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EDITOR'S COMMENTARY

Dear Colleagues

Welcome to the sixth edition of our newsletter.

Another year has come and gone. At a global level, Zika virus infection continues to be a strong focus of research activity. In Africa we've experienced a large outbreak of yellow fever in Angola and the Democratic Republic of Congo.

A setback for Africa and the global polio eradication initiative has been the recurrence of paralytic poliomyelitis due to wild poliovirus (WPV) in Africa. In August 2016, new cases of WPV type I poliomyelitis were detected in Borno, Nigeria, the first cases on the African continent in more than two years. As at 14 December 2016, 4 cases of paralytic poliomyelitis were reported in Nigeria. This outbreak has evoked a large vaccination campaign in Nigeria, and in Borno alone more than 1.7 million children have been vaccinated. At the global level, the possibility of eradicating polio during the next few years is still within reach, with only 34 cases of WPV infection reported in three countries in 2016, Afghanistan (12 cases), Pakistan (18 cases) and Nigeria (4 cases).

In this edition of the newsletter yellow fever outbreaks in Africa including the 2016 outbreak are reviewed, the Nigerian National tuberculosis conference is featured, recently published WHO guidelines on antibiotic resistance and infection control and prevention are discussed, the proceedings of the 2nd workshop on the HIV exposed uninfected infant and child that took place in Durban on 17 July 2016 are summarised, the 8th annual Ugandan paediatric and adolescent conference is discussed, and we conclude with commentary on two interesting publications in our regular journal watch slot.

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

In December 2017 we look forward to experiencing the 10th WSPID conference in China. This meeting will discuss important regional paediatric infectious diseases problems including infections that are prevalent in China. AfSPID will again be hosting a symposium at this important conference.

Kind regards, Brian Eley

YELLOW FEVER OUTBREAKS IN AFRICA

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Introduction

Few diseases have attracted more attention from medical historians than yellow fever (YF). It was one of the most feared diseases from the 15th to 19th centuries when large scale outbreaks in port cities of North and South America, Africa, and Europe caused devastating epidemics. Walter Reed reported that the disease was transmitted to humans by Aedes aegypti.1 Twenty-eight years later, yellow fever virus (YFV) became the first mosquito-borne virus to be identified.² YF is currently classified as a re-emerging disease and is a significant cause of high morbidity and mortality, with an estimated 200,000 cases each year and 30,000 deaths.³ The spectrum of clinical disease varies from mild flu-like illness to classical tri-phasic hemorrhagic fever, with hepatorenal involvement. Only 15–25% of cases progress to intoxication while 20–50% of patients with end organ impairments die. Majority of the cases are in Africa where it is endemic in over 33 countries." Although a highly effective vaccine is available, epidemiological data suggest an alarming resurgence of virus circulation in Africa over the last 20 years.5 failure to implement sustained vaccination programs reflects larger problems of poverty, civil war, and inaccessibility of rural areas where outbreaks occur.⁶

Evolution of yellow fever virus

Comparison of nucleotide sequences of YFV strains indicates the virus arose at a relatively early stage in flavivirus evolution, at least thousands of years ago. 7.8 Evolutionary studies suggest YFV originated in Africa, as the deepest phylogenetic split among viral genotypes is between those isolates sampled from East and West Africa. The fact that only two genotypes of YFV occur in the Americas, whereas at least 5 genotypes are described in Africaalso points to Africa as the evolutionary cradle of YFV. 9-11 However, the first account of a disease with symptoms that can be recognized as YF occurred in

Guadeloupe and Yukatan in 1648.12 Studies of rates of nucleotide substitution and divergence of clades offer convincing evidence that YFV was introduced into the Americas about 400 years ago from West Africa.7 This genetic record is highly consistent with historical course of slave trade. YF was first described in early 17th Century, when the Portuguese and other European countries began importing slaves from Africa to continental South America and the Caribbean to work on sugar plantations. Ae. aegypti vectors were likely to have been introduced to the New World at about this time. Actual means of introduction of YFV could have been by viremic humans or Ae. aegypti, since YFV transmission on board sailing vessels was not uncommon. Alternatively, the virus could have been carried on artificial containers or imported vegetation, by means of desiccated eggs laid by infected Ae. aegypti and/or other sylvatic vectors. Subsequent to devastating urban outbreaks within port cities on both the east and west coasts of South America, YFV established sylvatic enzootic cycle within the Amazon, Araguaia, and Orinoco river basins vectored by *Haemagogus* and *Sabethes* mosquitoes. ¹³

Transmission cycle

Three epidemiologically distinct infectious cycles occur between YFV transmission from mosquitoes to humans or non-human primates. In the sylvatic or Jungle cycle, monkeys are the hosts while *A. africanus* and other *Aedes* spp. are the vectors. In the savanna or intermediate cycle, found only in Africa, monkeys and humans act as hosts with *Aedes* spp as vector. Third is the "Urban" cycle where only *Ae. aegypti* is involved with human as hosts. *Ae. aegypti* is well adapted to urban centers and can be coinfected with dengue and chikungunya.

Epidemiology of yellow fever

From 1906-1922, cases of YF were rare in Africa, with very small outbreaks from 1922 to 1927 in West Africa. ¹⁴ Incidence of the disease decreased markedly from 1927 to 1930 and reappeared in 1931. The reappearance of cases of YF with no epidemiological link in several places all over West Africa and countries where the disease had not been reported for many years was explained by persistence of latent YF foci in these countries. In the epidemic periods, it was the European travelers in particular who were affected as they had no protection resulting from previous exposure. ¹⁵

Serological detection of antibodies against YFV in mice showed that high number of people in Sierra Leone and Southern Nigeria had been exposed, and this was less in Northern Nigeria. There were quite a number of positive sera in people living in Francophone West Africa, including west and south of Senegal, and along the upper course of the Senegal River, in the Macina area and the former Upper Volta Territory. 16 Sera samples of people tested positive in parts of former Togoland. On the other hand, the tests were negative in almost all the places studied in Guinea and Ivory Coast (except Grand Bassam). The highly positive results obtained in Kenya, Tanganyika and Northern Rhodesia were not sufficient proof that YF had previously existed in these countries, since serology was not 100% specific for YF. In places where YF was endemic, proportion of positive correlation of high immune status was fairly regular with age, whilst the immunity curve according to age was irregular in places where YF appeared sporadically.¹⁷ The disease appeared in June 1934 for the first time farther east, at Wau in Bahr-el-Ghazal Province in former Anglo-Egyptian Sudan. Where one third of individuals where immune to YF. 18 Sporadic cases were identified annually in East Africa until 1959, when an outbreak was recorded in the Blue Nile region and subsequently in neighboring Ethiopia. 19 From 1960 to 1962, a large outbreak occurred in southwest Ethiopia. More serological studies confirmed that YF was widespread in Uganda, Somalia, Ethiopia, and Kenya. The period 1986-1991 was an extraordinarily active period for YF in Africa. Globally, a total of 20,424 cases were reported with 5,447 deaths. This is the greatest YF activity reported to WHO since 1948 when YF reporting began. Between 1992 and 1993, a large outbreak was confirmed in the Rift Valley province of Kenya. Since then sporadic outbreaks have been made in East Africa, until the outbreak in southern Sudan in 2003. Between 2000 and 2014, YF outbreaks were reported in Uganda, Burkina Faso, Chad, Cote d'voire, Guinea, Mali, Paraguay, Togo, Venezuela, Congo and Nigeria.

Countries with 2016 outbreaks of YF in some Africa include Uganda, Angola, DRC, Kenya in East and Central Africa and Ghana, Guinea and Chad in other parts of Africa. Also, Columbia, Peru and Brazil reported outbreaks of YF in the year. From 26 March to 18 April, 30 suspected cases with 7 deaths were reported in Uganda. Affected people had no travel history outside of the country. First case in Angola with onset date on 5 December 2015 was identified in Viana municipality, Luanda province. On 21 January 2016, the National IHR Focal Point of Angola notified WHO of a YF outbreak. Between 4 and 12 April 2016, the National IHR Focal Point of China notified WHO of 2 additional imported YF cases. Over 11 laboratoryconfirmed YF cases imported from Angola have been reported in China. From 5 December 2015 to 20 October 2016 in Angola there were 4347 suspected cases, with 377 deaths (case fatality rate, CFR: 8.7%); 884 cases have been laboratory confirmed, with 121 deaths (CFR: 13.7%). Since the beginning of the outbreak, suspected cases have been reported from all 18 provinces; confirmed cases have been reported from 80 districts in 16 provinces while autochthonous transmission has been reported from 45 districts in 12 provinces.²² DRC is located in a geographical area known to be YF endemic, and autochthonous cases are regularly reported in the whole country. The last outbreaks were reported in Kasai Oriental in 2013 and in Province Oriental and Katanga in 2014.²³ From 1 January to 26 October 2016, 2987 cases were reported from 26 provinces; 78 confirmed cases were identified from 2800 suspected cases that were laboratory tested, with 16 deaths (CFR: 21%); Of the 78 confirmed cases, reported from eight provinces, 57 acquired infection in Angola, 13 were autochthonous, and eight were of sylvatic origin that are not related to the outbreak. One new confirmed, sylvatic case was reported from Bominenge Health Zone in Sud Ubangui province.²²

Six cases of yellow fever were recorded in the health zone of Sandoa in DRC with another case in Kasaji, also in the province of Lualaba. According to the bulletin of the Office for the Coordination of Humanitarian Affairs (OCHA), all these cases were confirmed after results of the samples tested by the Institute of Biomedical Research (INRB) of Kinshasa were positive. ²³

An entomological survey found a high density of Aedes aegypti larvae. High entomological density indicates a high risk of YFV amplification. These vectors have been found to circulate in abundance in the rain forest region in parts of West Africa. ^{24,25} The DRC government officially declared an outbreak of yellow fever on 23 April 2016 and the Ministry of Health activated the National Committee for Outbreak Management to respond to the outbreaks. Key response activities include: establishment of coordination mechanisms. social mobilization and community management, streetraining of health engagement, strengthening case through surveillance workers, dissemination of case definitions, screening and sanitary controls at Points of Entry and screening of refugees' vaccination status, reactive vector control activities,

sensitization of all health, facilities (public, private, and traditional practitioners) and vaccination of all individuals travelling to Angola. Technical support is required to improve laboratory capacities in terms of diagnosis, to avoid delays in laboratory confirmation of cases and improve surveillance. With support from WHO and partners, the country has developed a contingency plan to improve the country's preparedness for a possible response to larger YF outbreak. The plan is to vaccinate 8 health zones with at least 2 districts in Kinshasa and the 6 districts of Kongo Central where laboratory confirmed cases were identified (a total of nearly 2 million persons). If local transmission is laboratory confirmed, then other districts would be targeted accordingly.

Joint operations in Yellow Fever Strategic response plan

Informed by lessons in the early part of the year, a guideline was instituted for coordinated international response to interrupt transmission of the 2016 yellow fever outbreak in Angola, the Democratic Republic of the Congo, and a concurrent yellow fever outbreak in Uganda, including preparedness for the importation of cases in non-affected countries. It includes Joint Operations Plan that provides details of how the WHO and its partners are and will implement the framework's strategic objectives ²⁶

The goal is to end yellow fever outbreaks in affected countries and limit international spread. To do this, four objectives were outline. First, to end outbreaks in currently affected countries through targeted vaccination and other public health measures. Second, prevent morbidity and reduce mortality through early case detection and strengthened case management. Third, prevent international spread and lastly, prioritize research to improve access to yellow fever vaccine, and improve effectiveness of other prevention and control interventions. To achieve the first three, surveillance and risk assessment, vaccination, case management, vector control, social mobilization and risk communication are key. The fourth objective will require \$94.1m actualize). ²⁶

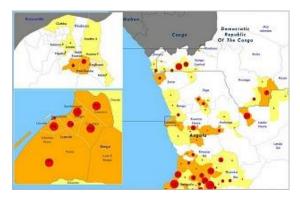


Figure1: Distribution of Yellow fever cases in Angola and the Demographic Republic of Congo as at 19 August 2016 (source: World Health Organization)

Vector competence

Aedes aegypti is the main vector for YFV. It exists as two subspecies: Ae. aegypti aegypti and Ae. aegypti formosus.²⁷ Aedes aegypti aegypti is found globally in tropical and subtropical regions, while Ae. aegypti formosus is mainly restricted to sub-Saharan Africa. Vector competence studies on Ae. aegypti from West Africa have shown these mosquitoes to be more refractory for YFV compared to Ae. aegypti collected from other parts of the world.²⁸ Sylvatic genotypes are transmitted between monkeys in forested areas, while cosmopolitan

genotypes are transmitted between humans in urban areas. The sylvatic genotype has been isolated from mosquitoes, monkeys, and humans in West Africa, but is genetically distinct from epidemic isolates. ^{29,30} Different genotypes as well as different lineages within genotypes can result in differences in both vector capacity and disease severity. ³¹ Genetic differences in YFV isolates are an important predictor of vector capacity. Seven genotypes of YFV are found worldwide, West African Genotypes I and II are endemic in West Africa. Genetic differences among YFV isolates are geographically associated with outbreaks in Africa. Specifically, West Africa genotype I is responsible for a majority of outbreaks and is genetically heterogeneous relative to other genotypes. ³²

Vaccination

Efforts to develop YF vaccines began soon after isolation of the virus in 1927. Attempts to produce inactivated vaccines during the early 20th century were unsuccessful, and subsequent vaccine development focused on live virus products. The first live-attenuated vaccine for yellow fever was developed between 1934 and 1935 in Francophone West Africa (Durieux et al., 1956), and its use dramatically reduced the incidence within five years of its introduction. Unfortunately, it was associated with a high risk of encephalitic reaction in children, with a fatality rate of 38% so its production was discontinued in 1980. The 17D live-attenuated vaccine in use today was developed in 1936, and a single dose confers immunity for at least ten years in 95% of the cases. In a bid to contain the spread of the disease, travellers to countries within endemic areas or those thought to be at risk require a certificate of vaccination. Between 2007 and 2016, 14 countries have completed preventive yellow fever vaccination campaigns: Benin, Burkina Faso, Cameroon, Central African Republic, Côte d'Ivoire, Ghana, Guinea, Liberia, Mali, Senegal, Sierra Leone and Togo, while Nigeria and Sudan have been implementing the campaigns.³³ However, there is a need to strengthen yellow fever vaccination requirements for travellers going to endemic countries in accordance with International Health Regulations. YF can easily be prevented by immunization, provided vaccination is administered at least 10 days before travel. WHO urges Member States, especially those where the establishment of local cycle of transmission is possible (where Aedes aegypti is present) to ensure that travellers to or from countries with current YFV transmission are vaccinated against YF. PAHO reports the global supply of yellow fever vaccines has been insufficient for years. The PAHO/WHO Revolving Fund provides about 50% of the demand in the region of the Americas but that is not the case in Africa. Current outbreak in Angola has stretched existing YF vaccine supplies.³⁵ Although there is a perfectly good vaccine, the trouble is that there is not enough of it in stock today, nor can there be for the next few years due to limitations on production of avian leucosis virus-free eggs, and the six months it takes to test and release each new batch (Woodall Jack, personal communication). This situation raises the question about vaccine availability now and in the immediate future. Therefore, the only way to get enough vaccine now is for WHO to make an emergency authorization allowing affected countries to use 5- or 10fold lower but still effective doses, saving stock for future

In DRC, reactive vaccination campaign in Feshi Health Zone in Kwango province ended after 152,492 people were vaccinated among a target of 146,449 (104.1%). The reactive campaign in Mushenge Health Zone in Kasai province began in October. Monitoring continues in the 62 Health Zones where the pre-emptive vaccination campaigns were conducted in August. WHO sent more

than 30 million vaccine doses to Angola, Democratic Republic of the Congo and Uganda since the beginning of the outbreak through the International Coordinating Group (ICG) global stockpile, with additional vaccine doses from the manufacturer Bio-Manguinhos in Brazil. As of 25 October 2016, 20 million vaccine doses have been approved for Angola and 9.4 million doses for Democratic Republic of the Congo. The number of vaccine doses currently available in the ICG global stockpile for emergency response is 6.9 million. The amount of doses already allocated to respond to the outbreak is not included in this number.²²

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NIGERIAN SOCIETY FOR PEDIATRIC INFECTIOUS DISEASES (NISPID) FEATURED AT THE NATIONAL TUBERCULOSIS CONFERENCE, 17-18 MAY 2016

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Stakeholders working on TB at the national and global levels converged in Nigeria global levels converged in Nigeria during the series of events that took place around the National TB Conference held from 16-18 May 2016 at Abuja, Nigeria's Federal Capital. Nigeria has the highest number of TB cases in Africa and is 4th among the countries that share the highest global TB burden. The National TB Prevalence Study of 2012 revealed figures that almost tripled the previous estimates. Despite the country's effort to address TB control the TB casedetection rate remains at an abysmal rate of 15%. With nearly 600,000 annual new TB infections it is projected that up to 60,000 cases occur amongst children.



Figure 1: Participants at a session of the 2016 National TB conference, Nicon Luxury hotel, Abuja, Nigeria

Presently through efforts of the Government and development partners, free TB treatment is offered to 95,000 adults and approximately 5,000 children each year. However, Nigerians with TB do not receive treatment, with implications for ongoing morbidity, disease transmission and annual mortality in the region of 170,000, worst affecting adults and children living with HIV infection.

Based on these challenges, the Stop TB Nigeria in collaboration with other partners organized the first National TB Conference held at Nicon Luxury Hotel Abuja. The theme of the conference was "The Hidden Face of Tuberculosis: Challenges in identification and Management among Vulnerable Groups in Nigeria". The goal of the conference was to improve synergy among all stakeholders working to end TB in Nigeria. The

 Leveraging on recent innovations in TB diagnostics and drugs

conference sub-themes were:

- The state of TB case-findings and prospects for TB control in Nigeria
- The national TB control programme which way forward: ownership for sustainability or partnership for continued support?



Figure 2: NISPID & AfSPID/WSPID Executive Committee Members Executive Committee Members at the 2016 National TB Conference, Nicon Luxury Hotel, Abuja, Nigeria; From L-R: Dr Regina Oladokun (NISPID Ex-Officio), Dr Lawal Umar (NISPID Secretary); Prof Osawaru Oviawe (NISPID President); Prof Mark Cotton (AfSPID President & World Society for Paediatric Infectious Diseases [WSPID] Vice President), the Guest Lecturer

The NISPID representative in the Stop TB Partnership Board of Nigeria Dr Lawal Umar (NISPID Secretary, sitting on behalf of the NISPID President), led the Scientific Sub-Committee of the Conference LOC. The conference attracted many international and national stakeholders working on TB and over 1,000 delegates attended the two-day event. Some of the special guests included:

- Wife of the President, Her Excellency, Hijiya Aisha Muhammadu Buhari, Nigeria's TB Champion, represented by the Wife of the Vice-President, Her Excellency, Mrs. Oludolapo Yemi Osinbajo
- Ambassador Dr Eric Goosby the UN Special Envoy on TB
- Dr Lucica Ditiu Executive Director, Global Stop TB Partnership
- Prof Isaac Adewole Minister of Health, Nigeria
- Mr Mike Harvey Mission Director, USAID Nigeria
- Dr Maarten van Cleef Global Director, KNCV/Challenge TB
- Prof Luis Cuevas Liverpool School of Tropical Science, Liverpool, UK
- Prof Mark Cotton AfSPID President/WSPID V/President, Stellenbosch University, Cape Town
- Prof John Idoko Director General, NACA
- Prof Osawaru Oviawe President of NISPID



Figure 3: NISPID, AfSPID/WSPID and Stop TB Partnership Chairman at the 2016 National TB Conference, Nicon Luxury Hotel, Abuja, Nigeria; From L-R: Dr Atana Ewa (Member, NISPID), Prof Luis Cuevas (Liverpool School of Tropical Medicine); Prof Osawaru Oviawe (NISPID President); Prof Mark Cotton (AfSPID President & World Society for Paediatric Infectious Diseases [WSPID] Vice President & Guest Lecturer); Dr Lawal Umar (NISPID Secretary); Dr Regina Oladokun (NISPID Ex-Officio); Prof Lovett Lawson (Chairman, Nigeria Stop TB Partnership Board).

Over 35 scientific papers were presented, prominent amongst which include "Overview of TB/HIV Co-infection in Nigeria" by Prof John Idoko, DG NACA, "Children with HIV and/or TB: How to fit into a National TB Program" by the Guest Lecturer, Prof. Mark Cotton (AfSPID President) Stellenbosch University Cape Town, S/Africa, "The Challenges of TB Control in Sub-Saharan Africa" by Dr. Maarten van Cleef, Director Challenge TB, and "Prospects for more reliable 'Game-changer' diagnostics for TB amongst vulnerable populations" by Prof Luis Cuevas, Liverpool School of Tropical Medicine.



Figure 4: A cross-section of awardees for outstanding contributions to TB control honoured at the 2016 National TB Conference, Nicon Luxury Hotel, Abuja.

GLOBAL GUIDELINES FOR ADDRESSING IMPORTANT INFECTION CHALLANGES

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In this brief report, recently published guidelines for addressing antimicrobial resistance and infection control practice are briefly summarised

Antimicrobial resistance

Antimicrobial resistance (AMR) is a threat to human health, development, and security. The evolving crisis of AMR, including the recent emergence of pan-resistant *Enterobacteriaceae* isolates is well described in the medical literature. Without intervention, mathematical modeling estimates suggest that by 2050, the annual number of deaths attributed to AMR would approach 10 million, exceeding the annual global mortality caused by cancer.¹

In May 2015 the World Health Organization (WHO) published a global action plan on AMR. ² At a high level meeting of the General Assembly of the United Nations on 21 September 2016, leaders of 193 countries reaffirmed their commitment to develop national action plans on AMR within 2 years, based on the WHO's global action plan.³

The overall goal of the WHO's global action plan on AMR is to treat and prevent infections with safe and effective medicines.³ To achieve this goal 5 strategic objectives were formulated by an expert committee, namely,

- Improve awareness and understanding of antimicrobial resistance through effective communication, education and training
- II. Strengthen the knowledge and evidence base through surveillance and research
- III. Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures
- IV. Optimize the use of antimicrobial medicines in human and animal health
- V. Develop the economic case for sustainable investment that takes account of the needs of all countries, and increases investment in new medicines, diagnostic tools, vaccines and other intervention

It is important to increase awareness of the magnitude of AMR and educate stakeholders in measures that can prevent or limit the evolution of resistance. Every time an antimicrobial is used inappropriately in the healthcare setting, the food industry or animal husbandry, the development of resistance can be accelerated. Inappropriate antimicrobial use is a consequence of ignorance and aberrant human behaviour. Surveillance and research are necessary to quantify the extent and impact of AMR at global, national and facility levels, and to determine the effectiveness of interventions and preventative measures.

Appropriate use of antimicrobial agents also contributes to the development of AMR. Therefore, the prevention of infection in healthcare facilities and communities through effective sanitation, hygiene and infection control measures reduces antimicrobial usage and hence lowers opportunities of developing resistance. Antimicrobial conservation or stewardship together with the implementation of facility-based antimicrobial guidelines will preserve the effectiveness of antimicrobial agents by reducing inappropriate use while maintaining access. The development of new antimicrobial agents, diagnostic tools and vaccines is dependent on increasing funding for research and development (R & D), simplifying the regulatory requirements that have to be fulfilled in order to

undertake R & D, and strengthening research collaboration.

Infection control & prevention

A new evidence-based guideline on the core components (CCs) of infection prevention and control (IPC) programmes was launched by WHO on 17 November 2016. This guideline acknowledges the adverse effects of healthcare-associated infection (HAI) in service delivery. At any one time up to 7% of patients in developed countries and 10% in developing countries will acquire at least one HAI. This guideline aims to support countries as they develop and execute their national antimicrobial resistance (AMR) action plans by providing evidence-based recommendations on the CCs of IPC programmes. The guideline addresses eight CCs of IPC and comprises 14 recommendations and best practice statements. These eight CCs are briefly summarized.

- 1. IPC programmes: An IPC programme with dedicated trained team should be in place in each health care facility and at the national level. At facility level, a minimum ratio of 1 full-time infection preventionist (nurse or doctor) per 250 beds should be available. However, there is a strong opinion that a higher ratio e.g. 1 per 100 beds should be considered due to increasing patient acuity and complexity.
- 2. IPC guidelines: Evidence-based guidelines should be developed and implemented for the purpose of reducing HAI and AMR. IPC guidelines should include (1) standard precautions, (2) transmission-related precautions, (3) aseptic techniques for invasive procedures, and (4) specific guidelines to prevent the most prevalent HAIs e.g. catheter-associated urinary tract infection, central line-associated bloodstream infection and ventilator-associated pneumonia. Guidelines should be complemented by education and training of relevant health care workers, and monitoring of adherence with guideline recommendations should be undertaken.

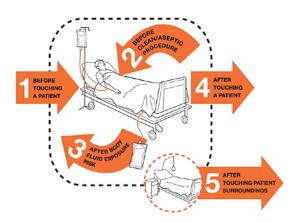


Figure 1: My five moments of hand hygiene (source: WHO)

3. IPC education and training: IPC training should be in place for all health care workers. Three categories of human resources were identified as targets for IPC training, IPC specialists, all health care workers involved in service delivery and patient care, and other personnel that

- support health care delivery such as administrative and managerial staff, axillary service staff and cleaners.
- 4. Surveillance: HAI surveillance should be performed to guide IPC interventions and detect outbreaks including AMR with timely feedback of results to relevant stakeholders. Surveillance should be conducted at both facility and national levels. At facility level, surveillance should be based on national recommendations and standard definitions, supported by adequate microbiology laboratory capacity. The following should be prioritized: (1) infections that have become endemic in the health care facility, (2) infections in vulnerable populations e.g. neonates, burn patients, ICU patients and immunocompromised patients, (3) infections that cause severe outcomes such as high case fatality rates, (4) infections caused by resistant organisms, particularly multi-drug resistant pathogens, (5) infections associated with selected invasive procedures e.g. intravascular devices, indwelling urinary catheters and surgery, and (6) infections that affect health care workers in clinical settings e.g. hepatitis B.
- 5. Multimodal strategies: IPC activities using multimodal strategies should be implemented to reduce HAI and AMR. A multimodal strategy consists of several elements or components (usually 3 to 5) implemented in an integrated way to improve outcome and change behaviour. The most common components include system change, education & training, monitoring, reminders/communication in workplaces and culture change. By contrast a bundle is an implementation tool aimed at improving the care process and patient outcomes in a structured manner. Multimodal strategies are encouraged at both facility and national levels.
- 6. Monitoring/audit of IPC activities and feedback and control activities: The main purpose of these activities is to effect behavioual change to improve the quality of care and practices.
- 7. Workload, staffing and bed occupancy at the facility level: Bed occupancy should not exceed the standard capacity of the facility and health care worker staffing levels should be adequately assigned according to patient workload.
- 8. Built environment, materials and equipment for IPC at the facility level: Patient care activities should take place in a clean and hygienic environment that facilitates practices related to the prevention and control of HAI, as well as AMR. Minimal health care facilities to accomplish this objective are specified in the guideline.

Conclusion

These policies are necessary for the prevention and control of AMR and HAI. As child health specialists and paediatric infectious diseases sub-specialists working in Africa, we should be advocates for the implementation of these guidelines in our health care facilities and should conduct relevant research to evaluate the effectiveness of these recommendations and be in the forefront of adapting these guidelines for our settings.

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REPORT OF THE 2nd HIV EXPOSED UNINFECTED (HEU) INFANT AND CHILD WORKSHOP

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The first HIV Exposed Uninfected (HEU) Infant and Child workshop was held in Vancouver in July 2015 and brought together enthusiastic clinicians, epidemiologists and basic scientists to review what is known about HEU infants and their clinical course, immunologic differences and risk for neurodevelopmental and infectious morbidity. This 2nd Workshop, held at the KwaZulu-Natal Research Institute for Tuberculosis and HIV (K-RITH) at the University of KwaZulu-Natal (UKZN) in Durban, built on the 1st Workshop by considering research methodologic challenges to facilitate the generation of high quality evidence translatable into action for HEU infants and children. The tone for the day was set by Mo Archary (UKZN) urging us to think more broadly about PMTCT aims and that instead of just preventing vertical HIV infection we should be striving for Promotion of the health of Mothers and Their Children Together (PMTCT).

Infant Feeding

Landon Myer (UCT) lead an engaging panel discussion on how to optimally measure and compare feeding exposures in HIV exposed and unexposed infants raising the tension between measurement for routine surveillance purposes, that needs to be pragmatic and focused on a few key questions, versus measurement for research purposes that may require more nuanced detail and sophisticated analytic techniques to understand the role of breastfeeding in reducing HEU infant morbidity. Nigel Rollins (WHO) highlighted the lack of reliable information on rates of breastfeeding in HIV-infected women, a critical piece of

information in accurately estimating postnatal HIV transmission rates.

Moleen Zunza (Stellenbosch University) shared her qualitative work showing that infant feeding choices are ongoing for mothers' despite having made an initial decision and that healthcare providers who are highly influential in these initial choices often lack the skills to adequately transfer messages to HIV-infected mothers about the risk-benefit ratio of infant feeding choices. Daya Moodley (UKZN) reminded us of the reality that whatever we have observed about infant feeding in a well-supported clinical research setting is unlikely to be achieved in the real world setting.

Infant HIV Diagnostics

Jean Maritz (Stellenbosch University) discussed HIV diagnostic dilemma's that are becoming apparent in the presence of prolonged infant postnatal prophylaxis and declining vertical HIV transmission. These include reduced sensitivity of standard HIV PCR tests and extended persistence of maternal antibodies beyond 18 months of age in up to 14% of HIV exposed but confirmed uninfected infants.

Specific HEU child challenges

Nigel Klein (University College London) took a critical look at the evidence for immune differences in HEU infants. With little evidence for quantitative differences in major lymphocyte subsets, there is fairly strong evidence for increased immune activation in HEU compared to HIV unexposed (HU) infants. Much of this evidence though comes from the pre-antiretroviral therapy (ART) era and there is yet to be a study that attempts to link immunological aberrations to clinical manifestations to better understand the relevance of these immune changes. A large prospective study that evaluates immunological differences in conjunction with clinical outcomes in the era of universal maternal ART is needed.

Kate Powis (Harvard) shared her work in Botswana, indicating that in the context of maternal ART HEU infants are experiencing impaired length growth that is only partly mediated by the higher prevalence of low birth weight in HEU infants. This indicates the urgent need to develop large scale pharmacovigilance and antiretroviral (ARV) safety surveillance that can keep up with the pace of expanding universal ART and changing regimens. Claire Thorne (University College London) discussed the challenges in establishing a consented cohort of HEU children for safety surveillance in the United Kingdom and how this has not been a feasible strategy even in a well-resourced setting. As an alternative, routine national data is being used to monitor death and cancer in children born to HIV-infected mothers.

Mary-Ann Davies (UCT) described efforts in the Western Cape leveraging the province wide patient unique identifiers to establish a provincial cohort of all pregnancies that can link mother-baby pairs to digitally available exposures including pharmacy records for ARV and other drugs. This will allow for evaluation of birth outcomes in relation to ART *in utero* exposure, hospitalizations for infectious and other events and future

association with rare events such as malignancies. Paige Williams (Harvard) took us through the advances being made in statistical methods to appropriately evaluate the safety of individual ARVs in the context of changing ART regimens over time, multiple concurrent ARV drug exposures and confounding by indication. Collaboration and pooling of data is going to be needed to achieve sufficient numbers of ART-exposed HEU infants to confidently establish safety. On this note Amy Slogrove (UCT) proposed that harmonization of outcome measures, particularly birth outcomes and infectious morbidity, could aid HEU researchers in more rapidly resolving outstanding questions through better comparability of studies across different settings.

The way forward

A small group will be taking this effort forward and aim to have a framework of harmonized outcomes to present to the HEU community at the 3rd HEU Infant and Child Workshop. Mark Cotton (Stellenbosch University) closed the workshop by reminding us of the importance of fathers and families in the PMTCT equation (PMTCT F² = Promotion of the health of Mothers and Their Children Together with the support of Fathers and Families). We thank UKZN for hosting this Workshop, Merck for sponsorship, SASPID and AfSPID for endorsements and all participants for their lively engagement. The 3rd Workshop is planned for July 2017 in Paris prior to the International AIDS Society Conference. All are welcome!

8TH ANNUAL UGANDA PAEDIATRIC & ADOLESCENT HIV CONFERNECE

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The 8th Annual Uganda Paediatric & Adolescent HIV conference held in Kampala Uganda from the 5-7th October 2016. The Annual Uganda Paediatrics and Adolescent HIV Conference is aimed at providing an opportunity to mobilize stakeholders; share scientific and programmatic knowledge; build on the present momentum necessary to achieve an HIV free generation; and provide care and treatment to all children and adolescent living with HIV. The conference is organized by the Ministry of Health with support from the AIDS Control Program, Academia from the Makerere University College of Health Sciences Department of Paediatrics and Child Health; key implementing partners like Baylor-Uganda; ANECCA, the JCRC, the Infectious Diseases Institute, Mild May Uganda, the Society of Adolescent Health in Uganda (SAHU), the Uganda Paediatrics Association (UPA), as well as other civil society organizations.

The theme for this year's conference was: Closing the gaps in Paediatric and Adolescent HIV/AIDS care now: Making 90/90/90 a reality"

Key highlights:

The conference was attended by national and international participants with an average of 620 daily. Most attendees were female at 61%, with a median age of 27(range 14-67); there was a heavy participation by adolescents and young people who organized the pre-conference. During an exit poll, adolescents reported increased awareness on their plight and rights to HIV prevention, care and treatment services.



Figure 1: conference participants

Uganda has recorded successes in the elimination of mother to child HIV transmission(eMTCT) and Antiretroviral (ART programs); the country currently faces an unprecedented HIV/AIDS burden among the adolescent age group as a significant proportion of vertically infected children survive and graduate into teenage years. Closing the gap in this context therefore means creating avenues for meaningful involvement of the young people, finding the hard to reach populations and ensuring that all mothers seek ante natal care early and get tested during pregnancy. In addition, Uganda, like many other countries in sub Saharan Africa needs to urgently find resources for services to sustain the early diagnosis and treatment agenda. There is need for inter-district /Inter-facility mechanisms to track lost infants and children. It is important to strengthen integration of HIV and other reproductive health (RH) services. And lastly, there is a need to develop a multisectoral approach to adolescent health. Adolescent health is a neglected area in Sub-Saharan Africa with little or no attention placed on this vulnerable population in the health sector. As we look towards achieving the 90:90:90 Global UNAIDS Targets. we must take bold steps in learning better how to deal with adolescents as health care providers.



Figure 2: younger conference participants

JOURNAL WATCH

Influencing antibiotic practice of prescribers

Review completed by Brian Eley

With the rapidly evolving crisis of antibiotic resistance, a key global challenge is the translation of awareness of resistance into effective antibiotic stewardship. Altering the behaviour of prescribing clinicians is critical for reducing unnecessary usage. This is easier said than done. Our decisions are habitual, automatic and influenced by the environment in which they are made, and therefore difficult to change. Hence, behavioural interventions aimed at improving antibiotic prescribing should be evaluated to ensure that they have the desired effect. One way to influence behaviour is to use social norms. For example, by simply pointing out that a beneficial behaviour is more prevalent than expected can increase the levels of that behaviour. This strategy was used recently in a pragmatic country-wide randomised controlled trial in England to influence the behaviour of high prescribers of antibiotics in general practice (GP).2

Publically available databases were used to identify GP practices whose antibiotic prescribing practices was in the top 20% of the country.

The trial was conducted in two stages: I. High prescribing practices were randomly assigned to two groups. Every GP in the feedback intervention group was sent a letter from England's Chief Medical Officer on 29 September 2014. The letter stated that the practice was prescribing antibiotics at a higher rate than 80% of NHS practices. GPs in the control group received no communication. Between October 2014 and March 2015, the rate of antibiotic items dispensed per 1000 population was 126.98 in the feedback intervention group versus 131.25 in the control group, a difference of 3.3%, incidence rate ration=0.967, p<0.001; representing 73406 fewer antibiotic items dispensed. II. The sample was re-randomised into two groups and in December 2014 GP practices were either sent patient-focussed information that promoted reduced antibiotic use or received no communication. The patient-focussed intervention did not significantly affect the rate of antibiotic items dispensed per 1000 weighted population.

These results show that an intervention incorporating social norm feedback on high antibiotic usage can significantly reduce use over a period of 6 months. This intervention offered 3 main advantages compared to face-to-face interventions for improving antibiotic stewardship, its relative inexpense, scalability, and low barriers to implementation. Thus antibiotic stewardship programmes should consider incorporating prescribing feedback into their activities.²

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Kaposi sarcoma risk in sub-Saharan Africa, Europe and Asia

Review completed by Brian Eley

To evaluate the burden of Kaposi Sarcoma (KS) in HIVinfected children and adolescents a collaborative research study was completed. This project involved 24 991 HIVinfected children and adolescents on combination antiretroviral therapy (cART) in 36 paediatric cohorts located in eastern Africa, southern Africa, Europe and Asia, yielding important findings. Twenty six developed KS after commencing cART. Incidence rates per 100 000 person-years (PYs) were 86 in eastern Africa (95% confidence interval [CI], 55-133), 11 in southern Africa (95% CI, 4-35), and 81 (95% CI, 26-252) in children of sub-Saharan African (SSA) origin in Europe. The KS incidence rates were 0/100 000 PYs in children of non-SSA origin in Europe (95% CI, 0-50) and in Asia (95% CI, 0-27). KS risk was lower in girls than in boys (adjusted HR [aHR], 0.3; 95% CI, .1-.9) and increased with age (10-15 vs 0-4 years; aHR, 3.4; 95% CI, 1.2-10.1) and advanced HIV/AIDS stage (CDC stage C vs A/B; aHR, 2.4; 95% CI, .8-7.3) at cART initiation. These results show that the KS risk is substantial in HIV-infected children and adolescents on cART of SSA origin, probably driven by high HHV-8 prevalence, particularly in eastern Africa and to a lesser extent in southern Africa.

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CONFERENCE & SOCIETY NEWS

- 5th Biennial Congress of the African Society for Immunodeficiencies (ASID) will be held at the Zambezi Sun Hotel, Victoria Falls, Livingstone, Zambia from 12 to 14 April 2017. For more information consult the ASID website: http://www.asid.ma
- 10th WSPID conference takes place in Shenzhen, China, from 2 to 5 December 2017. Information on the venue and conference dates will be made public shortly For more information visit the Paediatric Infectious Diseases Society website: http://www.pids.org/ or the conference website http://www2.kenes.com/wspid_2017/ AfSPID will once more host a dedicated symposium at this conference.
- **18**th 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/

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

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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.

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