Africa's response to childhood infection

The AfSPID BULLETIN

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Editor: Brian Eley; Editorial board: Sabrina Bakeera-Kitaka (Uganda), Adegoke Falade (Nigeria), O Idoko (Nigeria), Mark Cotton (South Africa); Address your articles, case reports, comments & letters to Brian Eley: Brian.Eley@uct.ac.za

IN THIS ISSUE

FROM THE EDITOR'S DESK

Dear Colleagues

Welcome to the first edition of our newsletter.

In this edition we review the formation meeting of our new society, Mark Cotton presents his vision for the society, Beckie Tagbo and Adegoke Falade describe the state of paediatric infectious diseases in West Africa, the new strategic plan to end polio is summarised, recent developments in the peer-review literature are highlighted, and upcoming conferences are discussed including progress towards finalising the AfSPID symposium at the forthcoming World Society for Paediatric Infectious Diseases (WSPID).

Research and publications are the lifeblood of academics. The Journal Watch section provides you with an opportunity to communicate your published research findings to fellow African colleagues. In this issue a few easy to access, publications involving African researchers are featured. Information about 'home-grown' research projects & publications is encouraged. Please send in brief reports on recent publications; summarise main findings and discuss the implications of these findings.

To make this newsletter a vibrant forum for exchanging information, we need a steady stream of contributions. I therefore invite you start writing and to submit your contributions as soon as possible. Send me information on forthcoming relevant conferences in your country or region, research developments that you've been involved with, short articles on outbreaks or epidemics in your setting, articles on clinical ID, clinical and research training, or interesting and instructive case reports, or simply write a short commentary or review on a recent ID development. Letters to the editor in which you respond to a published report are encouraged. Aim for a word count of 100-1000 words. However, larger articles will be considered.

I hope that you find this first edition interesting

Kind regards, Brian

FORMATION OF AfSPID

The formation of African Society for Paediatric Infectious Diseases (AfSPID) arose from collaboration between the Nigerian Society for Paediatric Infectious Diseases (NISPID) and the Southern African Society for Paediatric Infectious Diseases (SASPID); NISPID was established in 1999 and SASPID in 2008.

A public meeting was held in August 2010 at the 26th International Pediatric Association Congress of Pediatrics at the Sandton Convention Centre, Johannesburg, South Africa. This meeting was attended by 150 clinicians and academics from approximately 30 countries. This meeting was co-hosted by NISPID and SASPID. The major decision reached at this meeting was to proceed with the formation of an African Paediatric Infectious Diseases Society. Furthermore there was agreement that the new society should foster communication, sub-specialist training, engage in continuing medical education, promote & collaborate in relevant research and advocate for the interests of children through the prevention and treatment of infectious diseases.

The foundation meeting of the new society took place on 8 November 2012 at the 1st International African Vaccinology Conference at the Lagoon Beach Hotel, Cape Town on 8 November 2012. Thirty five clinicians and academics were in attendance. The meeting was chaired by Mark Cotton, (University of Stellenbosch, South Africa).

There was consensus that an executive committee should be formed to lead the society and that this committee should comprise at least 2 representatives from eastern, southern, western and central/northern Africa. The following individuals were elected onto the founding executive committee:

Executive committee

President: Mark Cotton (South Africa)

Vice-Presidents: Amha Mekasha (Ethiopia), Adegoke Falade (Nigeria)

Secretary: Sabrina Bakeera-Kitaka (Uganda)

Treasurer: Natasha Samuals (South Africa)

East Africa: Amha Mekasha (Ethiopia), Sabrina Bakeera-Kitaka (Uganda), Judy Orikiiriza (Rwanda)

Southern Africa: Mark Cotton & Brian Eley (South Africa), Mutsa Bwakura-Dangarembizi (Zimbabwe)

West Africa: Adegoke Falade (Nigeria), John Yenan (Cote D'Ivoire)

Central & North Africa: Gisèle Kazadi (Democratic Republic of Congo)

Additional decisions

The following committees were formed:

Advisory board (so support the president): G Hussey, B Eley, L Frigati, C Wiysonge

Training committee: L Whittaker, P Musoke (nominated by S Bakeera-Kitaka), B Eley, A Nekasha (nominated by M Bwakura-Dangarembizi), AG Falade, H Mujuru & T Avenant

Editorial board to support B Eley (editor of the newsletter): S Bakeera-Kitaka, AG Falade, O Idoko, M Cotton

Some of the first tasks assigned to the newly elected office bearers include (1) starting a newsletter (B Eley), (2) starting a online discussion group (Bernard Onoja), and (3) finalising the programme for the forthcoming AfsPID symposium at the 8th WSPID conference in Cape Town on Friday 22 November 2013 (Mark Cotton).

VISION FOR AfSPID

Mark Cotton, President of AfSPID

Division of Paediatric Infectious Diseases, Tygerberg Children's Hospital, Stellenbosch University, Cape Town, South Africa. mcot@sun.ac.za

Infectious diseases are a major threat to children and their families. The more experience and knowledge we generate, the better our ability to address this threat. AfSPID aims to increase networking on the continent and elsewhere in order to increase our resources and to compare experiences, update one another on new trends in infectious diseases and also to be a resource of infectious diseases expertise for the continent. We aim to increase training opportunities and help the new generation of paediatric ID specialists to develop.

We plan to continually build on our momentum. Our editor, Brian Eley, outlined the first steps in the formation of AfSPID. The newsletter will be an important vehicle for communication and learning. Please submit news items. We plan to introduce a case report section in our next edition.

We hope many of you can attend the WSPID 2013 conference in Cape Town. Please attend if you can. There will be a focus on malaria, malnutrition, TB and neonatal infections. We will be able to interact with colleagues from many parts of the world and will be able to contribute our unique perspectives. We will be hosting the 2nd AfSPID parallel session and plan to cover Africa's response to Millenium Development Goal #4 - reducing under-5 mortality by two-thirds.

ASfPID IN WEST AFRICA

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AfSPID (and by extension, AfSPID-West Africa) is just a few months old following its inauguration on 8 November, 2012 at AfSPID meeting in Cape Town, South Africa. The President is M Cotton (SA) and the Vice-Presidents are A Mekasha (ET) and AG Falade (NG)

AfSPID-West Africa, which is just as young as AfSPID, has AG Falade and JP Yena as her nominated Representatives. AfSPID-West Africa was charged with the responsibility of rallying her members together in the West African sub-region. We soon swung into action by creating awareness and gathering contacts of local societies and their members (both old and new).

State of Local Societies

Apparently most countries in the sub-region do not previously have any local societies except for Nigeria which has a well-established and registered local society known as Nigerian Society for Paediatric Infectious Diseases (NISPID).

We have succeeded in mobilizing Ghana and The Gambia to begin the process of establishing local societies. Efforts have been made to reach out to Togo as well.

The details of the 3 local societies so far reached are shown in the table below:

	Country	President / country representative	Members	Remarks
1	Nigeria	K Osinusi	113	Well established & registered
2	The Gambia	CN Oluwalana	10	In the process of formation
3	Ghana	L Renner	2	In the process of formation
4	Togo	?	?	No feedback yet

Awareness

There are plans to attract professionals to the local societies and by extension to AfSPID West Africa through intensive awareness creation, networking and organization of meetings. One way already being employed is through the local paediatric associations/societies. The Nigerian society already has a plan to hold a meeting/workshop this 2013. The Ghanaian society intends to work with her Paediatric society to establish a local paediatric infectious diseases society in that country.

Infectious Diseases Training and Interest in the Field

Training in infectious diseases is relatively very young in the sub-region and training activities are generally very low. However, interest in the field has grown tremendously over the years especially with the advent of HIV/AIDS pandemic and the awareness created by the World Society for Pediatric Infectious Diseases (WSPID) Congresses and NISPID.

Research

Through the World Health Organization (WHO) African Region, new vaccine surveillance sites have been established in most countries in the West African sub-region. The target diseases are rotavirus diarrhoea and Paediatric Bacterial

Meningitis (*Haemophilus influenzae b*, *Streptococcus pneumoniae* and *Neisseria meningitides*). This is in addition to previously established surveillance on polio and measles. There is a sub-regional and regional network through which huge uniform data are currently being generated in the sub-region, in a standard and comparable manner to support decision making by various governments. This has dramatically changed the previous situation of lack of locally generated data. Therefore, evidence based policy decisions on new vaccine introduction can now be made using local real data rather than estimates and extrapolations.

Challenges

The major challenges to growing the field are the very low level of awareness and training opportunities as well as lack of quality laboratory support. It is hoped that over time, these challenges would be overcome.

POLIO ERADICATION

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 Brian.Eley@uct.ac.za

In 1988 the world Health Assembly adopted a resolution calling for global eradication of polio by the year 2000. A multi-decade initiative by the Global Polio Eradication Initiative (GPEI), which was launched by the World Health Organization in 1988 has reduced the incidence of poliomyelitis by >99%, However, eradication has been difficult to achieve because of socio-political obstacles such as war, social disruption, political indifference, distrust of polio vaccines and the emergence of vaccine-derived poliovirusus in many locations. Recent global developments have renewed efforts to eradicate this highly infectious disease.

Major achievements of the GPEI

- All but 0.1% of polio has been eradicated i.e. from a caseload of 350,000 in 125 countries in 1988 to 233 cases in 5 countries in 2012. As at 27 March 2013, 16 cases have been reported from 3 countries in 2013.
- Eradication of wild poliovirus type 2 in 1999
- India stopped wild poliovirus transmission in 2011: The last case of paralytic polio in India occurred in a 2-year old girl in Howrh district, West Bengal on 13 January 2011. On 25 February 2012, India was officially removed from the list of polio-endemic countries by WHO reducing the number of endemic countries to three (Nigeria, Pakistan and Afghanistan).

Way forward

A new strategy, the Polio Eradication and Endgame Strategic Plan 2012-2018 compiled by the GPEI provides a roadmap for permanently disrupting the transmission of both wild poliovirus and vaccine-derived poliovirus. The plan includes the withdrawal of type 2 from Oral Polio Vaccine (OPV), the introduction of Inactivated Polio Vaccine (IPV) in all countries, and data-directed approaches to overcome existing operational problems.[1] Challenges remain particularly in the endemic areas along the border of Pakistan and Afghanistan and in northern Nigeria. The new plan has received strong support from vaccine experts. More than 400 scientists, clinicians and technical experts from 80 countries have signed a scientific declaration on polio eradication in support of the new strategic plan. This declaration was launched on 11 April 2013.[2]

References & further reading

1. Polio Eradication and Endgame Strategic Plan 2012-2018, 29 March 2013 (latest draft) URL: http://www.polioeradication.org/Portals/0/Document/Resources/StrategyWork/EndGameStratPlan_20130329_ENG.pdf
2. Scientific Declaration on Polio Eradication plus the full list of signatories may be viewed on the Emory Vaccine Center website http://vaccines.emory.edu/poliodeclaration/

JOURNAL WATCH

Routine antibiotics for severe acute malnutrition

Severe acute malnutrition makes a substantial contribution to childhood morbidity and mortality. High prevalence of infections among children hospitalized with malnutrition has led to the recommendation that routine antibiotics be administered to children with severe acute malnutrition, including those treated as outpatients. This recommendation has not been tested in a clinical trial.

Thus a group of researchers performed a randomized, double-blind placebo-controlled trial in which children aged 6 – 59 months with severe acute malnutrition and attending 18 outpatient feeding clinics in rural **Malawi** were randomized to receive amoxicillin, cefdinir (a third generation oral cephalosporin) or placebo for 7 days. Severe acute malnutrition was defined as oedema (indicative of kwashiorkor) or a weight-for-height z score < -3 (indicative of marasmus) or both (indicative of marasmic kwashiorkor). All children received ready-to-use therapeutic food as part of the treatment. The study's primary endpoints were the mortality rate and the rate of nutritional recovery. 2767 children were enrolled.

The mortality rates in the three groups were 4.8% (amoxicillin), 4.1% (cefdinir) and 7.4% (placebo), indicative of a 35.6% reduced mortality rate in the amoxicillin group and a 44.3% reduced mortality rate in the cefdinir group. The rate of recovery was significantly lower among those who received placebo than those who received either amoxicillin or cefdinir.

These findings suggest that children with severe acute malnutrition who qualify for outpatient treatment remain at risk for serious bacterial infection and that routine antibiotic therapy should be administered as part of their nutritional rehabilitation.

Reference: Trehan I, et al. *N Engl J Med* 2013; 368: 425-35

Phase 2b tuberculosis vaccine trial

One of the major vaccinology research goals is the development of tuberculosis vaccines with improved protection against tuberculosis and / or improved safety compared to the existing BCG vaccine. In the present phase 2b trial conducted in **Cape Town**, a modified Vaccinia virus Ankara expressing antigen 85A vaccine (MVA85A) was evaluated. 2797 BCG-vaccinated infants aged 4-6 months were randomized to receive either MVA85A or placebo (an equal volume of candida skin test antigen). The primary outcome was safety,

but efficacy was also evaluated. After a median follow-up of 24.6 months, more children who received MVA85A had at least one local reaction (89% *vs* 45%), but the number who had systemic and serious adverse events did not differ i.e. 80% *vs* 76% and 18% *vs* 18% respectively. Efficacy against tuberculosis was 17.3% (95% CI: -31.9, 48.2 and against *M. tuberculosis* infection -3.8% (95% CI: -28.1, 15.9).

In conclusion, although MVA85A was unable to confer protection against tuberculosis or *M. tuberculosis* infection, this trial was considered important because it was the first rigorously conducted infant tuberculosis vaccine trial since BCG was evaluated in 1968. More TB vaccine trials are likely to follow in the foreseeable future. Furthermore, several important questions regarding MVA85A remain unanswered. These questions are discussed in a related editorial.

Reference: Tamaris MD, et al. *Lancet* 2013; 381: 1021-28

Editorial: Dye C & Fine PEM. *Lancet* 2013; 381: 972-973

IL-12p40 deficiency

Interluekin-12 p40 deficiency is an autosomal recessive disorder which causes increased susceptibility to mycobacterial infection. An analysis of 49 patients from 30 kindreds originating from **Tunisia**, India, Pakistan, Iran and Saudi Arabia provided valuable genetic, immunologic and clinical information about this disease, which affects patients in North Africa. IL-12p40 deficiency causes low IFNγ production, increasing susceptibility to various organisms including mycobacteria.

The mean age of first infection in 44 symptomatic children was 1 year (range: 1 month to 7.6 years). The presenting infections in 30 index patients were BCG disease (27 patients: 19 with disseminated infection and 8 with regional disease), *Salmonella* infection (1 patient), *M. tuberculosis* infection (1 patient) and environmental mycobcaterial infection caused to *M. chelonae* (1 patient). 20 of the 30 patients manifested with BCG disease as their only mycobacterial infection throughout their lifetime.

Mycobacterial infection was the dominant infection type occurring in 42 of 44 symptomatic patients. BCG accounted for 95.2% of mycobacterial infections. Disseminated TB occurred in 2 patients and *M chelonae* in 2 patients. Other documented infections included *Salmonella* species, *Klebsiella* species, *Nocardia* and *Candida* species. Global mortality was 28.6% and the mean age of death: 7.1 years. Mortality was mainly due to disseminated BCG disease.

The paper provides detailed information about the patterns of infections documented in IL1-12p40 deficiency. An interesting feature of this disease is that despite being associated with increased mycobacterial susceptibility, multiple mycobacterial infections are rare.

Prando C, et al. *Medicine (Baltimore)* 2013; 92: 109-122

Xpert MTB/RIF in Ugandan children

Studies from South Africa, Tanzania and Zambia have recently reported on the diagnostic performance of Xpert MTB/RIF in children with suspected pulmonary tuberculosis. In the present study Ugandan researchers based at Mulago hospital in **Kampala** evaluated Xpert MTB/RIF on induced sputum specimens in 235 children, median age 36 (IQR: 16-74.5) months with suspected TB. The performance of a single Xpert MTB/RIF test was compared to TB culture results.

Sensitivity of Xpert MTB/RIF was 79.4% (95% CI: 63.2-89.7) and specificity 96.5% (95% CI: 93-98.3). The test performance was similar in HIV-infected and uninfected children. Xpert MTB/RIF identified twice as many TB cases as did smear microscopy. Factors associated with a positive Xpert MTB/RIF result included age > 5 years, TB contact history and a positive tuberculin skin test result.

Comment: The performance of Xpert MTB in the present study was better than in recent South African and Tanzanian studies where Xpert MTB/RIF test produced sensitivities of 58.7% and 46.4% respectively on the first sputum specimen. Both those studies showed that the sensitivity of Xpert MTB/RIF may be significantly improved when more than one sequential sputum specimen was collected & processed by Xpert MTB/RIF. The new Ugandan study provides further evidence that Xpert MTB/RIF may facilitate rapid confirmation of childhood TB and assist in the diagnosis of drug-resistant TB in Africa.

Sekadde MP, et al. *BMC Infect Dis* 2013, 13: 133

Mortality in severe malaria

An evaluation of more than 26,000 children with severe *Plasmodium falciparum* malaria admitted to six hospital research centres in **Banjul, Blantyre, Kilifi, Kumasi, Lambaréné & Libreville** was completed. The overall mortality was 4.3%. Median time to death varied across the centres from 8 hours in Libreville to 40 hours in Kilifi. Fifty-eight percent of the deaths occurred within 24 hours (designated early mortality); 19% of all deaths occurred 24-47 hours after admission (intermediate mortality) and 23% occurred thereafter (late mortality). When combining data from all sites, factors predicting early, intermediate and late mortality were deep breathing, prostration and hypoglycaemia. Deep breathing, prostration and coma were consistently associated with early mortality at all sites. However, there was considerable variability in the factors predicting mortality at individual sites, suggesting that the patterns of severe malaria are different between sites.

Kendjo E, et al. *Plos One* 2013; 8(3): e58686

Immunization in Africa

Three **Cape Town**-based researchers provide commentary on the state on immunization programmes in Africa, highlighting achievements and remaining challenges. For those of you who've attended the recent 1st International Vaccinology Conference in December 2012, this paper summarises the *status quo* in Africa. Furthermore, this commentary includes a useful graphic showing the evolution of vaccine coverage in Africa between 1980 and 2010, and discusses measures that are needed to overcome current challenges and take advantage of the new decade of vaccines.

Machingaidze S, et al. *PLoS Medicine* 2013; 10(3): e1001405

CONFERENCE & SOCIETY NEWS

3rd ASID conference: The 3rd conference of the African Society for Immunodeficiencies takes place in Sun City, South Africa, from 6 to 9 June 2013. ASID was formed in November 2008 in Morocco to develop and promote the field of primary immunodeficiency diseases (PIDDs) in Africa. There is considerable overlap between the PIDDs and the field of paediatric infectious diseases. Approximately 80% of children with PIDDs manifest with infectious diseases presentations. For more information on ASID and the conference consult the ASID website: http://www.asid.ma/

5th International workshop on HIV Pediatrics: This major annual workshop on HIV infection in children & adolescents takes place on 28 & 29 June 2013 in Kuala Lumpur, Malaysia. For more information consult the conference website: www.virology-education.com

FIDSSA 5: The 5th conference of the Federation of Infectious Diseases Societies of Southern Africa takes place in the Drakensberg, South Africa from 10 to 12 October 2013. FIDSSA is an amalgamation of 6 societies including the Southern African Society of Paediatric Infectious Diseases (SASPID). Invited plenary speakers include several international ID authorities. Information on the conference may be obtained from the FIDSSA website: http://www.fidssa.co.za/

WSPID 2013: The 8th World Congress of the World Society for Pediatric Infectious Diseases takes place at the Cape Town International Convention Centre, South Africa from 19 to 22 November 2012. Many of the leading paediatric ID experts will be in attendance. AfSPID will be hosting a symposium at this conference on the last day of the conference. More information including the programme may be obtained from the conference website: http://www2.kenes.com/wspid/Pages/home.aspx

17th ICASA (ICASA 2013): The 17th International conference on AIDS and STI's in Africa hosted by the Society for AIDS in Africa takes place from 7 to 11 December 2013 in Cape Town South Africa. For more information consult the conference website: www.icasa2013southafrica.com

HOW TO JOIN AfSPID

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

- Name, surname, title
- Country of residence
- Job description (registered ID specialist, clinician / researcher / academic / registrar / nurse / masters or doctoral fellow / other / any combination of the above)
- Your institution / affiliations
- Contact details