Africa's response to childhood infection

The AfSPID BULLETIN

Volume 6 (1) Newsletter of the African Society for Paediatric Infectious Diseases January 2019

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EDITOR'S COMMENTARY

Dear Colleagues

Welcome to the eighth edition of our newsletter. I wish you a successful and productive 2019.

Today we welcome Professor Regina Oladokun to the editorial board of the newsletter. She will also assist me as the deputy-editor of the newsletter and take the lead in soliciting articles and news from colleagues in the West African sub-region. Regina is based at Ibadan University, Nigeria where she heads paediatric infectious diseases in the Department of Paediatrics, University College Hospital, Ibadan. She completed her paediatric infectious diseases training in the unit that I head, at Red Cross War Memorial Children's Hospital and the University of Cape Town and successfully completed the exit examination set by the Colleges of Medicine of South Africa, qualifying as a paediatric infectious diseases sub-specialist in May 2015. In this edition of the newsletter, Regina writes to us about her vision for paediatric infectious diseases in West Africa.

Paediatric Infectious Diseases training for qualified paediatricians is an important consideration for African institutions. In a future edition of the newsletter I will provide you with a detailed description of my own experience in establishing a training programme.

The African continent has experienced a large number of outbreaks during 2018, including Hepatitis E and Anthrax in Namibia, Monkeypox in Nigeria, Lassa fever in Nigeria and Liberia, Rift Valley Fever in several countries in East Africa, Chikungunya in Sudan, Plague in Madagascar, Crimean-Congo haemorrhagic fever in Uganda and Cholera in at least 10 Eastern and Southern African countries.

Perhaps the event that has captured the attention of many health professionals in Africa and overshadowed other outbreaks on our continent in 2018 was the return of Ebola to the Democratic Republic of Congo (DRC). Two outbreaks occurred in DRC in 2018. The 9th recorded outbreak of Ebola in DRC occurred in Équateur province in the northwest of the country. It started on 3 May 2018, the last case manifested with symptoms on 2 June 2018, and the outbreak was declared over on 24 July 2018. This outbreak affected 54 individuals and resulted in 33 deaths, a case fatality rate of 61%. Traditional measures were used to contain this outbreak including early identification of cases, isolation and care of cases, contact tracing, safe and dignified burials and appropriate community engagement. An important supplemental intervention was ring vaccination using the recombinant vesicular stomatitis virus – Zaire Ebola virus (rVSV-ZEBOV) vaccine. A total of 3481 people were vaccinated, including front-line health professionals and individuals who were exposed to confirmed Ebola virus disease (EVD) cases. This targeted vaccination strategy is believed to have contributed appreciably to the control of this outbreak.

Unfortunately, 7 days after the 9th outbreak ended, a new outbreak, the 10th outbreak in DRC, commenced North Kivu province in the north east of the country. It quickly spread to the neighbouring Ituri province. This ongoing outbreak has been difficult to manage because rebel groups have been fighting for control of this area of DRC. As at 20 December 2019, there have been 560 EVD cases and 336 deaths, a case-fatality rate of 60%. These numbers indicate that this outbreak is the second largest Ebola outbreak in the world since the causative agent for Ebola was discovered in 1976. A ring-plus vaccination strategy was implemented in August 2018 using the rVSV-ZEBOV vaccine. More than 49,000 individuals have already been vaccinated. Furthermore, several monoclonal antibodies and antivirals have also been approved for compassionate use in EVD cases, and at the end of November the Ministry of Health of DRC announced that a randomized control trial has begun to evaluate the effectiveness and safety of a multi-drug intervention in the treatment of Ebola patients.

I would like to briefly acknowledge two other notable developments on the African continent. Firstly, in June 2018 trachoma caused by *Chlamydia trachomatis* was eliminated from Ghana, two decades after the World Health Assembly resolved to tackle this infection, which is the leading infectious cause of blindness. Thus, Ghana is the first country in the World Health Organization's African region to achieve this ground breaking milestone. Secondly, a new virus was isolated in the cerebrospinal fluid of a 3-year old Ugandan girl who had contracted fatal encephalitis. The Ntwetwe virus, named after the village in Uganda where the unfortunate patient lived, is a novel orthobunynavirus. The viral aetiology of encephalitis has been poorly studied in sub-Saharan Africa. If we do embark on comprehensive aetiological studies, other novel encephalitis-causing viruses may yet be discovered in Africa. I encourage you to read the paper of this important discovery in Clinical Infectious Diseases, 9 June 2018; DOI: 10.1093/cid/ciy486

We look forward to the next WSPID conference, which takes place from 5 to 8 November 2019 in Manila, The Philippines. The development of the scientific programme for the conference is nearing completion. AfSPID will be hosting a society symposium on outbreaks in Africa. Hopefully many of you will attend.

This edition of the newsletter includes a communiqué from the president of AfSPID, a case report from Ethiopia, commentary on paediatric HIV guidelines, news of the launch of the Gambian Society for Paediatric Infectious Diseases and our regular journal watch slot.

I hope that you enjoy this edition of the newsletter.

Kind regards, Brian Eley

A VISION FOR PAEDIATRIC INFECTIOUS DISEASES SUB-SPECIALITY IN WEST AFRICA

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Introduction and problem statement

Infectious diseases are responsible for more than 50% of childhood morbidity and mortality in sub-Saharan Africa. As such, it is pertinent to develop sub-specialty capabilities in the West African sub-region to facilitate understanding of the diagnostic and therapeutic interventions necessary to manage these conditions.

Most trainees in general paediatrics are exposed to a variety of diseases and heavy caseload of infectious diseases (ID) during their training in the sub region. However, the ID aspect of the training is largely unstructured with limited opportunity to develop advanced knowledge of medical microbiology and immunology of the diseases, plus lack of use of advanced diagnostic and treatment modalities. As a result, training and expertise in this sub-specialty lag significantly compared to the skills, knowledge and experience available in more developed countries.

Paediatric ID sub-specialty is all encompassing and entails the pathogenesis, disease spectrum, diagnosis, management and prevention of infectious diseases such as HIV/AIDS, tuberculosis, malaria, bacterial infections, sepsis, vaccine preventable diseases, soft tissue, joint and bone infections. Other aspects include other viral, fungal conditions, antimicrobial therapy, immunisations and much more. The modalities for carrying out the paediatric ID service include the clinical consultations on outpatient and inpatient basis as well as infection control. Educational activities occur through ID and antimicrobial stewardship ward rounds, microbiology culture meetings, case review meetings and journal clubs. Having received basic laboratory training, the Paediatric ID specialist has to interact with the laboratory in the interpretation of results, in relation to clinical cases. Research activities and surveillance are also important in the ID sub-specialty.

Status of Paediatric Infectious Diseases in Nigeria

Stand-alone paediatric ID units exist in less than 10% of the teaching hospitals in the country. Sensitisation to raise awareness about the portfolio of paediatric infectious diseases has begun in the last few years and is being championed by the Nigerian Society for Paediatric Infectious Diseases (NISPID) through symposia organised at the yearly Paediatric Association of Nigeria conferences.

Nigeria presently lacks a well-structured training curriculum that meets the needs of doctors in the sub-specialty of Paediatric ID. Five years ago, I took up the challenge to undergo Fellowship training in paediatric ID at the Red Cross War Memorial Children's hospital, Cape Town, through the African Paediatric Fellowship Programme. The paediatric ID sub-specialty training appears to be the first of its kind in Africa and has a well-structured training curriculum that meets the needs of doctors in sub-Saharan Africa. Training in Cape Town was most desirable to me because of its relevance and the similarities of the paediatric infections and other health conditions in both South Africa and Nigeria. The training facilitated the capacity building needed in the structuring of a sub-specialist paediatric ID programme in the West African sub-region.

The West African College of Physicians (WACP) and the National Postgraduate Medical College of Nigeria are moving towards sub-specialisation within their residency training programmes. With first-hand experience in paediatric ID training, I was placed in a strategic position to contribute to the development of the Paediatric ID sub-specialty training curriculum. The skills acquired will also be utilized in implementing the programme at my institution.

Another achievement from my sub-specialty training in paediatric ID is the production of an antimicrobial handbook for management of Paediatric Infectious Diseases. The book is to guide antimicrobial choice in the management children with infectious diseases in the sub-region (Oladokun RE, Osinusi K. (Editors). A Handbook of Paediatric Infectious Diseases & Antimicrobial Therapy. Inspiration House, Ibadan. 2018). The variability of diseases and the context of their management in different regions of the world call for adaption of guidelines for the local environment.

Paediatric ID training in the West African sub-region

Creating subspecialty training in paediatric ID within the West African sub-region is essential given the persistence of conditions such as tuberculosis, vaccine preventable conditions, the general increase in antimicrobial resistance, primary and secondary immunodeficiency diseases, and new or emerging infectious diseases.

Sub-specialty training will improve the quality of care for children with infectious diseases and associated immunological conditions. It will also raise awareness and facilitate research required for a better understanding of the local and regional infectious diseases epidemiology and management protocols. It will produce relevant data required for the development of local and region-specific public health interventions and evidence-based policy making that will improve child survival.

The Paediatric ID sub-specialty training curriculum was approved by WACP. The training curriculum is based on concepts and content of established training programs in South Africa, US and UK and is adapted, where appropriate, for the local needs and conditions within the sub-region.

The entry point is the Membership (Part I) examination of the WACP in paediatrics or its equivalent and the duration

of training is three years. The first year of training will include rotations in core clinical areas of paediatrics such as Neonatology, Emergency paediatrics, General paediatrics and Community paediatrics etc. Subsequently, the training will consist of rotations in clinical service in paediatric infectious disease and laboratory posting in medical microbiology and virology. There will be provision for an elective posting for 6 months at an established paediatric infectious diseases training programme outside the sub-region through regional and international linkages. Time is also allocated for research. Trainees will be required under supervision to conceptualise, design, execute and report research in paediatric infectious diseases. Training will be evaluated through a log book of clinical cases managed, laboratory experience and academic activities carried out by the trainee as well as an exit examination.

Prospects for Paediatrc ID in the West African sub-region

Sub-specialty training
One training centre that meets the criteria for implementing the WACP Paediatric infectious diseases training programme is the Paediatric Infectious Diseases Unit, Department of Paediatrics, University College Hospital (UCH), Ibadan, Nigeria, has recently put in a request for accreditation as a regional training centre for Sub-speciality training in Paediatric ID.

The Department of Paediatrics, UCH is the pioneer Department of Paediatrics in Nigeria and has been in the forefront of residency training for general paediatricians in the West African Sub-Region and also serves as the examination centre for the Membership and Fellowship examination of the West African College of Physicians. The Infectious diseases unit in the Department of Paediatrics provides specialist services for infectious diseases and immunodeficiency conditions and is involved in many research projects. The unit will collaborate with the Medical Microbiology Department of the UCH with laboratory rotations. There is also an existing expression of interest to collaborate elective postings in paediatric infectious diseases with colleagues at the Paediatric Infectious Diseases Unit, Red Cross War Memorial Children's Hospital Cape Town South Africa and the Division of Paediatric Infectious Diseases at the University of Nebraska Medical Center, United States of America.

The unit has two Paediatric ID sub-specialists, both certified by the Colleges of Medicine of South Africa. Additionally, Professor Regina E. Oladokun is a Fellow of both the National Postgraduate Medical College of Nigeria and the WACP, while Dr Babatunde O. Ogunbosi is a Fellow of the National Postgraduate Medical College of Nigeria. Both have vast experience in medical teaching and training at the undergraduate and postgraduate levels. They also have a track record of research in the field of Paediatrics ID and are actively involved as resource personnel for the National programmes on HIV, TB, Malaria and other infectious diseases of public health importance. They play lead roles in the UCH in issues related to antimicrobial stewardship, infection prevention and control, and Rapid Response for Communicable Diseases.

Establishment of Paediatric ID units across teaching hospitals
It is important to ensure that Paediatric infectious diseases units are established in tertiary health facilities across the country. This will ensure that case management of infections is optimal. Additionally, the training of resident doctors will be facilitated as they will gain a comprehensive understanding of the diagnostic and therapeutic interventions necessary to manage the entire spectrum of paediatric infectious diseases. The Nigerian Society for Paediatric Infectious Diseases is expected to play a leadership role in this regard.

Protocols for infectious diseases
Protocols need to be developed locally. As new information become available in the face of changes from research and clinical experience in the field, it is important that existing protocols for management of paediatric infectious diseases are updated regularly. Relevant standards of treatment that are peculiar to the practice environment need to be taken into consideration.

Research

As infectious diseases remain a leading cause of childhood morbidity and mortality in children in sub Saharan Africa, the large caseload in the region presents opportunities for rigorous designs that can answer the numerous research questions left unanswered. Unfortunately, limitations in funding, molecular laboratory and state of the art diagnostic capacities limit the scope of research. Collaborative research involving experts and researchers from more advanced settings are encouraged to improve the research capabilities and output from the sub-region.

Conclusion

The planning and implementation of the training programme as well as other activities to promote the paediatric sub-specialty in Nigeria and the West African region are on-going. A centre is soon to be accredited for training. It is hoped that ultimately through these efforts, the overall goal of improving child health indices in the country will be achieved.

PRESIDENT'S REPORT

Professor Mark Cotton, President of AfSPID and Vice-President of WSPID)

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AfSPID has featured on the World Society of Paediatric Infectious Diseases (WSPID) conference agenda since the Melbourne meeting of 2011. The foundation meeting took place at the annual VACCFA conference hosted by Prof. Greg Hussey in November 2012.

AfSPID Exco

The Exco is unchanged since its founding in 2012.

AfSPID Constitution

This was adopted in 2015

Financials

AfSPID eventually obtained its own account at ABSA Bank in September 2018. The account requires 2 members (Currently Prof Brian Eley and myself) to individually approve transactions. Until now, finances were managed through SASPID's account, also at ABSA. AfSPID is now in a better position to obtain and disburse funding. The income is from WSPID to fund a symposium at its biennial World Congress

The Newsletter

A big thanks to Prof Brian Eley for this most important output, always interesting and topical and welcome to Prof Regina Oladokun, our new deputy editor.

WSPID Update

- A WSPID board meeting took place in San Francisco in September 2018 to review WSPID's activities and to review plans
- The next WSPID conference is in Manilla in the Philippines November 5 – 8, 2019. The program looks as excellent as previous meetings, and covers all areas of interest. (https://wspid2019.kenes.com/scientific-program/) Please check it out. We will be having an AfPIDS session and are looking for suggested speakers and topics
- WSPID will be hosting a smaller regional meeting somewhere in Africa and focusing on antibiotic resistance as a global and regional threat. AfSPID will play an important role as the local organizing committee. Our plan is to bring as many emerging paediatricians and ID fellows together. We plan to organize scholarships for this purpose.
- WSPID is also in negotiations with ESPID (The European Society for Paediatric Infectious Diseases) for access to its educational activities, notably antibiotic resistance. Annual membership for access costs E50 per individual. WSPID has allocated US$2500 per region for co-sponsorship for individual doctors who would like this opportunity. It should be of great benefit to specialists in training but is open to all AfPIDS members.

The Future

After a slow start, there is now much to do and many opportunities to grow our society. More than ever, there is a need for more face to face contact.

Wishing everyone a good break and looking forwards to the New Year.

INAUGURAL MEETING OF GAMBIAN SOCIETY FOR PAEDIATRIC INFECTIOUS DISEASES

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At the 42nd Annual General and Scientific meeting of the West African College of Physicians which held in Freetown Sierra Leone from 4 – 8 November 2018, paediatricians from the Gambia working in infectious diseases held a meeting with a view to starting a Gambian Society for Paediatric Infectious Diseases (GaSPID). The meeting held on Sunday 4th November 2018. Being a country with a limited health workforce, sourcing meaningful numbers of members had so far made such an association difficult to start. In the past few years there has been an increase in the number of potential members. The Gambian group approached Dr Oladokun to share her experiences with the Nigerian society for paediatric infectious disease (NISPID).

The meeting was attended by Drs Uduak Okomo, Joseph Okebe, Olubukola Idoko (The Gambia) and Regina Oladokun (Nigeria). The discussions included some background regarding the NISPID and Dr Idoko gave some background on the African Society for Paediatric infectious Disease and the group discussed activities of these sister bodies. There were also discussions around the need to explore requirements for legal status and registration for such an association in The Gambia. Other paediatric infectious disease associations were mentioned as were important Paediatric ID conferences and meetings. The group plans to hold a meeting in The Gambia during 2019.

Attendees at the meeting (left to right) Drs Uduak Okomo, Joseph Okebe, Regina Oladokun and Olubukola Idoko.

CASE REPORT: PRIMARY IMMUNE-DEFICIENCIES: COMMON CONSULTS FOR THE AFRICAN PEDIATRIC INFECTIOUS DISEASES' CLINICIAN

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Case report

A six year old girl presented for her latest symptoms of cough and fast breathing and was admitted to our center for treatment of a severe pneumonia. She had multiple bouts of pneumonia since her infancy and had also been on follow-up at our pediatric cardiology and dermatology clinics for dilated cardiomyopathy and eczema. A consult for the pediatric infectious diseases' service was made to rule out an underlying immune defect. Mind you, as almost all African countries, Ethiopia does not have clinical immunologists or a concerned training program.

She was underweight, stunted. Her examination showed notching of her lower incisors, bilateral inguinal lymphadenopathy, cyanosis, flaring, retractions, wheezing and coarse crepitations, S3 gallop, a grade 2 pan-systolic murmur at her apex, hepatomegaly, partially lost scaly thumb nail and extensive eczematous lesions.

She was non-reactive for HIV antibodies. Her work-up showed eosinophilia (absolute counts of more than

3000/mm^3) with an otherwise normal lymphocyte (6504/mm^3) and neutrophil count (3744/mm^3) determined from the complete blood count and differential count results. She had two markedly elevated IgE determinations of 1500 IU/ml and 9400 IU/ml (normal age-related levels being less than 307 IU/ml) with an otherwise normal IgG of 950 mg/dl (normal age-related range: 504 – 1464 mg/dl), IgA of 115 mg/dl (normal age-related range: 27 – 195 mg/dl) and IgM of 145 mg/dl (normal age-related range: 24 – 210 mg/dl) (all determined at a lab abroad).

Feature	Score
Highest serum IgE level	10 (serum IgE level > 2000 IU/ml)
Episodes of pneumonia over lifetime	8 (> 3 episodes of pneumonia over lifetime)
Highest absolute eosinophil count	6 (absolute eosinophil count: > 800/mm^3)
Eczema (worst stage)	4 (severe eczema)
Number of upper respiratory infections per year	4 (estimated number of infections > 6/year)
Onychomycosis	2
Other serious infections	4 (severe infection present in past medical history; pericarditis in this case)
Age at initial presentation (in years)	7 (presentation in infancy or neonatal period)
Total score for our patient	45
Score: Unlikely if < 20; Indeterminate if 20 - 40; Suggestive if > 40	

Table 1: U.S. NIH Hyper IgE syndrome diagnostic score for our patient

Based on the U.S. NIH diagnostic criteria assessment of her presentation (Table 1), she was diagnosed with a rare form of primary immune-deficiency: hyper-immunoglobulin E syndrome or Job's syndrome[1]. There was no similar set of symptoms or a history of recurrent infections among her parents, siblings and close family members. There was no history of consanguinity. Based on the clinical features which included dental notching and the non-informative family history, she was presumed to have the autosomal-dominant form of the disorder[2].

Upon the revised 2017 classification of primary immune-deficiencies, there are currently nine categories (Table 2). Hyper-IgE syndrome is classified as a combined immuno-deficiency with associated or syndromic features[3]. This was the third case report of hyper-IgE syndrome from a sub-Saharan country[4,5].

Primary immune-deficiencies in Africa

A lot is unknown about primary immune-deficiencies in Africa. Most reports and registries exist in the North African countries and South Africa. As is the case globally, reports from Morocco, Tunisia, Egypt and South Africa suggest a predominance of antibody deficiencies[6,7]. An electronic search of studies from Africa (excluding the North African countries and South Africa) yielded only a single case report (DiGeorge syndrome) in addition to the aforementioned three reports on Hyper-IgE syndrome[1,4,5,8].

The child with a predominantly antibody deficiency commonly presents after six months of life after trans-placentally acquired maternal IgG starts to wane. Recurrent infections by encapsulated bacteria and chronic sino-pulmonary infections are often seen. Examination is notable for small tonsils and lymph nodes.

Immunodeficiencies affecting both humoral and cellular immunity are notable for earlier onset with a wide spectrum of bacterial, viral, fungal and protozoal infections, failure to thrive and eczema. Our patient's parents could afford to pay for complete blood count and differential count, serum immunoglobulin concentrations and thus rule out severe primary antibody and combined deficiency.

No.	Category	Notable examples
1	Immunodeficiencies affecting cellular and humoral immunity	Severe combined immunodeficiencies
2	Combined immunodeficiencies with associated or syndromic features	Wiskott-Aldrich syndrome, Ataxia-telangiectasia, Hyper IgE syndrome
3	Predominantly antibody deficiencies	Common variable immunodeficiency, X-linked agammaglobulinemia, Selective IgA deficiency, Transient hypogammaglobulinemia of infancy
4	Diseases of immune dysregulation	Chediak-Higashi syndrome
5	Congenital defects of phagocyte number, function or both	Leukocyte adhesion deficiency, Chronic granulomatous disease
6	Defects in intrinsic and innate immunity	Chronic mucocutaneous candidiasis, Mendelian susceptibility to mycobacterial disease
7	Auto-inflammatory disorders	Familial Mediterranean Fever,
8	Complement deficiencies	Terminal complement deficiencies, Properdin deficiency
9	Phenocopies of primary immunodeficiencies	Autoimmune leukoproliferative disease

Table 2: The 2017 IUIS phenotypic classification for primary immune-deficiencies

More than 350 primary immunodeficiency diseases have already been fully characterized. Many primary immunodeficiency diseases have unique features that may facilitate recognition. Leukocyte adhesion deficiencies (defects of phagocyte function) result in delayed separation of umbilical cord and leukocytosis (neutrophil count >30,000/mm^3). Chronic Granulomatous Disease, another defect of phagocyte function, increases susceptibility to both bacterial and fungal infections including unusual microorganisms such as *Burkholderia cepacia, Serratia marcescens, Nocardia* species and *Aspergillus fumigatus*.

Wiskott-Aldrich syndrome classified as a combined immunodeficiency with associated or syndromic features manifests with thrombocytopenia, small platelets, recurrent bacterial and viral infections, eczema, lymphoma and autoimmune disease. Ataxia-telangiectasia, another combined immunodeficiency with associate or syndromic features, may present with recurrent respiratory function, truncal ataxia, and oculocutaneous telangiectasia.

Chediak-Higashi syndrome, a disease of immune dysregulation, manifests with partial albinism, recurrent infections and giant lysosomes on peripheral blood smear, bleeding tendencies, hepatosplenomegaly and hemophagocytic lymphohistocytosis. While deficiency of early complement components cause infection by

encapsulated bacteria and systemic lupus erythematosus, deficiency of terminal complement components that form the lytic complex are associated with Neisserial infections including recurrent meningococcal infections.

Within our limitations, we have tried to formulate a far from perfect working diagnosis. Improving diagnostics is one facet of timely detection and preventing measures for affected children. Determinations of serum immunoglobulin (IgG, IgA, IgM & IgE), complete blood count and differential count and CH50 tests are components of a basic work-up of children suspected of having a primary immunodeficiency disease yet unavailable in most African countries. More advanced testing includes the measurement of lymphocyte subsets i.e. T cells (CD3), T-helper cells (CD4), T-suppressor cells (CD8), natural killer cells (CD16/56) and B-cells (CD19), the respiratory burst assay, the AH50 assay and genetic testing.

Some interventions are possible in African countries such as optimal immunization practice, antimicrobial prophylaxis and infection control measures. African clinicians should advocate for the routine use of immunoglobulin replacement therapy because intravenous immunoglobulin has been included in the essential drug list of the World Health Organization. However, stem cell transplantation is currently beyond the capacity of most African health systems[9].

Hence, focused clinical immunology education for African pediatric infectious diseases' clinicians is of utmost importance. These patients are likely to be reported by these physicians because of the undeveloped clinical immunology practice in the continent.

The African Society of Immunodeficiencies (ASID) (www.asid-africa.org) was formed in 2008 with the aim of advancing the practice of Clinical Immunology across Africa. It holds biennial meetings with the 6th congress to be held in Dakar, Senegal from 11th – 13th April, 2019.

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COMMENTARY: CONTROVERSIES IN HIV TREATMENT GUIDELINES: A PAEDIATRICIAN'S PERSPECTIVE

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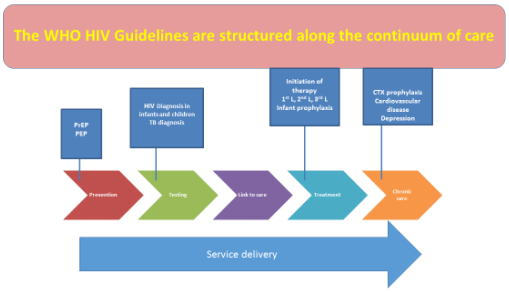

Survival of perinatally HIV-infected children has been transformed with the advent of antiretroviral therapy (ART)[1]. The availability of an increasing number of antiretroviral agents and the rapid evolution of new information introduced substantial complexity into treatment regimens for persons infected with human immunodeficiency virus (HIV)[2].The complexities were even more pronounced for children and adolescents living with HIV more so because their treatment is dependent on body weight and formulations include liquids and tablets.

In the 2002 WHO Treatment Guidelines initiation of anti-retroviral therapy (ART) was based on a CD4 count of less than 200 cells among adults; and for children less than 15% for the CD4 percentage. These guidelines continued to evolve based on an increased CD4 cell count, and moving towards more simplified regimens. The 2016 current adoption of "**Test and Treat**" for all persons living with HIV (PLHIV) irrespective of CD4 count, clinical staging or age provided that ART be initiated within 7 days of testing for children and 30 days for adults[3].

Other significant changes included the retention of Tenofovir (TDF) 300mg; 150mg of Lamivudine (3TC), and 600mg of Efavirenz (EFV) **TDF/3TC/EFV 600mg** as preferred first line regimen for adults; introduction of Dolutegravir (**DTG 50mg)** for use as an alternative in first line regimens in adults and children aged **10 and above;** introduction of once daily dosing with Abacavir (**ABC 120mg/3TC60mg)** in children; and the introduction of Lopinavir boosted with ritonavir(**LPV/r) pellets** for use in first line regimens for children under 3 years. A major challenge arising from the use of pellets was that elderly caregivers have been known to underdose these children with 3 pellets instead of 3 caplets.

Differentiated Service Delivery Models

With the overwhelming numbers of clients chocking the health system, the WHO recommended differentiated

service delivery models which are efficient strategies for provision of HIV and TB prevention, care and treatment services to address the needs of different sub-populations of clients. The differentiated service delivery model is a shift of service delivery from **"one size fits all"** to **"client centered"**[3]**.** The previous care and treatment models required frequent clinic visits, leading to high travel expenses. However, for children and adolescents, when the service delivery model is centered around the parent who may be doing well on treatment, this could easily be a disservice for the child who may not be adhering equally well. Moreover there is a general lack of child and adolescent specific spaces which would conform to the practice of client centered care.

Service Delivery models depend on the health status of the client i.e.

- **Stable clients** – adults on ART for more than 12 months, virally suppressed with no concurrent illness or co-morbidity and demonstrated good adherence. These require less frequent clinic visits
- **Complex/Unstable clients** - newly initiated on ART, < 12 months on ART, children, pregnant women, non-virally suppressed adults, clients with co-morbidities. These require critical attention

Differentiated service delivery models (DSDM) in children whose caregivers may be responding differently to ART or are at a different stage in their HIV care. Community volunteers support the DSDM, and clients are excited because they don't have to come to the clinic for their pill refills. Unfortunately, sometimes the children and care givers response to ART doesn't match, and this creates a quagmire.

HIV testing services (HTS)

HTS with linkage to prevention, treatment and care is recommended for all adolescents with a focus on those from key populations. Informed consent and HIV testing: Adolescents aged 12 years and above can consent on their own for HTS without the approval of their parent/guardian.

Strategies for improving uptake of HTS among adolescents:

- Use a peer-led approach where adolescent peers are trained to provide pre and post-test counseling as well as performing HIV tests.
- Offer services at the convenience of adolescents through flexible working hours, walk-in services for those without an appointment, weekend or same-day appointments.
- Offer services in a place that ensures privacy and confidentiality.
- Provide age-appropriate information such as benefits of knowing one's HIV status.

Risks of universal ART for children

There is no doubt that ART is beneficial, but it is also associated with toxicities. Preclinical and clinical studies have demonstrated short-and long-term adverse events on ART, including hematological, renal, cardiovascular, bone and metabolic abnormalities[4]. The short term side effects are frequently observed on initiation of ART, with dizziness and gastrointestinal disorders (diarrhoea, nausea and vomiting) more commonly observed. Dizziness and other central nervous system disorders (concentration problems, sleep disorder, psychotic reactions and seizures) are particularly observed with efavirenz and potentially result in sub optimal ART adherence and subsequent ART failure. Older children and adolescents have been known to refuse the ART initiation. Despite several efforts to scale up Paediatric access to ART has only 51% of the 1.8 million children under-15 years living with HIV globally were receiving ART at the end of 2015, compared to 72% of HIV-infected pregnant women[5].

Risk of resistance development

The rapid introduction of universal ART without the necessary planning and preparation may increase the burden on busy health facilities and lead to lower quality of the services and potential drug stock outs. This may overall increase the risk of selecting drug resistance that would further limit future treatment options for the adolescents and babies that may be born to them[6,7].

Sustainability challenges

As the global community strives to achieve global treatment targets by 2020 and aspires to reach the fast-track targets for children and adolescents, more efforts need to be in place to ensure that the quality of HIV services is improved and sustained. Measures are needed to enable timely and reliable viral load monitoring for early identification of virological failure. Moreover as viral loads are rolled out and turn out significantly high, decisions on how to switch and when to switch become a challenge. Whereas AIDS-related deaths have fallen for other age groups, mortality among HIV-infected adolescents rose by 50% from 2005 to 2012. In fact, AIDS was and remains one of the leading causes of death among adolescents worldwide [8].

More implementation challenges

The practicability of birth testing/ identification of HIV infected babies at birth is demonstrated in this short case scenario to represent several similar case. GM (not her real initials), was an 18 year old peri natally infected ALHIV who stopped taking her ART for 6mo because she was expecting her 1st baby, the doctor started the baby on full ART (AZT, 3TC, NVP) at birth, baby was DNA PCR negative at 6 weeks, but had very low growth parameters, mother had opted for formula feeds. Subsequently baby tested sero positive at 18 months. This case emphasizes the value of an HIV antibody test at 9months of age to prevent resistance development among babies who fail on prevention of mother to child transmission.

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RESEARCH: ANTIPYRETIC USE PRE- AND POST-ROUTINE VACCINATION IN THE GAMBIA: PERCEPTIONS AND PRACTICE

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Introduction

Fever is a common adverse event following vaccinations in children. Measures to control this adverse event in the context of routine paediatric vaccinations include the use of prophylactic or post vaccination antipyretics. Some studies have however documented poorer immune responses to vaccination in infants who receive antipyretics along with vaccinations. Some antipyretics are known to have anti-inflammatory effects and may therefore modify the systemic and local reactions to vaccinations such as fever redness, swelling, and pain around injection sites. Differences induced in systemic and local reactions following such antipyretic use may be important in comparing clinical trial results and interpreting the results of trials where immunogenicity is an end point.

Methods

We assessed the attitude, perceptions and practices related to the use of prophylactic or therapeutic antipyretics in routine immunization clinics in The Gambia during the final early infant series vaccination visit (4-month visit).

Results

A total of 39 health care professionals (HCP) involved in vaccination and 585 infant caregivers (ICG) were interviewed across The Gambia. 11% and 50% of the HCP felt that children required antipyretics pre and post vaccination, respectively, and 28% would routinely ask parents to administer antipyretics post vaccination. 29% of infant caregivers would [sometimes (7%) or always (22%)] give antipyretics prior to vaccination, while 86% would give them [sometimes (25%) or always (61%)] post vaccination. 53% reported that they were concerned about side effects of vaccination.

Discussion

Adverse events following vaccination are a concern to HCP and ICG alike, and many administer antipyretics either before or after vaccination. Further studies are required to explore the effects of such antipyretic use as the routine administration of antipyretics prior to and following vaccination noted may modify the immune response and local responses to vaccinations.

Photo credit: Mr Abdou Gibba

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2) Recently updated Curriculum Vitae (please note that your referees will need to have valid institutional email addresses. Personal addresses will not be accepted.)

3) Supervisor letter of support (Needs to be completed by the supervisor that will be supporting the trainee on his/her return. You should find a supervisor in your interested field or your direct HOD (This shouldn't be a South African supervisor but one in your home country where you will return to after you have completed the programme). The letter should state why there is a need for the candidate to complete this training, how the training will impact the hospital's needs and what plans will be put in place for the doctor after the training period) This supervisor will be instrumental with regards to formalizing a training plan for the trainee(keeping the needs of the hospital in mind) and keeping contact with the trainee to ensure that the trainee is on track with the training plan. The supervisor will receive 3-monthly APFP assessments in which they will be able to see the progress that is being made by the trainee.

4) Copies of your degree certificates and transcripts

5) Valid passport (Photo page only)

6) IELTS results (if available)

Application can be sent to:

Dr L Mubaiwa, Programme Director

Email: MUBAIWAL1@ukzn.ac.za

OR

Mr Brian Zaca, Programme Coordinator

Telephone: +27 31 260 4811;

Email: zacab@ukzn.ac.za

JOURNAL WATCH

Reverse zoonotic bacterial transmission

Review completed by Brian Eley

Zoonoses are infectious diseases that can be naturally transmitted from animals to humans. Of all viruses, bacteria, fungi and parasites that infect humans, an estimated 61% are zoonotic, and may originate from either domestic or wild animals. Emerging infectious diseases, defined as infections whose incidence in the human population has increased in the past 2 decades or whose incidence or geographic range is rapidly increasing or threatens to increase in the near future, are more than twice likely to be zoonotic than non-emerging infections. Frequent human-animal interaction and consumption of non-certified pathogen-free animal products increases the risk of zoonotic transmission. Poor and marginalised communities bear the brunt of zoonoses on the African continent.

There is less awareness among infectious diseases clinicians about reverse zoonotic diseases i.e. human to animal disease transmission, featured in the journal article. Until the present study was undertaken, reverse zoonoses such as infecting your cat with influenza, or your bird with tuberculosis have been documented on every continent except Antarctica. The researchers of the present study screened faecal samples of 24 species of seabirds at 4 Southern Ocean localities for enteric bacteria. In addition, backyard poultry in the Falklands were sampled. These poultry support human settlements in the Falklands and are in close contact with Sub-Antarctic and Antarctic wildlife. Their major findings included the detection in seabirds of *Salmonella* serovars and *Campylobacter* species typically associated with humans, antibiotic resistance of some bacterial strains and detection of specific *Campylobacter* genotypes previously reported almost exclusively in humans and domestic animals in high income countries. These findings suggest that transmission of human enteric bacteria to seabirds populations has occurred in the Southern Ocean ecosystems. The researchers conclude by calling for stricter biosecurity measures in Antarctica to limit the impact of human activity on the local ecosystems.

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CONFERENCE & SOCIETY NEWS

6th African Society for Immunodeficiency (ASID) Congress takes place in Dakar Senegal from 11 to 13 April 2018. For more information visit the ASID website: http://asid-africa.org/en/

37th Annual Meeting of the European Society for Paediatric Infectious Diseases, ESPID *2019*, will take place in Ljubljana, Slovenia, from 6 to 11 May *2019*. For more information visit the meeting website: https://espidmeeting.org/

11th International Workshop on HIV Pediatrics will be held in Mexico City, Mexico from 19 to 20 July 2019. For more information visit the conference website, http://www.virology-education.com/event/upcoming/10th-workshop-hiv-pediatrics/

11th World Society for Pediatric Infectious Diseases (WSPID) conference will be held from 5 to 8 November 2019 in Manila, The Philippines. 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.

8th Federation of Infectious Diseases Societies of Southern Africa Congress will be held from 7 to 9 November 2019 at the Indaba Hotel & Conference Centre, Johannesburg. For more details visit the FIDSSA website: www.fidssa.co.za

The 20th edition of International Conference on AIDS and STIs in Africa (ICASA) will be held in Kigali, Rwanda from 2 to 7 December 2019. For more information visit the conference website, icasa2019rwanda.org/

19th 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/icid/

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THE AfSPID BULLETIN

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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 word count (excluding references): 3000 words with no more than 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 (excluding references): 1500 words with no more than 15 references, and 3 tables, illustrations and/or pictures.

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