caregivers of HIV-infected children on ART improves patient retention and virological suppression.[1,2] The current study provides further support for this low-cost intervention.[3] Ferrand *et al*. completed an open-label, randomised controlled trial among children aged 6 -15 years in Zimbabwe. Community-based support for their caregivers lowered the odds of virological failure or death by 54%.[3] This intervention should be strongly considered in paediatric ART programmes that experience high lost-to-follow-up and treatment failure rates.

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Recurrence of adverse events following immunization

Review completed by Brian Eley

Mild adverse events following immunization (AEFI) such as fever or local reactions at the site of injection are not associated with permanent sequelae. Similarly, severe reactions such as febrile seizures and hypotonic-hyporesponsive episodes do not cause long-term adversity. With the exception of anaphylaxis and encephalopathy after a dose of vaccine there are no absolute contraindications to the receipt of further doses of the same vaccine. However, parents may resist subjecting their children to further immunization with vaccines associated with severe AEFI. In the current systematic review, Zafack, *et al.* estimated the risk of recurrence of a spectrum of AEFI including allergic manifestations, injection site reactions, apnoea, hypotonic-hyporesponsive episodes, fever and seizures. These pooled estimates should assist practicing paediatricians when counselling parents of children who previously experienced AEFI.

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Drug-drug interactions between lopinavir/ritonavir and 1st- and 2nd-line anti-tuberculosis drugs

Review completed by Brian Eley

Since the results of the P1060 randomised control trial were disseminated, lopinavir/ritonavir-containing antiretroviral therapy (ART) has become standard of care for young HIV-infected children irrespective of whether or not they had experienced exposure to peripartum nevirapine.[1,2] Tuberculosis (TB) co-infection often complicates the course of paediatric HIV infection.

Rifampicin-containing anti-TB drug regimens used in the treatment of drug-susceptible TB induces CYP3A4 and p-glycoprotein expression reducing the trough concentrations of lopinavir significantly in young children co-treated with lopinavir/ritonavir-containing ART. This effect of rifampicin can be attenuated by prescribing additional ritonavir.[3] Treatment of multi-drug resistant TB (MDR-TB) includes combinations of first and second-line anti-TB drugs to which the isolate is susceptible. Current international consensus recommends a combination of four TB drugs to which the MDR isolate is susceptible plus pyrazinamide.[4] Whether or not anti-TB drugs used in the treatment of MDR-TB, particularly the second-line agents, affect the exposure of lopinavir and/or ritonavir during HIV and TB co-treatment is addressed in the current study by van der Laan *et al*.[5] The effect of a drug regimen comprising high-dose isoniazid, pyrazinamide, ethambutol, ethionimide, terizidone, a fluoroquinolone and amikacin was evaluated. The findings showed that these drugs when administered in combination with lopinavir/ritonavir did not significantly affect the pharmacokinetic parameters or either lopinavir or ritonavir. While these results are reassuring for practising clinicians, further research is required to determine whether other anti-TB drugs also used in the treatment of drug-resistant TB in children and adolescents, including para-aminosalicylic acid, clofazimine, linezolid, moxifloxacin, delamanid and bedaquiline, affect the exposure of lopinavir/ritonavir during co-treatment.

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CONFERENCE & SOCIETY NEWS

18th International Congress on Infectious Diseases will be held in Buenos Aires, Argentina from 1 to 4 March 2018. For more information visit the International Society for Infectious Diseases website, http://www.isid.org/icid/

10th International Workshop on HIV Pediatrics will be held in Amsterdam, The Netherlands from 20 to 21 July 2018. For more information visit the conference website, http://www.virology-education.com/event/upcoming/10th-workshop-hiv-pediatrics/

22nd International AIDS conference will be held in Amsterdam, The Netherlands from 23 to 27 July 2018. For more information visit the conference website, https://www.aids2018.org/

The Southern African HIV Clinicians Society Conference 2018 will be held at the Gallaghar Convention Centre, Johannesburg, South Africa from 24-27 October 2018. For more information visit the conference website: http://www.sahivsoc2018.co.za/

11th WSPID conference will be held in Bali, Indonesia, from 7 to 9 November 2019. Information on the venue and conference dates visit the Paediatric Infectious Diseases Society website: http://www.pids.org/. AfSPID will once more host a dedicated symposium at this conference.

The 20th Edition of International Conference on AIDS and STIs in Africa (ICASA) will be held in Rwanda. For more information visit the Society for AIDS in Africa website, http://saafrica.org/

HOW TO JOIN AfSPID

There is currently no subscription fee. To join AfSPID, and to receive the newsletter and information about the society, including forthcoming events please send Natasha Samuels, samuels@sun.ac.za a brief email message indicating your interest in joining AfSPID together with the following information:

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THE AfSPID BULLETIN

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All contributions: The name, surname, job title, affiliation and email address of each author should be positioned immediately below the title of the article. The text should be single-spaced in 12-point Arial or Times New Roman font. The use of sub-headings is encouraged. References should be listed at the end of the manuscript in numerical order as first cited in the manuscript. References should be formatted in the Vancouver style, refer: http://www.southampton.ac.uk/library/resources/documents/vancouverreferencing.pdf (Citing & Referencing Guide: BMJ Vancouver style). If a reference contains less than 6 authors then list all authors. If a reference contains 6 or more authors, list the first 3 authors followed by et al. Tables, illustrations (figures) or pictures should preferentially be accompanied by an explanatory legend. Tables, illustrations and pictures should be the author's own work. Illustrations and pictures should be of high resolution quality. Ideally, pictures or unmodified illustrations from published mauniscripts or websites should not be copied, unless the corresponding author obtains written permission from the source publisher. Submit the manuscript in Microsoft Word.

Letters to the editor: Maximum of approximately 400 words and 6 references, with one illustration or table.

Review article or commentary: Maximum of approximately 3000 words (excluding references), 40 references, and 6 tables, illustrations or pictures.

Research feature: Research feature should be preceded by a 200 - 300 word biosketch of the featured young researcher. The research commentary should have a maximum of approximately 3000 words and 40 references.

Conference report: An introductory paragraph is recommended in which the conference details and focus is described. The conference report should focus on new developments and what they mean for African settings. Maximum of approximately 2500 words, 40 references, and 6 tables, illustrations or pictures.

Case report: The main elements should be an introduction, the case report and the discussion. Maximum word count of approximately 1500 words, 15 references and 3 tables, illustrations and/or pictures.

CONTACT DETAILS

Should you wish to submit articles, case reports, comments or letters for publication in the AfSPID Bulletin, please email your contribution to Brian.Eley@uct.ac.za