



# The AfSPID BULLETIN

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## EDITOR'S COMMENTARY

Dear Colleagues

Welcome to the ninth edition of our newsletter.

The 11<sup>th</sup> World Society for Paediatric Infectious Diseases congress (WSPID 2019) took place in warm and humid conditions at The Philippines International Conference Center in Manila, The Philippines from 5 to 8 November 2019. The conference was a success, attended by 1290 participants from 77 countries, and 517 abstracts were accepted for oral or poster presentation.



**Figure 1: The Philippines International Conference Center**

On the first day of the conference the Education Committee of WSPID hosted a research workshop, convened by Dr Andi Shane (USA) and Dr Sally Gatchelian (The Philippines). This workshop is an important educational initiative of WSPID to strengthen research among younger conference attendees. The workshop was attended by 43 invited junior researchers,

invited speakers and the WSPID Education Committee. The programme comprised a mixture of didactic lectures on aspects of research presented by leading researchers and oral presentations given by 5 junior researchers who were selected on the quality of their submitted research abstracts. Two mentors (senior researchers) were assigned to each of these 5 researchers to assist them with the preparation of their oral presentations.



**Figure 2: Dr Lingyun Guo (China) flanked by her two mentors, Professor Lisa Gonzales (left) and Professor Brian Eley (right). Dr Guo gave an oral presentation on her research project entitled 'The Diagnostic Value of Metagenomic Next-Generation Sequencing for Pathogen Identification in Paediatric Infectious Diseases'**

Scientific programme of the conference included 18 WSPID symposia organised by the international scientific committee, society symposia organised by regional paediatric infectious diseases societies affiliated to WSPID, oral presentation sessions during which important research findings were presented and meet the professor sessions focussing on paediatric ID topics. African speakers were well represented on the programme.

The African Society for Paediatric Infectious Diseases (AfSPID) held its symposium on the last day of the conference. It was chaired by Professor Amha Mekasha (Ethiopia) and Dr Isaack Mohammed (Mauritius). Three talks were presented.

Professor Christian Happi, Redeemer University, Nigeria, presented a talk on Lassa Fever. Recent estimates suggest that Lassa Virus causes 2 million human infections and 5000-10000 deaths per annum. He described the contribution that genomic research has made in advancing the biology of Lassa virus, for example, yielding insights into the biogeography, evolution and spread of Lassa virus during the 2013-2015 West African epidemic. He also described advances in the development of reliable diagnostic tests, and the role that real-time next generation sequencing played in supporting the management and control of the 2018 outbreak in Nigeria.

Dr Francis Kiweewa of the Makerere University- Walter Reed Project, Kampala, Uganda was next to present. He described the safety and immunogenicity of the Ad26.ZEBOV/MVA-BN prime-boost vaccine. This vaccine was approved for use in the current Ebola outbreak in the Democratic Republic of Congo in October 2019.

The final presentation in this session was given by Dr Paula Vaz based at Fundação Ariel Glaser, Maputo, Mozambique. She described the impact of recent cyclones Idai and Kenneth that devastated Mozambique in 2019 within 6 weeks of each other, causing immense suffering. Dr Vaz described the measures that were implemented to successfully moderate the risk of infectious diseases outbreaks, particularly cholera and malaria in the aftermath of these natural disasters including wide scale cholera immunisation.

The AfSPID symposium was followed by a general meeting of the society. Professor Mark Cotton, President of AfSPID was elected the new President of WSPID. The next WSPID conference takes place in November 2021 in Cancun, Mexico

During 2019 several workshops & conferences were held on the African continent that featured paediatric infectious diseases. I would like to highlight one such event, a pre-conference ID update course organised by Professor Regina Oladokun on 20 & 21 January 2019 in Ibadan, Nigeria. This course preceded the 50<sup>th</sup> Annual Paediatric Association of Nigeria Conference (PANCONF 2019), was attended by approximately 80 delegates and featured a spectrum of talks on childhood infectious diseases, including HIV infection, tuberculosis, viral haemorrhagic fevers, rational antibiotic prescribing, antibiotic stewardship, malaria and primary immune deficiencies. This was an important course, the first in Nigeria focussing exclusively on childhood infectious diseases.



**Figure 3: Participants at the Paediatric ID update course, organised by Professor Regina Oladokun in January 2019**

To strengthen the newsletter and ensure its sustainability, the editorial board will be progressively enlarged over the next few years. Today, two members join the editorial board, Dr Tinsae Alemayehu of Ethiopia and Dr Ombeva Malande of Kenya & Uganda. Both are qualified paediatric infectious diseases sub-specialists.

Dr Tinsae Alemayehu did his Doctorate of Medicine and his residency training in Pediatrics and Child Health at the College of Health Sciences, Addis Ababa University. He earned his sub-specialty certificate in Pediatric infectious diseases in 2018 after completing a two-year fellowship program co-administered by the Addis Ababa University and McGill University, Canada. Dr Tinsae served as an Assistant professor of Pediatrics at his alma mater from 2014 – 2019. He also briefly co-directed the Addis Ababa – McGill University Partnership program in Infectious diseases. He played an integral role in establishing the first antimicrobial stewardship practice in an Ethiopian hospital in 2017. He now works as a pediatric infectious diseases' specialist at the only referral infectious diseases and travel medicine center in Ethiopia while lecturing at

the St. Paul's Hospital and Millennium Medical College as a guest. Dr Tinsae has authored fourteen articles in peer reviewed journals.

Dr Ombeva Malande is a vaccinologist & paediatric infectious diseases sub-specialist. He completed a Masters of Medicine (MMed) degree in Paediatrics & Child Health at Makerere University. He is a certified fellow of the College of Paediatricians of South Africa (infectious diseases subspecialty). He has recently finalised a Masters of Philosophy (Paediatric Infectious Diseases) degree at the University of Cape Town, and is pursuing his Doctor of Philosophy degree in vaccinology. He is a Lecturer of Paediatrics & Child Health, Egerton University, and an Honorary Lecturer at Makerere University. He is the director of the East Africa Centre for Vaccines and Immunization (ECAVI), a vaccines systems support, research, advocacy and training program in Eastern Africa, as well as the convener of the widely acclaimed ECAVI vaccinology course for health professionals. His research interests include vaccines/immunisation, antibiotic stewardship and emerging resistance patterns and clinical presentation and outcomes for extended spectrum beta-lactamase (ESBL) producing and Carbapenem resistant Enterobacteriaceae (CRE) in the African paediatric setting.



**Figure 4: New members of the Editorial board, Dr Tinsae Alemayehu (left) & Dr Ombeva (right)**

This edition of the newsletter includes reports on the PANCONF 2019, Chikungunya in Ethiopia, childhood tuberculosis management in Ghana, the East Africa centre for vaccines and immunization (ECAVI) course, vaccine surveillance in Nigeria and our regular journal watch slot.

I hope that you enjoy the contents of this newsletter.

Kind regards, Brian Eley

## **ANTIBIOTIC STEWARDSHIP (AMS) IN PAEDIATRIC PRACTICE IN THE STOPLIGHT AT PANCONF2019**

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The Paediatric Association of Nigeria (PAN) held her 50<sup>th</sup> Annual general Meeting and 6<sup>th</sup> international Conference from 20<sup>th</sup> to 5<sup>th</sup> January 2019 at the International

Conference Centre, University of Ibadan, Nigeria. At this auspicious time in the life of an organization that has played a leading role in the child health and training of paediatricians for half a century, the Paediatric Infectious Diseases group under the aegis of the Nigerian Society for Paediatric Infectious Diseases (NISPID), deemed it fit to address a topic that has taken centre stage globally, antimicrobial resistance (AMR). Antimicrobial resistance has become a threat to global health with estimated 10 million deaths annual by 2050 if the current trajectory is maintained.<sup>1</sup> Their approach was hinged on the fulcrum of antimicrobial stewardship, an activity we are or should, as paediatricians, be all engaged in antimicrobial stewardship being a set of coordinated interventions aimed at improving and assessing appropriate use of antimicrobial agents by promoting selection of ideal antimicrobial regimen ensuring the right agent, dose, route and duration. This is expected to achieve best clinical outcomes, reduce toxicity and adverse events, prevent development of resistance strains and possibly reduce cost of care.<sup>2</sup>

To this end, a meet the expert session was organized on the 25<sup>th</sup> January 2019 to discuss this most important topic. On hand to discuss this were eminent panelists and seasoned Paediatric Infectious Disease experts from the Northern and Southern hemisphere. Prof Brian Eley is the lead of the Paediatric Infectious Diseases department at the University of Cape Town and Red Cross War Memorial Children's Hospital. He is a leading voice on antimicrobial stewardship in South Africa. Prof Stephen Obaro is from the Children's Medical Centre at the University of Nebraska but has a vast network and deep experience of the Nigerian landscape about issues related to bacteriology, infectious in children and the antimicrobial stewardship across the breadth and length of Nigeria. This comes from years of research and engagement with different public and private health institutions in Nigeria. The third discussant was Prof Regina Oladokun of the University College Hospital, Ibadan (UCH) where she heads the Paediatric Infectious Diseases unit and also leads the Antimicrobial Stewardship (AMS) Committee of the hospital, probably the first and only AMS Committee in the country.

The session was attended by a large number of conference participants drawn from across the country and included paediatricians practicing at different levels of health care in both the public and private sectors. This attests to the interest, or challenges paediatricians face with respect to antimicrobial stewardship and thus their enthusiasm to learn more, share experiences and deepen the process of rational antibiotic use in their respective practices and training institution.

The discussion was kicked off by Prof Oladokun with a brief overview of what AMS is all about. She expounded on the global challenge of AMR and the potential of mitigating this challenge by AMS programmes in health institutions. The different components of an AMS programme, the composition and key players, the approaches to AMS and the challenges were highlighted. The panelist discussion centred on what AMS meant for the larger health system in Nigeria. Prof Obaro made the point of having a holistic view which includes the chemist or local medicines peddler that dispenses antibiotics or a concoction of antibiotics, especially where health services are not available and or inaccessible. On the approach to establishing AMS programmes in health facilities, Prof Eley made the point of starting with basic activities that health care providers can identify with. This starts with creating awareness, providing education and information backed with local data and facts to get the buy-in of the health care community.

A critical factor in establishing AMS programmes is the support of the management structures in the health facilities, especially in the phase of dwindling resources for health. This was the experience of Prof Oladokun from her efforts in establishing the AMS committee at the UCH. Another critical factor is ensuring all-inclusiveness of the various actors in the health institutions. This includes the infectious diseases physician who often leads the team, the clinical microbiologist, clinical pharmacologists, representative of central administration, the pharmacy, the laboratory scientists, ICT experts and representative of the total quality management department, or clinical governance unit as it is called in other climes. However, according to Prof Eley, the AMS committee does not have to be sophisticated and may include a few physicians who are keen on appropriate use of antibiotics.

Judging from contributions from the participants, this discussion was long overdue and guidance was sought on various challenges they face with respect to rational use of antibiotics or AMS. Issues raised included the veracity of laboratory results, in the absence of quality control or certification of the laboratories where these results emanate, which makes it difficult to use for patient management. In some settings the antibiogram presented do not reflect the expected minimum standards, but rather a reflection of sensitivity discs provided by drug companies. At other times the options presented have excluded recommended antibiotics for the specific microbe while in some centres there is total absence of microbiology laboratories.

The ability of patients to procure and sustain the prescribed antibiotics backed by appropriate laboratory result was also an issue of concern. Interruption in treatment regimens often made it difficult to ascertain if an antibiotic regimen has failed or it is due to poor compliance as most patient access health, including antibiotic provision, on a cash-for-service basis. In other instances, antibiotics provided by health insurance schemes such that make proper AMS difficult, as they are often restricted in scope and at times considered inappropriate. More worrisome, when antibiotics are available, is the challenge of fake drugs. In a setting where hospital pharmacies do not meet the antibiotic demand of the hospital and the mechanisms for monitoring the source and quality of antibiotics used by patients are weak or non-existent, adequate audit of the system becomes impossible.



**Figure 1: Panelists of the ID workshop, from left to right: Dr Babatunde O. Ogunbosi (Ibadan), Professor Stephen Obaro (Nebraska), Professor Brian Eley (Cape Town), Professor Regina Oladokun (Ibadan), Dr Holly Rawizza (Harvard), Dr Ese Ebruke (IFAIN), Dr Dayo Adetifa (KEMRI, Kilifi) & Dr Theresa Ajose (IFAIN)**

It is obvious from the meeting that there is a need for more engagement between the health authorities, regulatory agencies, pharmaceuticals and health care providers on issues relating to AMR. AMS programmes need to be established and supported in the most basic of health facilities and all stakeholder need to collaborate in all ways possible if the challenge of AMR is to be mitigated. It is commendable that professional bodies like PAN and NISPID have brought this very important issue to the front burner and this should be encouraged. The session was generously sponsored by Human Diagnostics in partnership with CC-Bio innovations, Nigeria Ltd.

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## CHIKUNGUNYA OUTBREAK IN ETHIOPIA

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### Introduction

Chikungunya is an alphavirus infection transmitted by *Aedes* mosquitoes, especially *Aedes albopictus* and *Aedes aegypti*. It was first reported in 1953 in the border areas between Tanzania and Mozambique – its name derived from the language of the Makonde people and meaning “that which bends up” pointing to the severe joint pain associated with the virus.<sup>1</sup>

Chikungunya infection is characterized by a saddleback pattern of fever and multiple small joint arthralgia. It is transmitted by the *Aedes* mosquitoes which may also transmit Dengue, Yellow fever and other illnesses. Though joint complaints and fever predominate, patients may also experience erythematous macular or maculopapular rash, nausea, vomiting and headache 2 – 5 days after onset of illness.<sup>2</sup> The ankles and wrists are most affected by arthralgia which is worsened by gripping on affected joint.<sup>3</sup> Bleeding tendencies are less common and together with encephalitis are mostly reported from high risk groups like newborns, the elderly and the immune-compromised. Arthralgias can persist for weeks to months before resolution.<sup>4</sup>

Diagnosis is made by detection of virus in the first week of illness (period of peak viremia) and serologies (IgM appearing after first week of illness and persisting till three months and IgG appearing after two weeks of illness and lasting lifelong).<sup>5</sup> Most infections are self-limiting with treatment mainly based on symptomatic relief. Preventive strategies consist of vector control and personal protection. No effective vaccine exists.<sup>6</sup>

### Transmission

The *Aedes* mosquito is an aggressive daytime biter. Proximity of mosquito larval sites to homes is a major factor for chikungunya transmission.<sup>7</sup> Researchers

studying the Chikungunya outbreak in Reunion island showed a maximal temperature (higher than 28.5°C) and cumulative rainfalls (higher than 65 mm) in the month preceding infection, low socio-economic status, low altitude of dwelling, occupational inactivity, a lack of knowledge on transmission and obesity to be independent risk factors for acquisition of infection.<sup>8</sup>

### Epidemiology of Chikungunya infection in Africa

The majority of Chikungunya virus outbreaks in Africa were reported from the 1960s – 1980s. A large epidemic originating in 2004 in Lamu, Kenya spread to the Indian Ocean countries (2004 – 2006).<sup>7,9</sup> Chikungunya infection in African communities has been reported from 18 countries, mostly from east and central Africa (Figure 1).<sup>10</sup>



**Figure 1: African countries who have prevalence or outbreak reports for Chikungunya infection**

In recent times, Chikungunya outbreaks have been witnessed in various settings of the continent, refer table 1. In between these outbreaks, the virus is preserved by a sylvatic transmission cycle between arboreal mosquitoes and wild primates.<sup>11</sup>

Onset	Country of origin	No. suspected	No. confirmed	Genotype
Apr 2014	North Mozambique	114	8 of 114 samples	ECSA <sup>12</sup>
Sep 2015	Kedougou, Senegal	1409	10 of 14 collected samples <sup>13</sup>	
Feb 2016	Bula-Hawa, Somalia & Mandera, Kenya	1792 by June 2016	95 of 177 collected samples	the East, Central, and South African (ECSA) lineage of CHIKV imported from India (where it had caused an outbreak in 2010) <sup>14</sup>

Dec 2017	Mombasa, Kenya <sup>15</sup>	453 by Feb, 2918	32 of 453 collected samples	
May 2018	Red sea state, Sudan <sup>16</sup>	13,978 by October 2018 (7% aged < 15 years)	72 of 126 collected samples	
Jan 2019	Diosso, Congo rep.	6,149 by May 2019	61 of 173 collected samples	A226V mutation from a related <i>Aedes aegypti</i> – associated Central Africa CHIKV strains <sup>17</sup>

**Table 1: Chikungunya outbreaks over the past five years (2014 – 2019) in the African continent**

### Current outbreak in Ethiopia

As of 3 September 2019, more than 20,000 people have been infected by Chikungunya virus in an outbreak affecting mostly the eastern parts of Ethiopia – a fourth of which are children aged 15 years or less. <sup>18</sup>

The first ever confirmed case of a Chikungunya infection in Ethiopia was identified in June 2016 from the Suuf sub-district, Dollo Ado district of the Somali region of Ethiopia. The Dolo Ado district borders the Mandera county of Kenya, where a confirmed outbreak has been present since February 2016 (see Figure 2). Though the infection is known to exist in Kenya since 2004, the present outbreak in north-eastern Kenya is thought to have been imported from Somalia. <sup>19</sup>

The first reports of the outbreak in Ethiopia were made on the 8<sup>th</sup> March 2019 in the Ad'ar district of the Afar region. But the epicenter of the outbreak has been the Dire Dawa city administration, the largest city of eastern Ethiopia and the second largest in the nation. <sup>20</sup>

Chikungunya infection in the current outbreak has been reported (in decreasing frequency) from the Dire Dawa city administration (east Ethiopia), the Ad'ar district of Afar region (north-east Ethiopia), the Somali region (east Ethiopia) and the Dawro zone (south-west Ethiopia). Severe small joint pains were noted to be the predominant presenting feature with or without fever. Thus far, there have been no recorded mortalities. <sup>18</sup>

Dire Dawa city, the most affected area, sits in an arid environment. Average day time temperatures range from 28.3°C (in December and January) to 33.7°C (in May and June). The average rainfall ranges from 33 – 41 centimetres in the dry seasons to 401 centimetres in peak rainy season. There is erratic pipe water supply in the city which has forced inhabitants to utilize household water storage containers. These practices are attributed by experts for the reproduction of the vectors as well as the recent outbreaks of Dengue fever (first confirmed case in 2013) and Chikungunya fever.



**Figure 2: Political map of the border between Ethiopia and Kenya**

Insecticide spray campaigns, public education on use of mosquito nets and cleaning swamps and trainings for health workers in affected regions are being done to prevent further spread of Chikungunya infection in Ethiopia.

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## OVERVIEW OF CHILDHOOD TUBERCULOSIS MANAGEMENT IN GHANA

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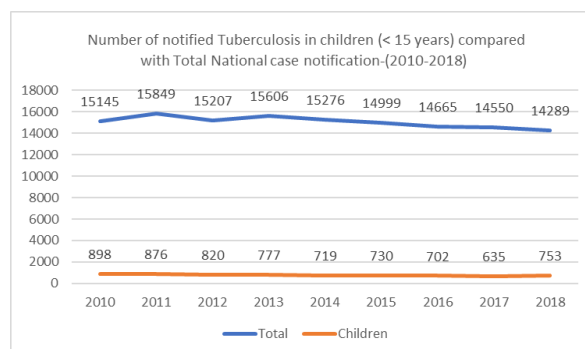
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### Introduction

Global attention on childhood Tuberculosis (TB) is a fairly recent phenomenon after a decade of neglect.<sup>1</sup> Childhood tuberculosis had been neglected in endemic areas with resource constraints, as children were considered to develop mild forms of disease and so contributed little to the maintenance of the tuberculosis epidemic.<sup>2</sup> Ghana within the global context is contributing towards Ending TB by 2030. This review article looks at the progress made in the management of Childhood TB in Ghana.

### National Tuberculosis statistics on children

The estimated TB incidence and incidence rate for Ghana in 2018 was 44,000 and 148/100,000 population.<sup>3</sup> The total number of reported cases as shown in figure 1, falls below the expected for the country. In 2018, out of the expected 44,000 cases, 14,289 cases were reported to the National Tuberculosis Control Programme (NTCP). Thus, the national TB notifications were 32% of the expected number of cases. Childhood TB cases nationwide averaged 5% of total cases notified which is far less than the expected 15–20% burden of tuberculosis.<sup>4</sup> The situation clearly reveals that TB in children is underdiagnosed. Cases are either not been found or misclassified as other diseases such as bacterial pneumonia and malnutrition.<sup>5</sup>



**Figure 1: National Childhood Tuberculosis trend from 2010 to 2018. Credit: Ghana TB Control Programme**

### Institutional structure

The NTCP is an agency under the Communicable disease Unit of the Ghana Health services. It is headed by the Programme Manager (PM) who is assisted by the Deputy Programme Manager (DPM). The DPM is responsible for childhood TB activities at the National level and work closely with the National Child TB working group (NCTWG). The Childhood TB champion (Paediatrician) leads and sets the agenda with other members for the NCTWG in conjunction with and financial support from the NTCP. Quarterly meetings are held with predetermined objectives. Most meetings have centred on improved case finding and data collection in children. The composition of the NCTWG are paediatricians, the NTCP, data managers, pharmacists, partners (WHO and UNICEF), and non-governmental organizations with interest in child health. Figure 2 shows the NCTWG meeting at the NTCP conference room, Accra.



**Figure 2 NCTWG quarterly meeting at NTCP office, Accra**

Another major role of the NCTWG is to support the NTCP to develop guidelines for the management of childhood TB in Ghana. Currently guidelines are being updated to reflect evidence-based practices in the discipline.

### Diagnostics

Diagnosing pulmonary TB (PTB) in children faces the same challenges as other parts of the world due to poor specimen techniques and paucibacillary disease.<sup>6</sup> It is not uncommon for PTB to be considered a differential after response to conventional treatment of pneumonia is poor. Diagnosing TB meningitis (TBM) follows same principle of looking deeper when response is poor. History of contact with someone with TB have often been asked in retrospect. Gastric lavage is the most performed specimen

collected technique and even though yield on Xpert MTB/RIF Ultra is better than microscopy, overall sensitivity is poor and ultimately diagnosis is often reverted to clinical.<sup>7</sup> Digital x-ray images are available at specified district hospitals for easy access to patients. Even though the NTCP procured the X-ray machine, the maintenance of the equipment is the responsibility of the facility. Aside from patients with suspected TB, all other users are charged. Logically, the more non-TB patients use the digital x-ray, the more the health facility generate revenue for both maintenance and other administrative purposes. Sometimes TB suspects have had challenges accessing the digital X-ray. Distance to a facility where digital x-ray is located is relative to the place of residence of the patient with suspected TB. Children with suspected TB depend on the willingness of adults (parents inclusive) to send them for imaging. The motivation is low the farther the distance. When x-rays are done, who interprets the results is another hurdle especially in district facilities where radiologists are not stationed. With advent of social media, a common platform has been created to share images with experienced paediatricians and radiologists for inputs towards the diagnosis of unconfirmed TB.

The NTCP has reference laboratories which have the capacity to routinely do TB cultures, line probe assays (LPA), and drug sensitivity testing for both first- and second-line TB medications.

### Capacity building

Childhood TB is rapidly evolving with new scientific evidence. These evidence guides NTCP policies. A study in South Africa suggested sputum induction was preferable to gastric lavage for diagnosis of pulmonary tuberculosis in both HIV-infected and HIV-uninfected infants and children.<sup>8</sup>

The NTCP has engaged a recently trained paediatric pulmonologist from Red Cross War Memorial Children's Hospital (RCWMCH) under African Paediatric Fellowship Programme (APFP) who is building capacity in Regional Hospitals to perform Induced sputum. The long-term vision is for regions to sequentially roll out district hospital training of nurses and clinicians to perform induced sputum. Hopefully, as specimen quality improves so will bacteriological yield.



**Figure 3: Trainer-of-Trainers workshop on sputum induction. Credit-NTCP**

### HIV/TB

National TB guidelines is explicit on screening all HIV positives for TB and *vice versa*. Adherence to the recommendation is not consistent. In some instances, HIV screening in children with TB is prompted by poor

response. Drugs for both HIV and TB are available at treatment centres. The main challenges are the combination of drugs in co-infected children. For younger age group (under 2 years), nevirapine is the non-nucleoside reverse transcriptase inhibitor (NNRTI) of choice. The interaction with rifampicin is well known but unavoidable for some co-infected children requiring both antiretrovirals (ARVs) and anti-TB medications.<sup>9</sup> Not all children are switched to triple nucleoside reverse transcriptase inhibitor (NRTI) especially when children involved are severely malnourished with moderate to severe anaemia (ruling out the use of zidovudine). Protease Inhibitors (PI) are reserved as second-line antiretroviral therapy (ART). When a child on second-line (PI based) develops TB, the routine 4 drugs (rifampicin, isoniazid, pyrazinamide and ethambutol) are administered without boosted ritonavir. Recent discussion has informed the decision to double the dose of PI in older children with TB during treatment. The National AIDS Control Programme (NACP) is engaging stakeholders on the way forward for making ritonavir syrup available for super-boosting<sup>10</sup> when needed for younger children who necessarily must be on dual therapy.

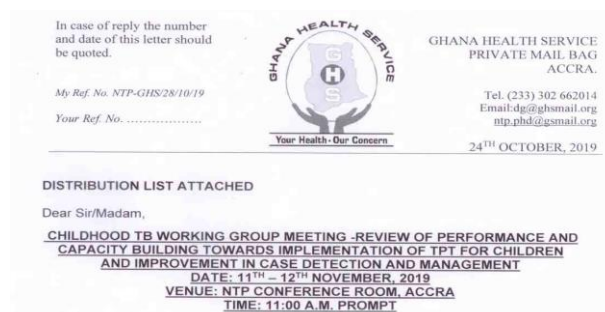
### Drug Resistant TB

Data from NTCP showed a total of 231 drug resistant TB (DR-TB) identified at the National level between 2010 and 2018. This data has not been disaggregated so exact figures in children (< 15 years) and treatment success rate was not readily available as at this write-up. A protocol for management of DR-TB in children based on updated WHO guidelines<sup>11</sup> have been developed with the help of a consultant. The national management guideline for DR-TB has appropriately being updated for children. Patients are preferentially treated in the communities with support from the District Health Management Team (DHMT) who also report to Regional Health Management Team. DR-TB drugs are supplied directly from the NTCP in agreement with the NCTWG and sent directly to the DHMT responsible for the child. Supplies are refilled after justification for use and progress report is submitted. Treatment decisions for DR-TB management in children are often clinical and drug choices are initiated on the national template which are modifiable based on close contact DR-TB drug sensitivity profile. Follow up is mainly on clinical and radiological response. In instances where the index case (household contact) is also on treatment, adherence is strictly supervised through direct observed therapy and sputum specimen followed up according to national policy guidelines.

### TB Preventive Therapy

Isoniazid prophylaxis therapy (IPT) is readily available for children below 5 years with documented exposure to TB contact. Newborns to mothers with TB are also well catered for with IPT after disease is ruled out in the neonate. BCG is however often given irrespective of the prophylaxis. This is often due to poor coordination between the immunization team and the clinicians. Children are treated in the community for 6 months with the caregiver going for regular monthly refill. The challenge is for these clients to be loss to follow-up especially when they are not monitored in the community. The tendency to stop treatment by the caregiver is often premised on the children been healthy.<sup>12</sup> But most importantly, these children need close monitoring within the IPT treatment period especially weight progressing. If Children on IPT begin to deteriorate on treatment, they should be switched to full short-course treatment for 6 months under supervision by health worker.

TB Preventive Therapy (TPT) broadens the scope of prophylaxis to include People with and without HIV living in high TB burden countries beyond the "golden 5-year rule".<sup>13</sup> It must be emphasised that TPT entails proper screening for active disease. The NTCP is building capacity to roll-out a successful TPT regimen in Ghana (Figure 4)



**Figure 4: Ghana Health Services prioritises activities of Childhood TB**

### Contact tracing and case finding

Childhood TB can be regarded as an emerging epidemic in areas where the adult epidemic remains out of control and *Mycobacterium tuberculosis* transmission is ongoing.<sup>14</sup> For every child diagnosed with TB (especially confirmed), there is someone in the child's community with active disease. The concept of contact tracing is well described in national guidelines but the true story on the ground does not seem consistent. Adults with confirmed or unconfirmed TB are appropriately put on treatment but the follow up on their children at the community level has been poor. Active follow up has proven to yield more results than passive follow up.<sup>15</sup> Clients often do not want to be identified by health care workers (HCWs) working within their catchment area due to stigma. This is a main constraint to active follow up because transport and other logistics must be provided so that HCWs can follow up on such clients residing in another DHMT catchment area. Moreover, HCWs services are in high demand within the hospital setting making it a challenge to release them for active follow up. This reveals a gap in the health care system where the DHMT within the community that the client resides is totally unaware of the client. To reduce cost, improve active follow-up and TPT implementation services, DHMTs should communicate and develop a functional tracking system for intensified active case finding and treatment.

### Advocacy by the Paediatric Society of Ghana

The Paediatric Society of Ghana (PSOG) collaborates very closely with the NTCP in advocacy, communication and social mobilization. The PSOG provided Paediatric Experts for the NTCP for a country-wide training programme on "childhood tuberculosis" management from 2016-2018. WORLD TB Day is marked yearly by the PSOG engaging the public through outreach programmes on radio stations, and visits to second cycle schools. School debates on childhood TB are also held between top schools who compete for a trophy.<sup>16</sup> Social media platforms have been created by the NTCP for most HCWs directly involved in TB care in Ghana. This innovation has made room for sharing of new research ideas and evidence-based clinical practices to inform clinic decisions at the district levels.

### Private Public Mix

Public and private health sectors both play crucial roles in the health systems of low- and middle-income countries.<sup>17</sup> Very few private sector health institutions get actively involved in child TB diagnosis and management. Almost all points of supply for anti-TB drugs are through established government or quasi-government health institutions. Private hospitals and clinics who suspect TB in children refer such cases to government institutions where investigations are done at no cost the patients. Moreover, treatment for TB is also free at all institutions. Anti-TB drugs are not readily available outside of government approved hospitals. Identifying at risk children whose parents would rather prefer private hospital to often congested government hospital delays early diagnosis and treatment. Certain communities are served only by private hospitals who are not well trained and equipped to suspect, investigate and treat children with TB. Referring such children with suspected TB to another facility will mean the clinician or health provider has thought of TB as a differential which is often not the case. If referral is done, the time between receiving the referral note and physically attending to care at the facility with ability to investigate and treat often takes a couple of days mainly because of lack of financial resources and poor understanding of the implication of childhood TB and its potential complications.

### Research

The NTCP supports selected facilities to undertake operational research on adaptations of study finding from settings that are fundamentally different from Ghana to suit cultural norms of local setting. Academic institutions also engage in observational and interventional research to inform both local and international knowledge in child TB care. For instance Kwame Nkrumah University of Science and Technology (KNUST) have studies on pharmacokinetics on antiretrovirals (ARVs) and anti-TB drugs routinely used by the national programmes.<sup>18,19</sup>

### Integrated care

In the past, the NTCP and the National AIDS Control Programme (NACP) have operated independently and submitted separate budgets to global funds for support. At the hospital level, there was minimal overlap in activities between the two entities. Patients have had to move to separate Health facilities to access care when they are co-infected. In a typical clinical setting, a child identified with moderate to severe malnutrition may or may not be screened for TB and HIV. This often depends on the orientation of the HCW attending to the child and the level of care. In the very rural setting, community health nurses may be the only trained health experts. Their basic training is in immunization and disease prevention. It is not uncommon for malnourished children to be put on nutritional rehabilitation irrespective of the underlying risk factors. Help with respect to ARVs and anti-TB drugs may eventually arrive if need be but this can severely impact mortality and morbidity.<sup>20,21</sup> There is therefore the need for more integrated services (TB, HIV, nutritional) among health providers in the interest of the sick child. For this to succeed programme managers (TB, HIV & EPI) who are policy makers must also talk to each other. It is easier for implementors at peripheral and community levels to coordinate their functions if instructions and directions for coordination comes from authorities.

In recent times, activities are well coordinated at policy levels for the NTCP and the NACP. Annual stakeholders meetings are synchronised with joint applications to global funds.<sup>22</sup> Health facilities are re-orienting to accommodate both HIV and TB at clinics where medications are also served at the same point of care.



## Stop TB partnership

This is a WHO partnership support for in-country civil society organizations (CSOs).<sup>23</sup> Civil society organizations are non-profit organizations that include non-governmental, faith-based, community-based and patient-based organizations as well as professional associations. Their health sector-related activities range from care and service provision to research, advocacy, lobbying and activism, and contribution to social welfare and support. Their main drive is usually to protect and empower the most vulnerable and to promote the communities they serve.<sup>24</sup> These groups are involved in screening of communities for TB including childhood contacts and referral to the nearest health facilities for further investigations when cases are suspected. STOP TB Ghana provides some funding to support activities of CSOs involved at the community level.

## Conclusion

The future is promising for childhood tuberculosis in Ghana so long as major stakeholders keep engaging each other towards an agenda for zero TB in children.

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## EAST AFRICAN CENTRE FOR VACCINES AND IMMUNIZATION (ECAVI) VACCINOLOGY COURSE FOR HEALTHCARE WORKERS: AN OPPORTUNITY FOR IMMUNIZATION SYSTEM STRENGTHENING IN AFRICA

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## Background

Vaccine-preventable diseases (VPDs) are a major contributor to morbidity and mortality in low-income countries (LICs).<sup>1</sup> Vaccination is an important child survival strategy especially in high-burden LICs where more than 10 million children under 5 die annually.<sup>1-3</sup> Immunization, a major pillar for attaining Sustainable Development Goal (SDG) 3 (aiming to reduce the under-five year-old mortality rate [U5MR] to less than 25/1000 live births by 2030) can prevent almost three million deaths annually.<sup>4-5</sup> Challenges facing immunization coverage in LICs include language barriers, transport-related access problems, terrain-related accessibility barriers, low education and socio-economic status of caregivers, refugee status, cultural barriers, religious beliefs, young age of caregivers, population mobility, vaccine hesitancy and negative messaging.<sup>6-11</sup> Research in LICs has identified healthcare worker (HCW) training as a major intervention needed to increase vaccination coverage.<sup>1,2,6,9,11</sup> The resurgence of VPDs which were earlier thought to be under control, such as measles, has heightened the need for innovative strategies to control this spread. In March 2019, 26 districts in Uganda were identified by the Ministry of Health (MoH) as experiencing recurrent measles outbreaks. This led to the MoH and Parliament initiating a measles action plan to combat the re-emergence of the disease in these districts, with enhanced HCW training and community/social mobilization being central to this plan.

The launch of the SDGs in 2016 to replace the Millennium Development Goals (MDGs), came with the clear realization that none of the countries in East Africa attained MDG 4 that aimed to reduce U5MR by two-thirds. According to the 2014 Kenya Demographic and Health Survey, the infant mortality was 39/1000 live births with U5MR of 52/1000 live births, implying that at least 1 in every 19 children born in Kenya in 2014 died before reaching their fifth birthday.<sup>12</sup> The 2016 Uganda Demographic and Health Survey reported an U5MR of 90/1000 live births, and an infant mortality rate of 43/1000 live births.<sup>11</sup> Measles, a re-emerging VPD in East Africa, currently poses the biggest challenge to immunization programmes around the world. The World Health Organization (WHO) African Regional Committee has adopted a regional measles elimination goal for 2020, urging all countries to achieve an incidence of confirmed measles of less than 1 case per million population and to attain the elimination of measles and make progress in the elimination of rubella and congenital rubella syndrome with effort to aim at MCV1 coverage of at least 95% at the national and district levels and SIA coverage to be 95% in all districts.<sup>14</sup>

## Evolution of the ECAVI Vaccinology Course for HCWs

The East Africa Centre for Vaccines and Immunization (ECAVI) is an initiative of health professionals, working with and through the Paediatric Associations in Eastern Africa, to promote advocacy, training, research and improving and strengthening immunization health systems; and promoting improved uptake and training on new and available vaccines; towards the control of morbidity and mortality associated with vaccine preventable diseases and cancers in Eastern Africa (including the five East African Community member states

Burundi, Kenya, Rwanda, Tanzania and Uganda, plus Sudan, South Sudan, Ethiopia, Eritrea, Djibouti and Somalia). While we acknowledge that a lot has been done to improve coverage and understanding about vaccines and immunizations in Eastern Africa, there are some gaps, which could still be filled. Somalia and South Sudan are countries emerging out of periods of prolonged conflict and displacements, with weak child survival and immunization health systems. Even Kenya and Tanzania, the more peaceful of the 11 nations in Eastern Africa, are not faring excellently in vaccine coverage and control of vaccine preventable illnesses.

Mortality indicators show that over half of all children Under 5 years of age who die in the Eastern Africa region do so directly or indirectly due to vaccine preventable illnesses, especially pneumonia, diarrhoea, measles, whooping cough, tetanus, TB and pertussis.<sup>6</sup> Pneumonia alone kills more children than malaria, TB and HIV combined.<sup>3</sup> The aim of ECAVI is to make a contribution however small, to the current immunization situation in Eastern Africa. Founded on 1 August 2014 and registered as an international non-governmental organization in both Kenya and Uganda, ECAVI promotes improved uptake and training on new and available vaccines, towards the prevention and control of morbidity and mortality associated with VPDs and cancers in Eastern Africa. ECAVI plays a leading role in organising vaccinology symposia during annual scientific conferences for paediatric associations across East Africa, and closely partners with the WHO, UNICEF and MoHs in the region, to launch new vaccines and update vaccination schedules for recommended Expanded Programme on Immunization (EPI) vaccines in the East African region.

It is hoped that through ECAVI a platform is created, and forum made for exchange and sharing of up to date and accurate information about vaccines in Eastern Africa. ECAVI also provides links to up to date statistics regarding vaccine and immunization coverage and indices within Eastern Africa. ECAVI continues to work closely with its collaborators to advance the pillars of training, health system support, advocacy and research. These included training sessions for immunization health workers in Wakiso District of Uganda and Hoima District of Uganda. ECAVI has also been actively involved in the roll out and supervision activities with the ministry of health and UNEPI in Kampala, Wakiso, Kaberamaido and Kanungu Districts in Uganda. Experts from ECAVI have worked as national supervisors and independent monitors during these national and country wide SIA activities. The Director and Program manager of ECAVI recently attended the Global vaccinology Training conveners and experts Workshop, which was held at Les Pensières Center for Global Health in Veyrier-du-Lac, Annecy, France, on 7th and 8th November 2018. It was a good forum to exchange thoughts, ideas and experiences with other conveners of vaccinology courses from around the world which shall help us of future courses.

ECAVI also organizes the Annual Children's Cancer run in Kampala, which seeks to create awareness about prevention of Cervical Cancer and other vaccine preventable illnesses in children through immunization, by making available all such information to parents and participants through the children's cancer run. ECAVI is a central member of the stakeholders and expert's forum on influenza and related disease surveillance, organized by Mériex Foundation called the Middle-East and Africa Influenza Surveillance Network (MENA-ISN), established in 2014. ECAVI recently won two research grants from WHO-CDC to conduct research in Kenya and Uganda. The study in Kenya was in Mathare valley informal settlement – on reporting of adverse events following immunization (AEFI) in informal settlements in Nairobi,

Kenya. The activity sought to find out whether there are any AEFI in Informal settlements of Nairobi county; to determine the knowledge, experience, perception, and practice level on AEFI reporting and surveillance among health workers serving informal settlements of Nairobi; to determine the knowledge, experience, and attitude of Health workers towards detecting and reporting AEFI in Informal settlements in Nairobi and to explore and find ways in which the community and health workers in informal settlements can be equipped with knowledge and skills to manage AEFI.

The study in Uganda was done in Hoima District, entitled Health System Strengthening of Immunization Services in Uganda, that aimed at understanding why Hoima district continues to register immunizable disease outbreaks in particular measles annually despite availability of an active national immunization program, to identify gaps in immunization health systems that contribute to low uptake and completion of immunization schedules and generate ways in which the capacity of Health workers in Hoima be strengthened in order to reach at least 90% of the unvaccinated children and support monitoring of National Immunization indicators.<sup>9</sup> ECAVI has prioritized health worker training and education as a central pillar and cog in improving immunization uptake in the region, towards the control of vaccine preventable diseases, and eventual reduction in under five morbidity and mortality in the region due to these diseases.



**Figure 1: Participants at the 4<sup>th</sup> ECAVI vaccinology course at Silver Springs hotel, Bugolobi, Uganda**

Since 2016 ECAVI, working with partners and stakeholders, has trained over 500 HCWs through its annual vaccinology course held over 5 days. Of those trained, 49% are from Uganda, 29% from Kenya, 6% from Tanzania, 5% from South Sudan, 4% from Nigeria, 3% from Somalia/Somaliland, 2% from Rwanda, 1% from Ethiopia, and 0.5% each from Sudan and Afghanistan. ECAVI plans to hold its sixth vaccinology course from 22-26 June 2020, in Kampala Uganda. This course will focus on current and new developments in the use of vaccines in the East African region, targeting 100 HCWs from across East Africa, in line with ECAVI's aim of training a 1000 HCWs over a period of 10 years. The course is designed for HCWs working in the field of vaccination administration and delivery [nurses, midwives, cold chain managers, EPI focal persons, medical doctors, masters students (MPH, MSc, and MMed), pharmacists, public health professionals, vaccine programme administrators] and HCWs who are interested in the clinical aspects of vaccines and immunization.

Central to successful organization of this course, has been the major role played by two key partners - the South African Vaccination and Immunisation Centre (SAVIC) at Sefako Makgatho Health Sciences University (SMU) in South Africa and the Network for Education and Support in

Immunisation (NESI) at the University of Antwerp, Belgium. These two organizations have a great experience and history for supporting advocacy, training and capacity building towards improved immunization systems in Africa. SAVIC and NESI have been central and pivotal to generation of course content, course administration, course delivery and its continuous evaluation/improvement. The full list of organizations partnering with ECAVI in organizing and running this course include the following:

- Makerere University (MU), Kampala, Uganda
- The South African Vaccination and Immunisation Centre (SAVIC) at Sefako Makgatho Health Sciences University (SMU)
- The Network for Education and Support in Immunisation (NESI) at the University of Antwerp, Belgium
- Uganda National Academy of Sciences (UNAS)
- Kabarak University (KU), Nakuru Kenya
- Uganda Paediatric Association
- Kenya Paediatric Association
- Kenya, Tanzania and Uganda EPIs
- Paediatric Association of Tanzania
- University of Nairobi (UON)
- The Centre for Health Advancement, Research and Resource Mobilization (CHARRM) based in East Africa.

#### **Justification for ECAVI Vaccinology Course for HCWs**

Vaccination is a key strategy for prevention of communicable diseases, which contribute more than two-thirds of the U5MR in the East African region. The overwhelming response by HCWs to previous ECAVI vaccinology course adverts, resulting in a growing waiting list of applicants, coupled with representation from beyond Eastern Africa, shows that many HCWs are eager for training on current and new vaccines and how to improve their immunization practices. Kenya and Uganda have recently experienced increased public resistance and negative sentiments against TT, measles-rubella, hepatitis B (Hep B) and oral polio vaccines (OPV), which may contribute to declining uptake. Of Kenyan and Ugandan children aged 12-23 months, 68% and 52% respectively are fully vaccinated.<sup>12-13</sup> This low coverage reflects dropout rates of 8% for pentavalent, 17% for OPV, and 9% for pneumococcal vaccine. In 2014 Uganda rolled out human papillomavirus (HPV) vaccination against cervical cancer; however, only 48% and 1% of the targeted girls respectively were reached for the first and second doses. The Uganda National EPI (UNEPI) attributes this low uptake of the HPV vaccine to inadequate community mobilization and poor HCW knowledge on the vaccine roll-out strategy. However, vaccine hesitancy, vaccine refusal and rumours of AEFI may have contributed as well. ECAVI aims at improving this situation, by contributing to immunization programmes through strengthening systems and education of HCWs. There are group and plenary sessions with the 100 participants interacting with over 20 facilitators to share views, research findings, experiences, successes, challenges and formulate possible interventions for improving their own roles which are part of the larger national immunization programmes. The

course also promotes education and knowledge among vaccinators, empowering them to be vaccine advocates and immunization champions. To ensure relevance and applicability, the expert facilitators are largely professors and senior lecturers from medical schools; MoH EPI officers, and stakeholders who participate in vaccination-related decision-making at the highest level in Eastern Africa.

### Content, administration and facilitators for the ECAVI Vaccinology Course

The course content includes:

- Introduction and history of vaccination in East Africa
- Basic immunology of vaccines (immune system, how vaccines work, current/new vaccines, and vaccines under development)
- Vaccine development and pharmacology (formulation/composition, indications and administration)
- Vaccine evaluation process: Preclinical, Phase I, Phase II and Phase III trials; and regulatory approval and registration
- Overview of Vaccine Preventable Diseases
- Vaccine safety and AEFI surveillance: Post-licensure and post-introduction monitoring of vaccine safety and effectiveness; recognition, management and reporting of AEFI
- Vaccine registration and WHO prequalification; the process of introduction of a new vaccine into a national immunization programme: important considerations; vaccination policy and immunization schedules in Eastern Africa
- Current safety issues and controversies regarding immunization (the media, language, terrain, beliefs, age, culture, communication on vaccines, vaccine hesitancy and negative messaging)
- Roles of Gavi, the WHO Global Vaccine Action Plan, EPI, National Immunization Technical Advisory Groups, and national and subnational SIAs
- Vaccines for special groups and populations (pregnant women, adolescents, adults, and immunocompromised patients)
- Vaccine related logistics (integrating immunization into health systems; cold chain management; communicable disease surveillance)
- Immunization data management and record keeping: monitoring and evaluation, data capture, storage, analysis and sharing
- Practical skills training in immunization, discussion, knowledge and experience sharing among participants



**Figure 2: Facilitators at the 2<sup>nd</sup> ECAVI vaccinology course, from left to right: Dr Ombeva Malande, Dr Carine Dochez, Ms Afaayo Rachel, Dr Sabrina Kitaka & Dr Irene Lubega**

The course administration team comprises the course convener, Dr Ombeva Malande, the course administrator, Ms Rachel Afaayo, and the course coordinators and faculty members/facilitators: Dr Sabrina Bakeera-Kitaka (MU), Dr Edison Mworozzi (MU), Dr Lawrence Owino Okong'o (UON), Dr Wesley Too (KU), Dr Ombeva Malande (MU/Egerton University), Professor Johanna Meyer & Dr Andrew Musyoki (SMU), & Dr Carine Dochez (UA). Other faculty members/facilitators include: Dr Deo Munube (MU), Dr Bongomin Bodo, Dr Annet Kisakye & Dr Katushabe Edison (WHO Uganda), Dr Driwale Alfred (UNEPI), Dr Rachel Afaayo (ECAVI), Dr Thulani Mhlanga (Pfizer South Africa), Dr Myriam Mahana (Sanofi Pasteur France), Dr Nekoye Otsyula (GSK), Dr David Muwonge (Sanofi Pasteur Uganda) & Dr Celia Nalwadda (UNAS).

### Participant selection

A maximum of 100 participants per course are targeted through adverts emailed to members of the various paediatric/medical associations, medical schools, selected hospitals, EPI programmes, and also posted on the ECAVI website and Facebook page. Any interested HCW must submit his/her CV with a formal application and motivation for attending, to the course administrator. A selection committee comprising the course coordinators and course administrator vets the applications and selects 100 participants for the course.



**Figure 3: Certificate award session during the 4<sup>th</sup> ECAVI vaccinology course**

### Teaching methods

The mode of course delivery includes formal lectures; case studies and scenarios; videos; debate and discussions; practical demonstrations; site visits; participant presentations; assessments and evaluations.

Participants answer a series of structured questions at the end of each day to reinforce key messages. They further complete a daily course evaluation/feedback for future course improvement. Participants who attend more than 90% of sessions earn continuing professional development points and receive a certificate of attendance.

### Conclusion and Lessons learned

The WHO recently declared vaccine hesitancy, which results in sub-optimal vaccination coverage and outbreaks of VPDs, as a threat to global public health. Vaccination coverage and adherence to immunization schedules can be improved through strengthening immunization programmes and educating HCWs. ECAVI's vaccinology courses address these issues by training and empowering HCWs to become local vaccine advocates and experts throughout the East African region. Moving forward, we identify the following ten areas urgently requiring attention and focus to improve immunization in Africa: Hesitancy and negative messaging (dealing with antivaccine groups); identification, management and reporting of AEFI; dealing with measles and tetanus in the older child as re-emerging diseases; the need to introduce Hepatitis B birth dose & Rubella Vaccine into the National EPI programs; dealing with the continuing Polio eradication bottle necks; dealing with influenza virus as an emerging threat (especially surveillance & vaccine provision); strengthening cold chain systems and vaccine stockouts/transportation/delivery to rural & remote areas of Africa; improved health worker training & support supervision; roll out and uptake of HPV vaccine – especially the second dose; and enhanced focus on use of maternal vaccination to prevent diseases in early infancy.

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## AN OVERVIEW OF NEW VACCINE SURVEILLANCE IN NIGERIA

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### Background

The Expanded Programme of Immunisation made tremendous gains in reducing disease burden and mortality globally, targeting common "childhood killer diseases" of tuberculosis, measles, poliomyelitis, diphtheria, tetanus and pertussis.<sup>1</sup> Initial gains recorded were short lived as children were still dying from many preventable conditions. It was estimated that 6.2 million children and adolescents under 15 years died in the year 2018 with 15-25% being attributable to diseases that could be prevented by vaccines.<sup>2</sup> New vaccines against some of these diseases have long been developed but have generally remained underutilized. Some of these new vaccines include rotavirus, *Haemophilus influenzae* type B, pneumococcal conjugate, hepatitis B, inactivated poliomyelitis, and rubella vaccines, amongst others.<sup>3</sup> The Global Vaccine Action Plan (GVAP), endorsed by the 194 member states of the World Health Assembly in May 2012 recognised the need to ensure equitable access to existing and new vaccines for people in all communities, and provides a framework to prevent millions of deaths by 2020 through more equitable access to existing vaccines for people in all communities. Furthermore, the plan laid out strategies to amongst other things increase deployment of new vaccines in developing countries where the burden of these conditions is highest.<sup>4</sup>

Surveillance for diseases covered by the new vaccines is an integral part of the GVAP. It provides critical baseline data to guide informed decision making for the adoption of these new vaccines; provides a platform for monitoring the impact of these new vaccines on disease epidemiology; and provides robust epidemiological data crucial for understanding of vaccine effectiveness and prioritizing research and development.<sup>4</sup> Considering the oft described weak health systems in Sub-Saharan Africa and the lack of robust data collection systems and laboratory capacity for microbiological confirmation for diagnosis of diseases, it becomes imperative that systems be developed to

ensure adequate capture of good quality disease epidemiology data, prior to and following introduction of these new vaccines. To this end, the new vaccine surveillance system for *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis* meningitis and rotavirus gastroenteritis was established in Nigeria as part of the Global and African Regional New Vaccine surveillance system with objectives of describing through sentinel surveillance sites the epidemiology of rotavirus gastroenteritis and paediatric bacterial meningitis, all in children less than five years of age hospitalised at the sentinel surveillance sites.

### Rotavirus gastroenteritis surveillance in Nigeria

The rotavirus surveillance commenced in 2010 in Nigeria in one site in South-East Nigeria (Enugu State). Considering the size and population of Nigeria and the perceived burden of rotavirus gastroenteritis three more sites were introduced over the next few years with one added in 2012 (Ilorin in North Central Nigeria) and two in 2017 (Zaria in North West Nigeria and Bauchi in North-East Nigeria).

Surveillance teams are organised at each of the sites with a paediatrician leading each site team with all sites coordinated by a National Coordinating mechanism involving the Federal Ministry of Health, States Ministries of Health and the World Health Organization.

All children aged less than or equal to 59 months hospitalised on account of diarrhoea are recruited consecutively at the surveillance sites and where present, sub-sites after fulfilling all inclusion and exclusion criteria. Relevant data is collected via a standardised case investigation form (CIF) including demographics, clinical information, vaccination status and disease outcome. Stool samples are analysed in the site laboratory rotavirus antigens using an Enzyme Linked Immunosorbent Assay (ELISA) following standard methodology. Samples analysed are also sent to the Regional Reference Laboratory at the Noguchi Memorial Institute, Ghana for genotype determination and quality control.

### Paediatric Bacterial Meningitis surveillance in Nigeria

Paediatric Bacterial Meningitis surveillance began in Nigeria in 2009 with one site in Lagos University Teaching Hospital in Lagos South West Nigeria. Subsequently, four other sites commenced surveillance for Paediatric Bacterial Meningitis with one site in 2011 (Enugu in South East Nigeria), and three more sites in 2012 (Ilorin in North Central Nigeria, Benin in South Nigeria and Bauchi in North East Nigeria).

Surveillance teams are composed and coordinated similarly to as described for the rotavirus gastroenteritis above. All children aged less than or equal to 59 months hospitalised with features in keeping with meningitis were recruited after fulfilling the inclusion and exclusion criteria. Children were deemed to have suspected meningitis if they were admitted with sudden onset of fever and one of the following signs: neck stiffness, altered consciousness with no other alternative diagnosis, or other meningeal signs; or if they were admitted with a clinical diagnosis of meningitis.<sup>5</sup> Following recruitment, necessary data was obtained using a standardised case investigation form inclusive of demographics, clinical symptoms and signs, vaccination status and outcome. Cerebrospinal fluid is obtained according to standard procedures. A detailed description of CSF processing for the surveillance has been described elsewhere.<sup>6</sup>

Frozen specimens were transported to the Regional Reference Laboratory at the Medical Research Council,

The Gambia for Species-specific quantitative polymerase chain reaction (qPCR) assays.

While the surveillance is still ongoing, some of the surveillance data has been published and can be found at the listed references.<sup>6,7</sup>

### Conclusion

New vaccine surveillance is generating quality data on epidemiology of paediatric bacterial meningitis and rotavirus gastroenteritis in Nigeria. Preliminary data suggests a high rotavirus burden in Nigeria and *S. pneumoniae* remains the leading cause of acute bacterial meningitis in children less than five years of age.

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## JOURNAL WATCH

### Neonatal infections and antimicrobial resistance in sub-Saharan Africa

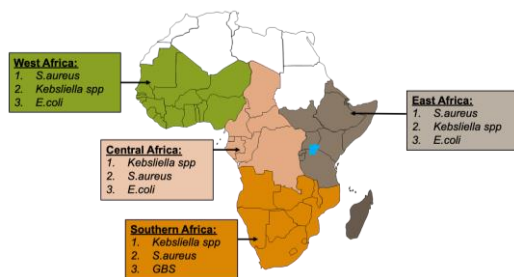
Review completed by Uduak Okomo, MRC Unit The Gambia at London School of Hygiene & Tropical Medicine. email: [uokomo@mrc.gm](mailto:uokomo@mrc.gm)

Serious bacterial infections in newborn babies - sepsis, meningitis, and pneumonia - are a leading cause of the 2.5 million annual newborn deaths. Countries in sub-Saharan Africa have the highest burden of serious neonatal infections in the world, but there is an important knowledge gap regarding the exact causes in these countries because diagnostic tools are rarely available or implemented. The burden of neonatal deaths is unevenly distributed across sub-Saharan Africa, being higher in West and Central Africa than East and Southern Africa, but similar data regarding the differences in the regional distribution of bacterial pathogens causing serious neonatal infections and antimicrobial resistance (AMR) are lacking.

In the largest systematic review of the causes of neonatal infection and AMR from sub-Saharan Africa, the researchers reviewed the available literature, 151 studies comprising data from nearly 80,000 newborns from 26 countries, to draw attention to the bacterial pathogens that caused neonatal infections, and the extent of antimicrobial resistance in sub-Saharan Africa over the past decade

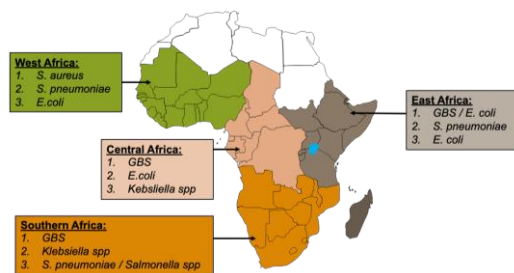
(2008 – 2018), focusing on regional differences. The paper also examined the quality of reporting among the reviewed studies, according to the Strengthening the Reporting of Observational Studies in Epidemiology for New-born Infection (STROBE-NI) checklist.

2019;19(11):1219-1234.doi: 10.1016/S1473-3099(19)30414-1.



**Figure 1: Aetiology of neonatal bacteraemia / sepsis, by region (2008-2018)**

Data was available from only 26 of the 48 countries in sub-Saharan Africa. There was wide variability in the reporting and recording of research findings across the identified studies. Their major findings show that the pathogen profile in sub-Saharan Africa is different from that found in high-income countries, with sub-regional geographical variation in the distribution of specific bacteria between and within regions. Since 2008, *Staphylococcus aureus*, *Klebsiella* species, and *Escherichia coli* have remained the most common reported causes of neonatal sepsis, the majority of *Staphylococcus aureus* cases were reported from West Africa. The main reported causes of neonatal meningitis are Group B *Streptococcus*, *Streptococcus pneumoniae*, and *Staphylococcus aureus*. Antibiotic resistance profiles for most of these pathogens demonstrated a high degree of resistance to the first- and second-line antibiotics recommended by the World Health Organization – namely ampicillin, gentamicin, and third generation cephalosporins such as ceftriaxone and cefotaxime. These findings suggest that reliable national and regional data are needed to track progress on reducing the burden of neonatal infections and AMR across sub-Saharan Africa.



**Figure 2: Aetiology of neonatal meningitis, by region (2008-2018)**

The researchers conclude by calling for more population-based neonatal infection studies and improved routine surveillance are needed to improve clinical care, plan health system approaches, and address AMR. Future studies should be reported according to standardised reporting guidelines, such as STROBE-NI, to aid comparability and reduce research wastage.

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Okomo U, Akpalu ENK, Le Doare K, et al. Aetiology of invasive bacterial infection and antimicrobial resistance in neonates in sub-Saharan Africa: a systematic review and meta-analysis in line with the STROBE-NI reporting guidelines. *Lancet Infect Dis*

## Prevalence estimates of fungal infection in South Africa

Review completed by Brian Eley, Paediatric Infectious Diseases Unit, Red Cross War Memorial Children's Hospital and the Department of Paediatrics and Child Health, University of Cape Town. Email: [brian.eley@uct.ac.za](mailto:brian.eley@uct.ac.za)

In this paper the burden of superficial and invasive fungal infection in South Africa is described. The analysis suggested that more than 3.2 million South Africans (7.1% of the population) are affected by fungal infections every year. The main drivers for this high estimate are the HIV and TB epidemics, and widespread poverty. While *Tinea capitis* was deemed the most frequently encountered fungal infection, causing more than 1 million cases per annum, the recently recognised *Emergomyces* is estimated to cause 100 cases per annum. This line of research is not completely new in sub-Saharan Africa. Estimates of the burden of fungal infection have previously been reported for Uganda, Nigeria, Tanzania and Kenya. We do need to pay more attention to fungal infection, including improved diagnostics and treatment, and strengthen the fungal infection research agenda in sub-Saharan Africa.

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## Whole Genome Sequencing for predicting first-line drug susceptibility or resistance of *Mycobacterium tuberculosis* isolates

Review completed by Brian Eley, Paediatric Infectious Diseases Unit, Red Cross War Memorial Children's Hospital and the Department of Paediatrics and Child Health, University of Cape Town. Email: [brian.eley@uct.ac.za](mailto:brian.eley@uct.ac.za)

The aim of this study was to determine the diagnostic reliability of whole genome sequencing (WGS) for predicting the susceptibility or resistance of *Mycobacterium tuberculosis* isolates to the first-line anti-tuberculosis drugs, isoniazid, rifampicin, pyrazinamide and ethambutol, when compared to the gold standard phenotypic susceptibility testing (The CRyPTIC Consortium and the 100,000 Genomes Project, et al.). In this large study more than 10,000 *M. tuberculosis* isolates sourced from 16 countries were analysed.

The results show that WGS is highly reliable for predicting susceptibility / resistance to the first-line anti-tuberculosis drugs. For example, the sensitivities of WGS were consistently above 91% for all 4 drugs and greater than 97% for isoniazid and rifampicin. Similarly, the specificities of WGS were consistently above 93%, reaching 99% and 98.8% for isoniazid and rifampicin, respectively. These impressive findings show that WGS can predict susceptibility / resistance of *M. tuberculosis* isolates to the first-line anti-tuberculosis drugs with a high degree of accuracy. Furthermore, this and other recently published studies have shown that susceptibility testing based on

WGS substantially reduces the workload, turn-around time and unit cost of resistance testing compared to classic phenotypic testing (Pankhurst, et al.).

Based on these results health authorities in England, The Netherlands and New York have already introduced WGS-based susceptibility testing. Whether or not this technology will be adopted by sub-Saharan African countries remains unclear.

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## CONFERENCE & SOCIETY NEWS

**19<sup>th</sup> International Congress on Infectious Diseases** will be held in Kuala Lumpur, Malaysia, from 20 to 23 February 2020. For more information visit the International Society for Infectious Diseases website, <http://www.isid.org/igid/>.

**38<sup>th</sup> Annual Meeting of the European Society for Paediatric Infectious Diseases, ESPID 2019**, will take place in Rotterdam, The Netherlands, from 25 to 30 May 2020. For more information visit the meeting website: <https://espidmeeting.org/>

**12<sup>th</sup> International Workshop on HIV Pediatrics** will be held in San Francisco, USA from 3 to 4 July 2020. For more information visit the conference website, <http://www.virology-education.com/event/upcoming/10th-workshop-hiv-pediatrics/>

**7<sup>th</sup> African Society for Immunodeficiency (ASID) Congress** takes place in Khartoum, Sudan in April 2021. For more information visit the ASID website: <http://asid-africa.org/en/>

**12<sup>th</sup> World Society for Pediatric Infectious Diseases (WSPID) conference** will be held in November 2021 in Cancun, Mexico. 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.

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