Africa's response to childhood infection

The AfSPID BULLETIN

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FROM THE EDITOR'S DESK

Dear Colleagues

Welcome to the second edition of our newsletter.

A year has passed since the first edition of our newsletter was circulated. Much has happened in the ensuing period. There have been exciting research developments and updated international guidelines, and several conferences have taken place on our continent.

The 3rd African Society of Immunodeficiencies (3rd ASID) conference took place in June 2013 at Sun City in parallel with biennial ALLSA conference. This conference attracted notable international and continental speakers who delivered talks on the entire spectrum of primary immunodeficiency diseases (PIDs). Particular highlights were talks by Capucine Picard on Mendelian susceptibility to infection and Stephen Holland on PIDs in adult patients. Continental speakers originated mainly from North Africa where the PIDs are highly prevalent.

The 5th Federation of Infectious Diseases Societies of Southern Africa conference took place at the Champagne Sports Resort in the Drakensberg in October 2013. The Southern African Society for Paediatric Infectious Diseases (SASPID) played an important role in organising this conference. SASPID's international speaker was Robert Heyderman, Director of the Malawi-Liverpool-Wellcome Trust Clinical Research Programme in Blantyre, Malawi. He presented a plenary talk on severe bacterial infection in Africa. He noted the importance of non-typhoidal *Salmonella* as a leading cause bacteraemia among children and adults in many parts of Africa including Malawi. Rob Davidson from Northwick Park Hospital, London presented a fascinating account of his experiences in managing visceral Leishmaniasis or Kala-Azar (VL) in Africa. VL is prevalent north and east Africa, particularly in Sudan, Ethiopia and Eritrea. It causes profound immunosuppression. Therefore, the main cause of death in patients with VL is opportunistic infection. He also highlighted the evolution of treatment options and mentioned therapeutic trials that he had participated in. Therapeutic options for Leishmaniasis have progressively expanded over the last 25 years. Therapeutic options include antimonial drugs such as sodium stibogluconate, amphotericin B, lipoidal formulations of amphotericin B, paromomycin, and miltefosine which is administered orally. Pentavalent antimonial drugs are the first choice in most developing countries. However, sodium stibogluconate is unacceptably toxic in HIV-infected individuals. One focus of current therapeutic research is the optimisation of combination therapy for VL. During the conference SASPID hosted a paediatric symposium focussing on *Staphylococcus aureus* infection, bacterial meningitis, intra-abdominal TB and a large gastroenteritis outbreak in the Northern Cape. In this newsletter, Nicolette du Plessis a paediatric ID specialist summarises her presentation on *Staphylocccus aureus* infection.

In November 2013, the 8th World Congress of the World society for Pediatric Infectious Diseases (8th WSPID) took place in Cape Town. More than 1350 delegates from 105 countries participated. Some of our society's members attended. A conference report focussing on developments regarding antibiotic resistance, antibiotic stewardship, pneumonia, and meningitis was recently published (Eley BS & Nuttall J. *Expert Rev Anti Infect Ther* 2014;12(4):419-22). Our society hosted a symposium at the 8th WSPID conference entitled "MDG4 reducing child mortality in Africa – regional perspectives". It featured speakers from Mauritius, Cameroon, Nigeria and Egypt. Two of the four talks, by Lawal Umar and Maha Mansour are featured in this edition of the newsletter.

In April 2014 the spotlight returned to Cape Town with the hosting of the 16th International Congress on Infectious Diseases. More than 2500 delegates from 120 countries participated. As with the 8th WSPID conference delegates were treated to a plethora of presentations of exceptional quality and scientific depth. The 16th ICID covered both adult and paediatric ID. For the benefit of those of you who did not attend this conference a few developments of relevance to Africa are summarised.

Also featured in this edition is a research project on schistosomiasis by Welcome Mkululi Wami & colleagues, progress with the role out of meningococcal conjugate vaccine in the meningitis belt by Olubukola Idoko, news from the journals and information about forthcoming conferences.

I would like to take this opportunity to thank all authors for excellent contributions.

I hope that you find this edition interesting. Please continue to send me your contributions so that this becomes a vibrant and exciting product of Africa.

Kind regards, Brian Eley

STAPHYLOCOCCUS AUREUS INFECTION

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The lecture started with the presentation of two teenage boys. The first patient presented with osteomyelitis of his right knee shortly after a soccer injury. His symptoms worsened over the course of 2 weeks and he developed renal failure as well as infective endocarditis. The second young boy also had a soccer injury, but he presented weeks after sustaining the injury in septic shock and multisystem failure. He required urgent cardiac surgery for a large aortic valve vegetation. Methicillin-sensitive *Staphylococcus aureus* (MSSA) was isolated from numerous specimens collected from both patients. A short review of *Staphylococcus aureus* infection was then presented. The current epidemiology, especially in developed countries, concentrates on the difference between community- and hospital-acquired methicillin resistant strains (CA-MRSA and HA-MRSA). South African data is segmented, but the CA-MRSA and HA-MRSA strains seem to be integrating and is difficult to assign to either the community or hospital setting. The colonisation and carriage rate differs greatly between MSSA and MRSA strains, and screening and decolonisation strategies should be considered separately. Clinical disease is similar, though CA-MRSA has been known to cause severe skin and soft tissue disease. Both sensitive and resistant *S. aureus* infections can cause serious and life-threatening disease. The risk of infective endocarditis once *S. aureus* bacteremia occurs can be as high as 11%. Laboratory diagnostics have evolved to molecular methods, especially for epidemiological and research purposes. The principles of collecting adequate samples, draining and aspirating infection sites, and careful interpretation of susceptibility results were addressed. Treatment principles remain similar, whether MSSA or MRSA are suspected. These include early and adequate drainage and surgical intervention where needed, in addition to correct antibiotic prescriptions that reflect susceptibility results and dosing recommendations.

Editorial Comment

A particular discussion point in the recent literature is the optimal dosing strategy of vancomycin for the treatment of MRSA infections in children. In adult practice a loading dose is recommended and the aim of therapeutic drug monitoring is to maintain a trough concentration of 15-20 μg/ml which is said to correlate with the desired AUC:MIC ratio of >400, providing adequate vancomycin exposure during treatment. A recent randomised control trial in children showed that a loading dose of vancomycin did not result in earlier achievement of the desired therapeutic trough concentration.[1] Recent pharmacokinetic modelling suggested that a trough concentration of 7-10 μg/ml may be sufficient to achieve a AUC:MIC of >400 in more than 90% of children with MRSA infection.[2] Thus the current position is that (1) we should use the IDSA 2011 dose recommendation for vancomycin of 15 mg/kg/dose 4 times per day, (2) a loading dose is not required, (3) the MIC of MRSA isolates should be routinely determined, (4) trough level monitoring may not be necessary if the MIC of the isolate in ≤ 1 mg/L, and (5) until optimal trough levels for children are established one should aim for a trough level of 15-20 mg/L if the infection is caused by an isolate with a high MIC (> 1 mg/L).[3]

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TOWARDS ATTAINING MDG4 IN WEST AFRICA: PROGRESS, CHALLENGES & PROSPECTS

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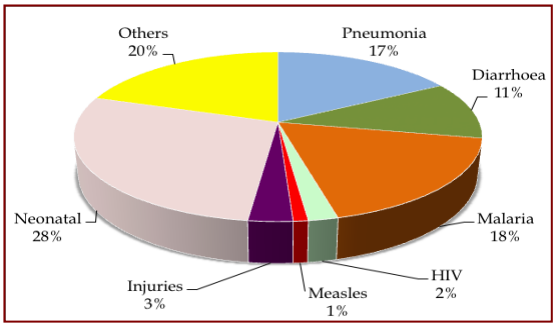
The UN Millennium Development Goal (MDG) 4 is a global declaration of commitment for child survival through a two-thirds reduction of under-five and infant mortality from the 1990 figures and attaining 90% measles immunization coverage for children aged 12-24 months by 2015.[1]

The 15 countries of West Africa have an average total population of about 316 million in 2011 (range: 0.5 million in Cape Verde to 160 million in Nigeria) and are mostly grouped as "*Lower Income*" and "*Lower Middle Income*" countries with at least half of citizens in eight countries living on less than $1/day. The Under-5 child proportion in each country range from 10.3% to 19.9% but Nigeria has the highest under-5 population of nearly 52.9 million, or 50.2% of the total in the sub-region.[2] They are also among the "75 Countdown" countries sharing over 95% of the global maternal and child deaths.[3]

Leading causes of under-five mortality in West Africa

Infections remain the leading causes of child mortality (Figure 1) and by the end of 2012, the countries of the sub-region were among the top 15 countries with the highest under-five deaths from pneumonia and diarrhoea, accounting for 23% of the total global 1.3 million deaths due to these infections; [4,5] Nigeria alone had 18% while Niger, Mali and Burkina Faso share 5%. Malaria has become largely concentrated in West and Central Africa, being responsible for 65% of the mortality burden for the top ten countries (3.1 million deaths). Nigeria alone has 46% of this total while Mali, Cote d'Ivoire, Niger and Burkina Faso together have 19%.[4,5]

Figure 1: Leading causes of under-five mortality in West Africa, 2012



Neonatal deaths closely follow with 28%; asphyxia and prematurity caused 57% while neonatal infections including sepsis, pneumonia and meningitis together caused 25%. Cote d'Ivoire, Guinea Bissau, Mali and Sierra Leone were among the top ten with the highest rates globally, while Nigeria shares 40% of the total global neonatal deaths with India and Pakistan.[4] HIV/AIDS is responsible for 1-4% of deaths across the sub-region and out of the total global under-five HIV-associated deaths of 103,000 in 2012 Nigeria had 23% or 24,000, which far outweighs the sum for the 14 other countries. Nigeria also has one of the lowest ART coverage (12%) for eligible children. The sub-regional average prevalence of stunting is about 40% while under-nutrition is associated with up to a third of under-five deaths. [4]

PROGRESS IN UNDER-FIVE MORTALITY REDUCTION

The sub-region recorded significant progress from 1990, when mortality rates were above 200/1,000 live births in eight countries. By the end of 2012 only eight countries had rates above 100/1,000.[4,5] The sub-region is however, still home to eight of the top 15 countries in the global ranking of under-five mortality rates (Tab. 1). The decline was largely attributable to measles deaths reduction by over 80%.

Table 1: Global ranking of under-5 mortality rates (U5MR/1000 live births) for West Africa, 2012

Country	U5MR	Rank	Country	U5MR	Rank
Sierra Leone	182	1	Togo	96	19
Guinea-Bissau	129	6	Benin	90	22
Mali	128	8	Liberia	75	32
Nigeria	124	9	Gambia	73	33
Niger	114	10	Ghana	72	36
Cote d'Ivoire	108	11	Senegal	60	43
Burkina Faso	102	14	Cape Verde	22	88
Guinea	101	15			

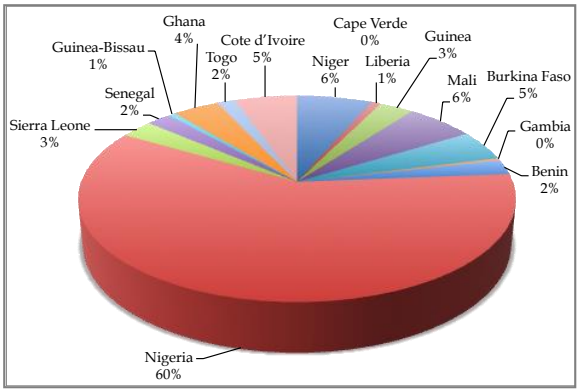
The sub-region's achievements as presented in the *2013 UNICEF MDG Report - "A Promise Renewed"*, with analysis of the UN Inter-agency Group on Child Mortality Estimates (IGME) data revealed reductions of 23% for neonatal, 33% for infant and 39% for under-five mortality respectively, but these were based on regional grouping with Central Africa.[4] When disaggregated, the reductions for West Africa suggest better progress with 30.4% for neonatal mortality, 42.7% for infant mortality and 49.7% for under-five mortality (Table 2), although still short of the two-third reduction targets. Measles immunization coverage improved from 58% to 79% but only five countries reached the 2015 target of 90%. [4]

Table 2: Progress towards attaining MDG4 targets in West Africa, 2012

	1990 (/1,000)	2013 (/1,000)	Reduction	Reduction from 1990 (%)
Neonatal Mortality Rate	46	32	14	**30.4**
MDG 4 Targets				
Infant Mortality Rate	110	63	47	**42.7**
Under-5 Mortality Rate	195	98	97	**49.7**
	1990 Coverage (%)	2013 Coverage (%)	Countries with <90% Coverage	Countries with >90% Coverage
Measles Immunization Coverage	58	79	10	**5**

In spite of the achievements Nigeria still remains globally prominent and responsible for 827,000 deaths or 13% of the global total as at the end of 2013, while carrying 60% of the burden at the sub-regional level (Fig 2). With a 2011 population of 162 million, Nigeria's under-five population of about 27.2 million is over half the region's under-five population, [2] partly accounting for its higher burden.

Figure 2: Under-five Mortality Burden in West Africa, 2012 (% of 1.5 million)



Niger and Liberia recorded the most impressive reductions with average annual rate of reduction (AARR) of 4.8% and 5.4% and reductions of 65% and 70% from the 1990 rates respectively.[4] These countries successfully scaled up interventions targeting malaria, pneumonia, diarrhoea, malnutrition and HIV.[2,3,4,5,11] In Niger 22% of under-five death reductions were attributed to improved care-seeking for pneumonia and diarrhoea, 25% to provision of insecticide treated mosquito nets (ITN) and 19% to nutrition interventions.[11,12,13] In Liberia by the end of 2010 ITN provision rose to 73% thereby halving malaria prevalence, prevalence of severe malnutrition fell to 2.2% due to enrolment of 50% of severely malnourished children in a *basic care package,* PMTCT and ART coverage improved to 69% of eligible women and to 44% of eligible children while neonatal tetanus has also been eliminated.[11,12,14]

THE CHALLENGES OF ATTAINING MDG4 IN WEST AFRICA

Foremost among the challenges that retard West Africa's MDG4 progress includes:

i. ***Inadequate funding***

Both domestic and external funding targets (MDG 8) were not met; the Overseas Development Assistance (0.7% of GNI of developed countries) fell due to the global economic meltdown. By 2011 only 5 countries complied with undertakings made at the*"2001 Abuja Declaration"* to set aside 15% of national budgets for health.[15,20]

ii. ***Poverty, hunger, malnutrition***

The sub-region has countries with highest mortality in children from poorest households, with serious to alarming levels of hunger as ranked on the *Global Hunger Index.* The enduring poverty and food insecurity have contributed to high rates of under-nutrition and increased child vulnerability to infections.[11,12]

iii. ***Poor utilization of health services***

Health seeking behaviour is generally poor with less 50% of children that have suspected pneumonia taken to health care providers. There is also poor use of ORS and Zinc for children with diarrhoea and antibiotics for those with pneumonia.[11,12] Sub-optimal routine immunization coverage and inconsistent immunization campaigns have contributed to resurgence of outbreaks of measles especially in Nigeria.[16]

iv. ***Poor human resources***

The sub-region has the severest shortage of health personnel with a density of less than 2.0/1,000. Where available, they have inappropriate skill mix with skewed distribution in favour of urban areas. [17,18,19]

v. ***Poor access to safe water supply and sanitation***
With high diarrhoeal disease burden especially in Niger, Mali and Burkina Faso, these countries still have less than 50% supply of safe water and environmental sanitation is poor. [4]

vi. ***High out of pocket expenses for health***
There is generally high out of pocket expense for health costing above 50% in half of the countries; it is as high as 94% in Cape Verde and 88% in Guinea. Governments' health expenditure is less than 15% across the sub-region. [2,6]

vii. ***Slow rate of maternal mortality reduction***

Maternal mortality ratio ranks amongst the highest in the world, further increasing the vulnerability of orphaned children.[3,4,19]

viii. ***Slow neonatal mortality reduction***
Reduction of neonatal deaths lags behind under-5 mortality decline with the average share among total under-5 deaths rising from 36% to 40% from 1990 to 2012.[3,4,5]

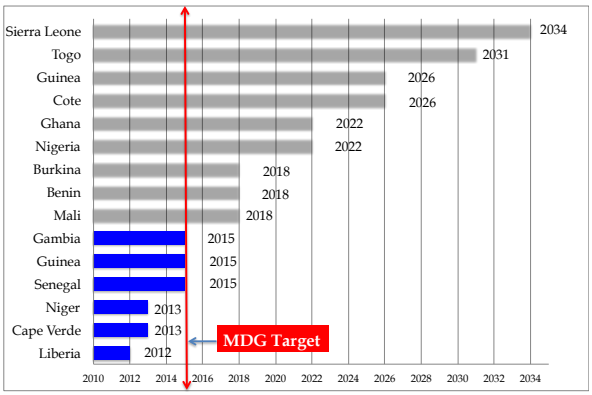
ix. ***Rapid population growth***
West Africa has about the highest population growth rates, constituting a challenge for adequacy of health service coverage. In Nigeria for instance, as the annual number of births rose from 4.3 million to 6.1 million between 1990 and 2008 and the number of births attended to by skilled providers doubled from 1.3 million to 2.7 million, the coverage rose by only 8% (31% to 39%). Had the number of births remained stable coverage could have reached 63%. [2,3,17]

x. ***Armed Conflicts***
Various conflicts threatened equitable service delivery, displaced populations into vulnerable refugee settlements, including civil wars fought in Sierra Leone, Liberia, Guinea-Bissau and Cote d'Ivoire, Coups d'état that occurred in Gambia, Niger and Guinea, as well as recurrent ethnic and sectarian clashes in Nigeria, Mali, Benin since 1990. [4]

PROSPECTS FOR ACHIEVING THE MDG 4 TARGETS

By end of 2013 only Liberia attained the 2/3rd under-5 mortality reduction goal and with just 770 days to the end of 2015 Niger, Cape Verde, Senegal, Guinea and Gambia are likely to attain the goal at their current AARR of 3.8-4.8%. As a sub-region however, West Africa is unlikely to reach the 2/3rd reduction goal because the AARR for other countries is much slower. Togo and Sierra Leone may indeed only achieve this goal nearly 2 decades after 2015 (Figure 3).

Figure 3: Year when West African countries are predicted to achieve MDG4



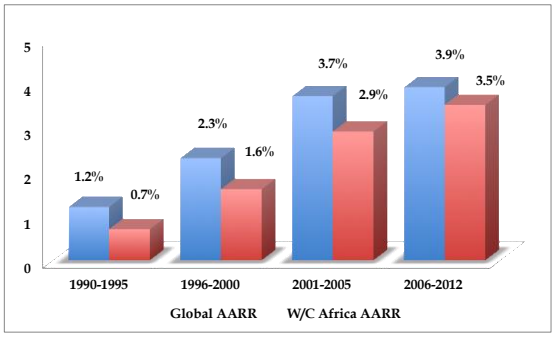
Controversy over Measurement of MDG Success: Achieving Targets or Faster Progress?

The official MDG reports (UNDP, World Bank and UNICEF) focus on achieving targets these have depicted sub-Saharan Africa, as either "off-track", "missing the target" or having a "grossly insufficient rate of reduction". Global development experts however, argue that as performance measures MDG success should focus on faster pace or acceleration of progress relative to pre-MDG period. [10] Further arguing that observed progress could as well have been unrelated to MDG efforts, they proposed an alternative analysis including the period preceding 1990 and disaggregated background achievements from those attributed to MDG efforts.[10] This has revealed some *"empirical findings"* suggesting that Africa's MDG progress is indeed faster than the global average, evidenced by: [10]

i. A 63% acceleration (post-2000) of Africa's under-5 mortality reduction against a global average of 32%.
ii. Nigeria, Burkina Faso and Senegal emerging among the world's top 10 for under-5 mortality reduction and among top 15 improvers of reduction by absolute pace of improvement.
iii. When rated by AARR and comparing progress from 1970, 75% of sub-Saharan Africa had accelerated its AARR between 2001 and 2010 over previous rates.

The 2013 UNICEF MDG Report also showed a five times rise in AARR for West and Central Africa compared to only a tripling of the global average from 1990 to 2012 (Figure 4). [4,5]

Figure 4: West/Central Africa's Rise of Under-5 Mortality Reduction



Recommendations

With elusive prospects, West African countries need to focus on strategies to further accelerate progress beyond 2015. This can be achieved by:

1. A review of terms of partnerships through country-led selection of needs, taking the lead in setting national goals and targets, and channeling partner support towards most essential interventions. [9]
2. Poverty alleviation plans and reduction of family out-of-pocket expenses for health. [4,19]
3. Increased budgetary allocation to prioritize health programmes, ensure universal access and rehabilitate infrastructure. [13,14,15,20]
4. Addressing human resource gaps through task-shifting and preferential deployment of skilled personnel to under-served areas. [3,4,11,17]
5. Improving political will to adopt and implement innovative strategies and health interventions. [4,19,21,23]

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MDG4 IN NORTH AFRICA: WHERE ARE WE?

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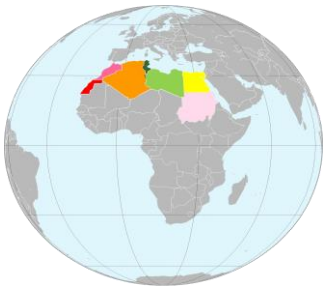
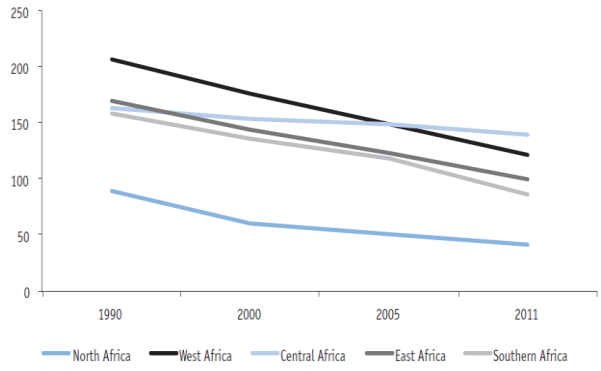
Northern Africa is the northern most region of the African continent, linked by the Sahara desert to Sub-Saharan Africa. According to the United Nations North Africa consists of seven countries or territories, namely Algeria, Egypt, Libya, Morocco, Sudan, Tunisia, and Western Sahara.

Figure 1: North Africa



Millennium Development Goal 4 (MDG4) aims to reduce mortality among children under 5 by two-thirds between 1990 and 2015. Globally, the under-five mortality rate has dropped 47%, from 90 deaths per 1,000 live births in 1990 to 48 per 1,000 live births in 2012. Africa has reduced the under-five mortality rate from 173 deaths per 1,000 live births in 1990 to 95 deaths per 1,000 live births in 2012-still far from its MDG4 target. Among African sub-regions North Africa has made the most progress in reducing the under-five mortality rate. It decreased from 73 deaths per 1,000 live births in 1990 to 22 deaths in 2012, a 69% reduction thus achieving the MDG 4 target.

Figure 2: Under 5 mortality rate by region



Infant mortality

Infant mortality rate (IMR) refers to the number of deaths per 1,000 live births. Globally, IMR has decreased from 63 deaths per 1,000 live births in 1990 to 35 deaths per 1,000

live births in 2012. Africa has reduced IMR gradually from 105 deaths per 1,000 live births in 1990 to 63 deaths per 1,000 live births in 2012. North Africa has reduced infant mortality by more than 50% from 56 deaths per 1,000 live births in 1990 to 19 deaths per 1,000 live births in 2012.

Neonatal Mortality

Globally, neonatal mortality has declined 37% from 33 deaths per 1,000 live births in 1990 to 21 deaths per 1,000 live births in 2012. Africa has reduced neonatal mortality rate from 44 deaths per 1,000 live births in 1990 to 32 deaths per 1,000 live births in 2012. Northern Africa has reduced neonatal mortality rate by 58% from 30 deaths per 1,000 live births in 1990 to 13 deaths per 1,000 live births in 2012 (more than half of under-five deaths).

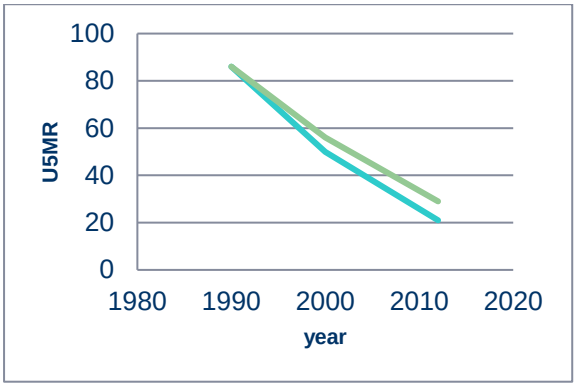
Progress in Egypt

Evidence shows that Egypt has achieved MDG4; U5MR declined from 86 deaths per 1,000 live births to 21 deaths per 1,000 live births in 2012, while the MDG4 target is 29 deaths per 1,000 live births. The annual rate of reduction is the highest in North Africa- 6.4%. IMR fell from 63 deaths per 1,000 live births in 1990 to 18 deaths per 1,000 live births in 2012.The neonatal mortality rate decreased from 33 deaths per 1,000 live births in to 12 deaths per 1,000 live births in 2012. Egypt has achieved its MDG4 target through:

- Implementing vaccination drives
- Campaigns against diarrhoeal-related diseases & promoting oral rehydration therapy
- Combating respiratory diseases such as pneumonia & bronchitis.
- Improvements in maternal health services

The current focus is on preventing death during the first 28 days of life due to low birth weight, premature birth and inadequate infant care.

Figure 3: Under-five mortality in Egypt



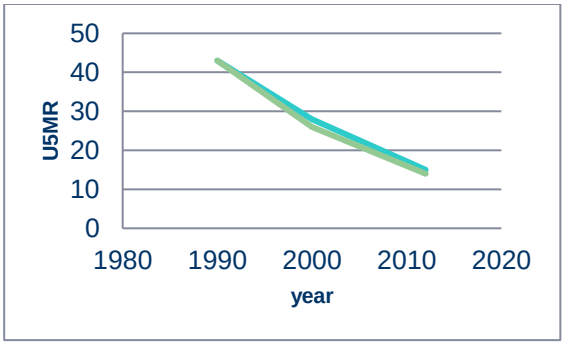
Progress in Libya

Libya is on the track to achieve MDG4. It represents the lowest U5MR in North Africa. U5MR declined from 43 deaths per 1,000 live births in 1990 to 15 in 2012, while the MDG4 target is 14 deaths per 1,000 live births. Annual rate of reduction is the third in North Africa- 4.7%. IMR fell from deaths 37 per 1,000 live births in 1990 to 13 deaths per 1,000 live births in 2012. The neonatal mortality rate decreased from 21 deaths per 1,000 live births in 1990 to 9 deaths per 1,000 live births in 2012. The reduction of U5MR was achieved through:

- Education of women and the wide distribution of health care facilities in urban and rural areas. This led to a sharp fall in infant mortality since the 1970s
- Vaccination campaigns aimed at vaccinating all the children in the country, both Libyans and non-Libyans.

To reduce the rate even further, Libya's health sector will need to create programmes that identify and eliminate the causes of death.

Figure 4: Under-five mortality in Libya

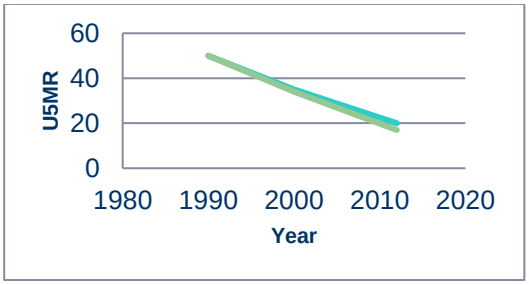


Progress in Algeria

Algeria is on the track to achieve its MDG4 target. U5MR declined from 50 deaths per 1,000 live births in 1990 to 20 deaths per 1,000 live births in 2012, while the MDG4 target is 17 deaths per 1,000 live births. Annual rate of reduction is the fifth in North Africa- 4.1%. IMR fell from 42 in 1990 to 17 deaths for every 1,000 live births in 2012. The neonatal mortality rate decreased from 23 deaths per 1,000 live births in 1990 to 12 deaths per 1,000 live births in 2012. This achievement was done through implementation of the “Child Survival and Development" programme that includes**:**

- AN effective prenatal programme and capacity building of health personnel for the management of both mother and child
- Strengthening the information system
- Programmes of immunization, rehydration and management of acute respiratory infections
- Social communication strategies to support maternal health programs
- Parent education programme for integrated early childhood development

Figure 5: Under-five mortality in Algeria

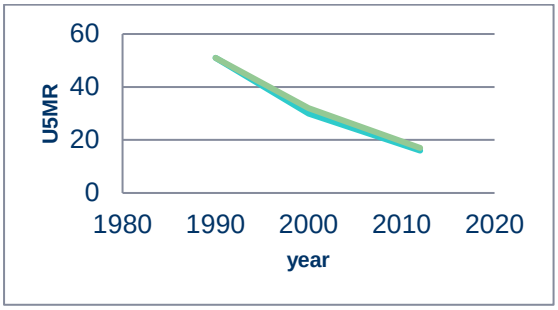


Progress in Tunisia

Tunisia has achieved its MDG4 target. U5MR declined from 51deaths per 1,000 live births in 1990 to 16 deaths per 1,000 live births in 2012, while its MDG4 target is 17 deaths per 1,000 live births. Annual rate of reduction is the second highest in North Africa- 5.3%. IMR fell from 40 deaths in 1990 to 14 deaths for every 1,000 live births in 2012. The neonatal mortality rate reached 10 deaths per 1,000 live births in 2012 while it was 24 deaths per 1,000 live births in 1990. Tunisia's success is due to:

- Great investment in health, in infrastructures and in the training of medical and paramedical personnel
- Development of more than ten national programmes in favour of the mother and child
- Great efforts were made to ensure a better regional distribution of health services
- Improvement in living standards and in housing conditions of the citizens, as well as in better education and in women's promotion

Figure 6: Under-five mortality in Tunisia

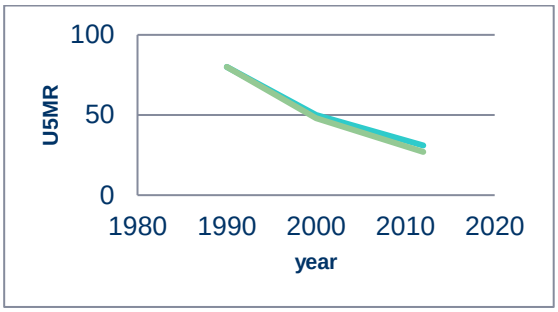


Progress in Morocco

Morocco is on the track to achieve its MDG4 target. U5MR has declined from 80 deaths per 1,000 live births in 1990 to 31 deaths per 1,000 live births in 2012, while its MDG4 target is 27 deaths per 1,000 live births. Annual rate of reduction is the fourth highest in North Africa- 4.3%. IMR fell from 63 deaths in 1990 to 27 deaths for every 1,000 live births in 2012. The neonatal mortality rate decreased from 35 deaths per 1,000 live births in 1990 to 18 deaths per 1,000 live births in 2012. Morocco has progressed in reducing U5MR through a programme of helping babies breathe, to reduce asphyxia-related newborn death by;

- Scaling up newborn resuscitation capacity
- Scaling up the application of essential newborn care and the reduction of newborn sepsis
- Focusing on high-risk babies and scaling up the application of Kangaroo Mother care
- Preventive and curative child health services such as vaccination and community case management of child illness such as diarrheal disease and pneumonia

Figure 7: Under-five mortality in Morocco

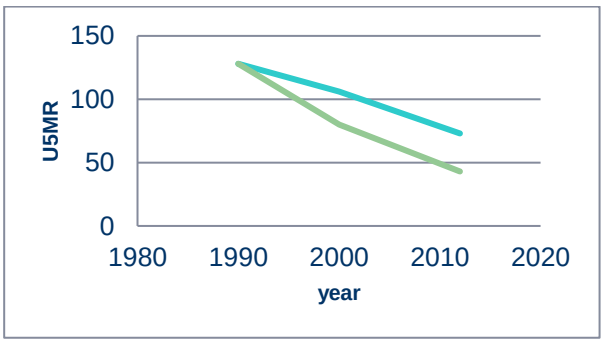


Progress in Sudan

Sudan is still far from its MDG4 target. U5MR declined from 128 deaths in 1990 to 73 deaths per 1,000 live births in 2012, while the MDG4 target is 43 deaths per 1,000 live births. Annual rate of reduction is the lowest in North Africa- 2.6%. IMR fell from 80 deaths in 1990 to 49 deaths for every 1,000 live births in 2012. The neonatal mortality rate decreased from 40 deaths per 1,000 live births in 1990 to 29 deaths per 1,000 live births in 2012. Child mortality is the result of:

- Widespread malnutrition, pneumonia, malaria, vaccine preventable diseases and diarrheal disease
- Lack of infrastructure and limited capacity
- The ongoing conflict in Darfur, where an estimated 1.8 million children have been affected by armed conflict
- Many children have been exposed to brutal violence
- Disruptions in essential services like water and education are also leaving their mark

Figure 8: Under-five mortality in Sudan



Summary

- North Africa has achieved MDG 4 reaching 22 deaths per 1,000 live births in 2012, a 69% reduction
- Infant mortality decreased to 19 deaths per 1,000 live births in 2012. Neonatal mortality declined to 13 deaths per 1,000 live births in 2012 constituting 58% of U5MR
- Egypt and Tunisia have achieved their MDG4 targets.

- Libya, Algeria and Morocco are on the track to achieve their MDG4 targets.
- Sudan is still far from its MDG4 target and needs to make a greater effort in all aspects of health care.

Table 1: U5MR & MDG4 achievements in North Africa

	U5MR			MDG target for 2015	Annual rate of reduction (%) 1990 – 2012
	1990	2000	2012		
N Africa	73	43	22	24	5.4
Egypt	86	45	21	29	6.4
Libya	43	28	15	14	4.7
Algeria	50	35	20	17	4.1
Tunisia	51	30	16	17	5.3
Morocco	80	50	31	27	4.3
Sudan	128	106	73	43	2.6

RESEARCH FEATURE

In this section we focus on the research of Welcome Mkululi Wami a PhD student at the University of Edinburgh, Institute of Immunology Infection and Research, working on the neglected tropical disease, urogenital schistosomiasis.

His research project focuses on developing statistical models to explore the interactions between exposure, infection and pathology associated with *Schistosoma haematobium* infection in preschool and primary school aged children. The findings will be important for future designs of field studies as well as improving the current intervention methods in the affected populations. He has a background in applied statistics and biostatistics. Previously, he worked as a Statistical Research Consultant, Statistician, Data Analyst and Junior Reward Consultant (Strategic Information Services). He has a Master of Science degree in Statistics: specialising in Biostatistics from Hasselt University, Belgium and a Bachelor of Science Honours degree in Statistics from the University of Zimbabwe, Zimbabwe. His recent peer-review publications are in the area of public health. During the course of his PhD training he has presented several conference papers related to his research. He enjoys working and connecting with professionals from across different fields.

PAEDIATRIC SCHISTOSOMIASIS IN ZIMBABWE

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Urogenital schistosomiasis (bilharzia), caused by infection with *Schistosoma haematobium* is an important, yet neglected tropical disease. It affects more than 100 million people worldwide, mainly in sub-Saharan Africa, where more than 90% of the morbidity cases are reported. The disease has a serious socioeconomic and public health impact in these affected regions. Children in endemic areas carry the heaviest burden of disease, and due to the chronic nature of the infection and continued susceptibility to re-infection, they can remain infected for most of their lives. Consequently, they are subject to schistosomiasis-related disease including bladder and kidney disorders, stunting, malnutrition and impaired memory and cognition.

In Zimbabwe, urogenital schistosomiasis is predominant among rural communities with poor sanitary facilities and limited access to safe water which necessitate regular contact with infective water. According to the recent schistosomiasis national survey, (Ministry of Health, Zimbabwe MOHCW, 2010), schistosome infection is among the top 10 causes of hospital admissions in the country, thereby emphasising its public health importance. In several countries currently implementing schistosome control programmes, the control strategies follow the directive by the World Health Assembly (WHA) in 2001, involving regular school based de-worming using praziquantel aimed at reducing morbidity and promoting childhood health. As a result, preschool children (≤ 5 years old) have been neglected in schistosomiasis control programmes. By focusing treatment upon the school-aged population, preschool children are thus denied the benefits of the praziquantel treatment given to their older peers, creating a potential health inequity.

The exclusion of pre-school children from control programmes arose as a result of the previous misconception that they carry insignificant infection levels, which has been exacerbated by the poor diagnosis of infection in the field. In addition, there is currently a paucity of studies comparing the different methods of detecting infection and associated morbidity in this younger age group. We recently conducted a study in Zimbabwe to determine the levels of infection in pre-school children and also compare the sensitivity and specifity of two methods that can be applied in the field to diagnose urogenital schistosome infection. The specific aims of our study were to compare the levels of *S. haematobium* infection in preschool and primary school children, detected by the parasitological diagnostic technique versus infection detected via the serological method, and assess the implications of these levels of infection for the World Health Organization (WHO) recommended treatment regimens.

Our study was conducted in two rural villages in Murewa district, in the north-east of Zimbabwe (31^{o}90'E; 17^{o}63'S). A total of 438 children (1-5 years, n=97; 6-10 years, n=341) were recruited from crèches, early child development centres, preschools and local primary schools. Parents/guardians with children not attending any of the education programmes (e.g., children <3 years old) in the area were invited to report to the school centre for enrolment into the study. Children were designated infected with *S. haematobium* based on parasitological examination if at least one egg was detected in any of their urine samples. Sera obtained from up to 5ml of venous blood collected from each child were tested for anti-egg IgM antibody responses using enzyme linked immunosorbent assays (ELISA), and children designated as positive if the serum level of their schistosome specific antibodies was more than 2 standard deviations above the mean antibody levels of age-matched negative controls. The Bayesian modelling technique was used to assess the accuracy of the two infection diagnostic techniques in the absence of a perfect gold standard diagnostic method. Generalized regression models were used to estimate the age-dependent infection prevalences determined using parasitology or serology.

The serological diagnostic technique was more sensitive (*Sensitivity*: 0.94; 95% CI: 0.89-0.98) than the parasitological diagnostic technique (*Sensitivity:* 0.57, 95% CI: 0.43-0.84). However, the study further showed a higher specificity for parasitology (*Specificity:* 0.94; 95% CI: 0.94-0.98) compared to serology (*Specificity*: 0.75; 95% CI: 0.78-0.97), in agreement with other published studies. The parasitological mean egg count per 10 mL urine in preschool children was 9.0 (Range: 0.0-380.0) and 19.8 (Range: 0.0-1030.0) in primary school children. The overall estimated infection prevalence determined using the serological diagnostic technique was 71.5% (95% CI: 67.2–75.7%) and was found to be significantly higher than the prevalence based on parasitology (37.4%; 95% CI: 33.0–42.0%), in accordance with the diagnostic accuracy results. Furthermore, the prevalence based on serology was significantly higher than prevalence determined using parasitology in both preschool and primary-school age groups. Following the WHO schistosome control guidelines, infection prevalence based on the serological diagnostic technique suggested a more frequent treatment regimen than that implied by the parasitological technique for this study population.

In conclusion, our study showed the presence of significant *S. haematobium* infection levels among preschool children, further reiterating the need for their inclusion in schistosomiasis control programmes to reduce the risk of developing severe schistosomiasis-related morbidity. In addition, the study findings highlight the importance of sensitive infection diagnostic tools as it has a bearing on the required treatment regimen for the study population. These findings are crucial for refinement and improvement of current schistosomiasis intervention strategies.

The research outlined above is part of a series of studies on schistosomiasis in Zimbabwe conducted by our research group (Parasite Immunoepidemiology Group, University of Edinburgh) and our collaborators at the University of Zimbabwe and National Institutes of Health Research, also in Zimbabwe.

More details of this study can be found in: Wami WM, Nausch N, Bauer K, Midzi N, Gwisai R, Simmonds P, Mduluza T, Woolhouse M, Mutapi F. Comparing parasitological *vs* serological determination of *Schistosoma haematobium* infection prevalence in preschool and primary school-aged children: implications for control programmes. *Parasitology*: 2014: 1-9. doi:10.1017/S0031182014000213

More details on study activities in Zimbabwe: http://pig.bio.ed.ac.uk/

Other references:

Ministry of Health and Child Welfare (MOHCW). 2010. Report on the National Soil Transmitted Helminthiasis and Schistosomiasis Survey.

INTRODUCTION OF A MENINGOCOCCAL A CONJUGATE VACCINE IN THE AFRICAN MENINGITIS BELT

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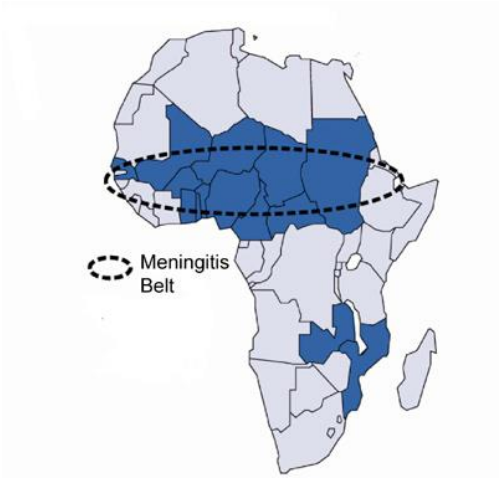
Major epidemics of mainly meningococcal A meningitis have plagued the region known as the African meningitis belt extending from Ethiopia to Gambia and Senegal since it was first described in 1963.[1-3] Epidemics were subsequently reported in neighbouring regions.[2] The largest epidemic to date occurred in 1996 with devastating effects including over 25,000 deaths.[4] Control strategies at the time involved reactive mass immunization campaigns following timely reporting of cases which had reached epidemic thresholds.[5] Reporting was however often not timely and available polysaccharide vaccines at the time did not offer protection to vulnerable children less than 2 years of age nor induce herd immunity.[6-9] This led in 2000 to the conclusion by a WHO expert group with endorsements from delegates and experts from African Health ministries, that the development of a conjugate vaccine for use in the region was an attractive strategy for epidemic control.[5] The Meningitis Vaccine Project (MVP) - a partnership between World Health Organization (WHO) and Program for Appropriate Technology in Health (PATH) with funding from the Bill and Melinda Gates Foundation was thus born in 2001.[10] Its goal was to eliminate epidemic meningitis as a public health problem in sub-Saharan Africa through the development, testing, licensure and widespread use of conjugate meningococcal vaccines.[5]

Figure 1: African Meningitis belt



Following extensive deliberation, it was agreed to develop an affordable meningococcal A conjugate vaccine through an innovative international partnership that involved collaborations between companies and independent experts including transfer of conjugation and fermentation technology to a developing country vaccine manufacturer, Serum Institute of India Limited (SIIL).[10] This unique 'push' strategy allowed cost per vaccine dose to be predetermined at < 50 cents which is less than the cost of existing polysaccharide vaccines.[5,10,11]

Vaccine Introduction

Following extensive clinical trials in India, Mali, The Gambia, Senegal and Ghana, marketing authorization was received in the country of manufacture India in 2009.[12] WHO prequalification was received, with licensure of the new vaccine (MenAfriVac(®)) in 3 African meningitis belt countries Mali, Niger and Burkina Faso in 2010 less than 10 years after MVP started.[13,14] This was on the basis of non-inferiority to the licensed polysaccharide vaccine using immunogenicity cut offs, leading to phased introduction of the vaccine in 1 -29 year olds within the African meningitis belt.[14] This single dose is expected to induce strong herd immunity.[15]

The vaccine introduction strategy is two pronged involving mass vaccination campaigns and integration into routine immunization programmes.[16] The mass campaigns are ongoing within the belt and are being done in phases in lager countries. A need basis with priority given to countries and regions worst hit by epidemics determined the sequence of vaccine introduction. These criteria included[12]:

- Disease burden.
- Country readiness
- Participation in the clinical trials for vaccine development.
- Financial viability.
- Vaccine availability.

Based on these criteria, 3 groups of countries were identified as follows[12]:

- **Core countries:** Burkina Faso, Chad, Ethiopia, Mali, Niger, the northern states of Nigeria, and Sudan.
- **Bordering countries with hyperendemic zones:** Benin, Cameroon, Central African Republic, Côte d'Ivoire, Democratic Republic of the Congo, the Gambia, Ghana, Kenya, the remaining states of Nigeria, Senegal, Togo, and Uganda.
- **Other at-risk countries without hyperendemic zones:** Burundi, Eritrea, Guinea, Guinea-Bissau, Mauritania, Rwanda, and Tanzania.

After these campaigns are completed, the main challenge will be protecting infants and young children not initially vaccinated.[16] Incorporation of MenAfriVac(®) into routine Expanded Programme on Immunization schedules or use in mass campaigns targeting children under five years of age should help to circumvent this.

In September 2010, Mali, Niger and Burkina Faso introduced the vaccine.[13,17,18] On December 6 2010, Burkina Faso became the first African country to introduce MenAfriVac(®) nationwide in a hugely successful mass vaccination campaign that targeted all 1 to 29 year individuals in the country. Administrative coverage rate for this campaign was 100.3% with more than 11 million people were vaccinated between December 6 and 15.[13] Since that time, 9 other African countries have introduced the vaccine including Mali, Niger, Nigeria, and Chad and over 153 million people have received the vaccine so far.[12]

Subsequent introduction in bordering or at risk countries will be decided by the International Coordinating group (ICG) on Vaccine Provision for Epidemic meningitis Control, which currently manages stock piles of polysaccharides vaccines for reactive campaigns. The process is a country-driven approach taking into account the epidemiologic context and the country's' ability to mount vaccination campaigns.[12]

Table 1: MenAfriVac(®) roll out plan. (Courtesy: Meningitis Vaccine Project)[12]

MENAFRIVAC ROLL OUT PLAN	2011	2012	2013	2014	2015	2016
GROUP 1						
Nigeria	✕	✕	✕	✕		
Chad	✕	✕				
Cameroon	✕	✕				
Sudan		✕	✕			
GROUP 2						
Ghana		✕				
Benin		✕				
Senegal		✕				
GROUP 3						
Ethiopia			✕	✕	✕	
Democratic Republic of Congo					✕	
South Sudan				✕	✕	
Ivory Coast				✕		
Togo				✕		
Uganda					✕	
Guinea				✕		
GROUP 4						
Gambia			✕			
Central African Republic					✕	
Erithrea						✕
Kenya					✕	
Burundi						✕
Guinea Bissau						✕
Mauritania				✕		
Rwanda						✕
Tanzania						✕

Impact

Although still in the early days, since the introduction of the vaccine significant reductions in disease caused by meningococcal A and meningococcal A carriage have been reported with almost complete disappearance in some countries.[19] This impact is likely due in part to MenAfriVac(®) introduction. Serogroup W and X meningitis however appear to be on the increase within the belt and may be one of the next challenges to tackle.[19] Strong laboratory support and surveillance systems are required to monitor continued impact on disease as well as impact on meningococcal carriage.

Socioeconomic impact has also been recently assessed and it is predicted that the introduction of MenAfriVac(®) is a cost-savings intervention (US$192 saved per disability-adjusted life year [DALY] averted) compared to the current strategy of reactive mass vaccination campaigns.[12,20] This is largely due to the effect the vaccine will have in inducing herd immunity not seen with polysaccharide vaccines, and the fact that it is cheaper than the polysaccharide vaccines. Further to this, the vaccine in 2012 gained WHO approval to travel outside the cold chain for up to 4 days.[21] This characteristic alone can half vaccine storage and transportation costs.

Conclusion

Introduction of this novel vaccine 10 short years after development is indeed a public health success story and is already showing promise of significant impact within the region. The unique strategy used to develop this vaccine may well serve as a model for other public health challenges in sub-Saharan Africa and beyond.

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HIGHLIGHTS FROM THE 16TH ICID

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The 16th International Congress on Infectious Diseases took place in the International convention Centre, Cape Town, the same venue as that of the 8th WSPID conference. Plenary lectures addressed the prevention of HIV through antiretrovirals, neglected tropical diseases, global challenges in infectious diseases, otitis media, influenza and Middle East Respiratory Syndrome – Coronavirus (MERS-CoV). Symposia were devoted to a wide spectrum of common infectious diseases problems and challenges. This review addresses a few topics that may be of interest to clinicians working on our continent.

Invasive non-typhoid Salmonellosis

Myrone Levine (University of Maryland and School of Medicine, Baltimore) presented an overview of the epidemiology of non-typhoid *Salmonella enterica* (NTS) focussing primarily on invasive infection.[1] More than 2500 serovars of NTS have been identified. Most disease is caused by two serovars namely *Salmonella typhimurium* and *Salmonella enteritidis*. These two serovars are important causes of bacterial gastroenteritis worldwide. In sub-Saharan Africa (sSA) they cause invasive NTS (iNTS) disease in young children, mainly <3 years of age. In many parts of Africa the incidence of iNTS disease is as high as that of invasive pneumococcal disease. Invasive NTS disease is associated with a high case fatality rate in excess of 20%. The case fatality rate is high in all age

groups, including children >60 months of age and adults. A novel *S. typhimurium* strain, ST313 causing invasive disease has emerged in sSA. Epidemics of multi-drug resistent ST313 have been documented in several countries. Risk factors for iNTS disease include malaria, HIV infection and malnutrition. Levine said that although the incidence of iNTS infection was recently shown to decline with falling malaria incidence, this decline was likely to be due to annual variation because recent research has recorded an increasing incidence.[2,3] A vaccine against NTS is urgently needed because we lack fundamental epidemiological information required to control iNTS. In particular, the reservoir and modes of transmission of NTS in Africa are not known. It is highly probable that when a vaccine becomes available it will be used in routine EPI programmes, possibly at 6, 10 and 14 weeks of age to ensure that young children are protected.

Sharon Tennant (University of Maryland and School of Medicine, Baltimore) discussed bivalent vaccines targeting *S. typhimurium* and *S. enteritidis*.[4] Live attenuated and conjugate vaccines strategies have been developed in parallel. Attenuated live strains of *S. typhimurium* (CVD 1931) and *S. enteritidis* (CVD 1944) were shown to be safe in mice. CVD 1931 and CVD 1944 were highly protective (85-91%) when vaccinated mice were subsequently challenged with *S. Stanleyville* (a Group B Salmonella serovar) and *S. Dublin* (Group D Salmonella serovar), respectively, indicating that live attenuated vaccines may generate cross-protection against other *Salmonella species.* Glycoconjugate vaccines have also shown great potential in mouse studies. Core polysaccharide-O polysaccharide (COPS) conjugated with carrier proteins generates functional immunity and protects against fatal *Salmonella* challenge. COPS conjugated to *Salmonella* flagellin does not affect the antibody response to flagellin and provides 92-100% protection in mice. Another approach involves conjugating COPS with *Salmonella* porins. Currently, the production *S. typhimurium* and *S. enteritidis* conjugates is being scaled-up. Tennant said that if bivalent vaccines are effective they should provide protection against up to 90% of invasive disease.

The fight against cholera in Africa

In a symposium entitled “Towards cholera elimination: A new era for an integrated strategies” speakers described several initiatives aimed at controlling cholera. Luc Hessel stated that Cholera remains a major public health issue with an estimated global burden of 3-5 million cases per annum causing 100,000 – 200,000 deaths. Despite advances in clinical management, control and prevention, cholera outbreaks continue to be reported annually from sub-Saharan Africa (sSA) and Asia. For example, during the first 11 weeks of 2014, an outbreak predominantly in the Democratic Republic of Congo (DRC) and Nigeria was responsible for 12,863 cases and 182 deaths, a case fatality rate (CFR) of 1.5%. Hessel introduced the Initiative against Diarrhoeal and Enteric Diseases in Africa and Asia (IDEA), a professional network involved in cholera control, prevention and elimination. IDEA is active in 13 countries in sSA and 9 Southeast Asian countries. In 2014 the IDEA advocacy agenda focuses on improvement of current food, water, sanitation and hygiene interventions, strengthening surveillance systems, and the introduction of cholera vaccination as part of an integrated strategy to eliminate cholera.[5]

Delphine Sauvagot introduced Africhol, which aims to improve cholera prevention and control in sSA through an evidence base on incidence and disease burden. Since the 7th cholera pandemic reached Africa in 1970 cholera has become endemic in many African countries, and remains a recurring cause of large, often multinational epidemics in West, Central and east Africa. At least 20 countries in Africa report cases to the WHO each year, Total annual cases from Africa reported to WHO consistently exceed 100,000 and CFRs range from 2.22 to 2.95%, but exceed 5% in ≥1 country per annum. The organisation has established a network of sentinel surveillance sites. Collaborating countries include Cameroon, Côte d’Ivoire, DRC, Guinea, Kenya, Mozambique, Tanzania, Togo and Uganda. Two new countries have recently joined i.e. Nigeria and Zimbabwe. Sauvagot drew attention to a recent supplement published by the *Journal of Infectious Diseases*, which provides an in depth analysis of the burden of disease and critical issues for diagnosing, treating, preventing and controlling cholera in Africa, and highlights surveillance activities supported by Africhol (*J Infect Dis* 2013;208 (Suppl 1), November 2013. The entire supplement may be accessed via the Africhol website).[6]

David Sacks (Johns Hopkins Bloomberg School of Public Health) discussed the Delivering Oral Vaccine Effectively (DOVE) cholera project. The DOVE project promotes the use of oral cholera vaccine (OCV) in an integrated manner. In 2010 WHO revised its policy regarding cholera vaccination, recommending that it be used for countries with cholera. The available cholera vaccines, Dukerol, Shanchol amd mORCVAX are safe and provide protection of >50% that lasts for 2 years in endemic populations. Furthermore WHO has created a stockpile of 2 million doses of OCV for emergency situations.[7] Sacks said that several challenges remain including (1) a small stockpile of 2 million doses, which should be increased to 20 million doses because the population at risk exceeds 1 billion, (2) the cost of the WHO pre-qualified Shanchol vaccine is currently 1.85 USD per dose and additional programme costs amount to 0.5-1.0 USD per dose, (3) lack of awareness of OCV among public health experts, (4) few countries have developed a strategy for integrating OCV into their national health systems, an exception is the DRC, which has developed a comprehensive national policy to respond to cholera, and (5) effective and accurate surveillance. He said that a control programme without surveillance is futile.[8]

Finally Franck Haaser and Didier Bompangue drew attention to initiatives to control and eliminate cholera in the DRC. The DRC is among the countries most affected by cholera outbreaks. Haaser, a water engineer said that epidemiological studies have shown that eastern DRC was a particular hotspot for cholera. A large infrastructural project to improve potable water access is being completed in Kalemie, Katanga province supported by the Global Alliance Against Cholera. A second project to improve the quality and safety of potable water in Uvira, South Kiva province has also begun.[9] Bompangue, an epidemiologist from the University of Kinshasa provided a detailed analysis of the history and epidemiology of

cholera in the DRC. During the first 6 global pandemics up to 1923 there were no reported cases of cholera in Africa. From 1970 onwards, cholera has occurred annually in the DRC. In eastern DRC cholera is endemic, while in western DRC it characteristically occurs in epidemics. Severn cities situated along Rift Valley lakes in eastern DRC are the main source of cholera. Bompangue drew attention to the new national policy for the elimination of cholera in the DRC. Seven strategic objectives are being pursued including improved surveillance, timely alert of outbreaks, strengthening prevention initiatives in targeted areas, improved case management, the overall of infrastructure for drinking water and sanitation, strengthening coordination, and operational research.[10]

Influenza: understanding the pathogenesis to improve outcome

The plenary talk on Influenza by Jonathan A. McCullers (St Jude Children's Research Hospital, Memphis, Tennessee) provided insights into the pathogenesis of secondary bacterial pneumonia (SBP) that may occur as part of an influenza infection. During the 2009 H1N1 influenza pandemic, SBP was present in 25-50% of severe or fatal cases. *Staphylococcus aureus* and *Streptococcus pneumonia* were the commonest associated bacterial infections. Several proposed mechanisms in the viral-bacterial synergism were presented. These included factors that enhance bacterial adherence e.g. sialidase activity of the virus inducing epithelial damage, factors facilitating bacterial access to normally sterile sites e.g. the Eustachian tube, factors altering the innate immune function, and bacterial factors that enhance viral replication.[11]

Mice model studies from St Jude Children's Hospital have shown that the influenza virus suppresses host immune function in animals infected with influenza virus in various ways, one of which is the depletion of alveolar macrophages in the airways.[12] This leads to impaired bacterial clearance by altering cellular innate immunity in the lungs with a resultant increased susceptibility to pneumonia. The peak occurs during day 3 to 7 but the effect can be present for up to 10 days after viral infection. Even with the use of antibiotics for the treatment of SBP, there is still significant morbidity and mortality. McCullers also presented the results of a study investigating the use of corticosteroids in SBP caused by *S. pneumoniae* following influenza infection in the mouse model previously mentioned.[13] Mice were intranasally infected with influenza virus followed by a small inoculation of pneumococcus on day 7 after influenza infection. Detection of SBP and severity of pneumonia was determined by measuring bacterial load of *S. pneumoniae* in the lungs of the mice using bioluminescence imaging. Ampicillin, used to treat the SBP once detected, eliminated infection in mild cases of pneumonia but was ineffective in the mice with severe pneumonia. Adjunctive dexamethasone therapy, administered once antibiotics for SBP were commenced, showed a 70% survival in the mice with severe pneumonia. Early dexamethasone commenced on day 3 after influenza infection and before SBP occurred did not improve survival in the ampicillin-treated mice with either mild or severe pneumonia. Corticosteroids suppress adaptive immunity causing decreased numbers of T-cells, leading to delayed influenza virus clearance and therefore increased lung injury.

Nosocomial infections in low and middle-income countries

Ursula Theuretzbacher (Centre for Anti-infective agents, Vienna, Austria) spoke about global resistance hotspots. Resistance-determining genes along with multi-drug resistant pathogens are widespread and increasing worldwide. Extended spectrum beta-lactamase producing *Enterobactericae* are increasing and the New Dehli metallobetalactamase (NDM) gene first identified in India in 2008, is now found worldwide. She went on to mention that antibiotics being used consumed in various forms with its use in animal farming as well water that is used in the irrigation of farms. The low to middle income countries are contributing significantly to the pool of resistance genes and the difficult to treat infections. These countries are lacking in economic resources, have weak antibiotic policies and medicine regulatory authorities, there is erratic access to antibiotics and there are wide differences in the standard of living. Treatment of highly resistant organisms will be difficult as the access to appropriate or even newer antibiotics may not be possible. This will lead to the further spread worldwide of resistant organisms.

Ramanan Laxminarayan (Centre for Disease Dynamics, Economics and Policy, Washington and Princeton University, USA) provided an overview of the factors driving antimicrobial resistance in low to middle income countries. These included: the non-prescription use of antibiotics, the appropriateness of the use of antibiotics, incentives from drug companies for healthcare providers, patient behavior and expectations, people can afford antibiotics, veterinary antibiotic usage in developed and developing countries and global travel that increases the spread of resistant pathogens. The sale of Carbepenems has increased worldwide despite the cost of the drugs.[14]

Shaheen Mehtar (University of Stellenbosch, South Africa) has developed a teaching program in Infection Prevention and Control (IPC) where practices and implementation can be applicable to the African setting. With the rates of healthcare-associated infections ranging between 2.5 and 14.8% in African hospitals, infection control plays an important in the further prevention and control of these infections.[15] The training ranging from a certificate of competence to a Masters degree has involved healthcare workers involved in IPC from throughout the African continent. A new education program has been launched which involves messages on mobile phones to educate society as well as healthcare workers in the rural areas.

Childhood & adult pneumonia in the era of Conjugate vaccines

David Murdoch (University of Otago, New Zealand) spoke about the difficulty of diagnosing the aetiology of pneumonia and that the newer advances in pneumonia diagnostics has been in the field of serology collection is important but may be difficult to obtain specimens required for either culture or serology e.g. lung aspirates, sputum, nasopharyngeal specimens that may be colonized with upper respiratory tract pathogens. Differentiating bystanders from true pathogens is difficult especially with

case-control studies showing similar respiratory pathogens found as often in cases and in controls. As a result of testing for a wider range of pathogens, multiple microbes are detected. And whether all the microbes detected are all contributing to the disease, is not always clear.

Shabir Madhi (NICD, Johannesburg) spoke about the spectrum and complications of pneumonia in the era of conjugate vaccines. Pneumonia still remains the leading cause of death in <5 years of age in the developing world. With the introduction of Pneumococcal conjugate and *Haemophilus influenza* type b conjugate vaccines into the national immunisation schedules in developed countries, there has been a decrease in the incidence of invasive pneumococcal disease and all cause pneumonia (up to 52% in the United States) following vaccination with PCV-7.[16] Since developing countries, with a high burden of disease, have only recently introduced pneumococcal conjugate vaccines (PCV), the impact of the vaccine on all cause pneumonia morbidity and mortality has not been shown yet. The talk also highlighted that although there was a reduction in all cause pneumonia, there was a temporal association between the introduction of PCV-7 and parapneumonic empyaema due to pneumococcal serotypes not found in PCV-7 particularly serotypes 1, 3, 14 which are included in the PCV-13.[17]

M Elderson (PATH, Seattle, USA) discussed new pneumococcal vaccines that are in development at PATH. These include vaccines that contain proteins common to all pneumococcus serotypes that could offer broad and affordable protection to children around the world.[18] The current approaches undergoing research include adaptations or modifications to the conjugate vaccine e.g. attaching a polysaccharide antigen to carrier proteins to elicit immune responses in young children, the development of a recombinant genetically detoxified pneumolysin protein (L460D) or pneumolysoid and the development of an inactivated pneumococcal whole cell vaccine.[19] The preclinical trials of the inactivated whole cell vaccine in mouse models showed good efficacy against invasive pneumococcal disease (T-cell mediated) and nasal carriage (antibody mediated).[19] Phase I clinical trials have also been completed, showing good immune responses to the vaccine by the subjects. The next step would to bring the vaccine candidate to a country in Africa to assess the vaccine's suitability for the the target population. PATH is also collaborating with the Serum Institute of India to develop a 10–valent conjugate vaccine that includes the serotypes prevalent in developing countries and would also be affordable to those countries.

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JOURNAL WATCH

Long-term co-trimoxazole prophylaxis for HIV-infected children

Cotrimoxazole prophylaxis administered before the start of antiretroviral therapy (ART) reduces morbidity, mortality and rates of hospitalisation in HIV-infected children. Whether or not children and adolescents receiving ART should discontinue cotrimoxazole prophylaxis is unclear. In this randomised non-inferiority trial conducted in **Uganda** and **Zimbabwe**, the effect of stopping versus continuing daily open-label cotrimoxazole was investigated, after the participants had received ART for more than 96 weeks. The median follow-up from randomisation to closure of the trial was 2.1 years. Participant who stopped cotrimoxazole experienced significantly higher rates of hospitalisation and death than those who continued. Most hospitalisations in the group that stopped prophylaxis were for malaria and other infections, particularly pneumonia, sepsis and meningitis. These findings argue strongly for long-term cotrimoxaozole prophylaxis in conjunction with ART in sub-Saharan Africa, and should prompt revision of global guidelines for managing cotrimoxazole prophylaxis in HIV infected children and adolescents.

Reference: Bwakura-Dangarembizi M, et al. *N Engl J Med* 2014; 370: 41-53

Causes of fever in children in Africa

Malaria has been a major cause of fever among children in Africa. However, with the decline in malaria transmission in many parts of Africa it is important to improve our understanding of the causes of fever. The researchers recruited children less than 10 years of age with a temperature ≥38°C at two outpatient clinics, one rural and the other urban in **Tanzania.** A comprehensive clinical assessment was completed and blood and nasopharyngeal specimens were collected for an extensive battery of diagnostic tests. Final diagnoses were determined using algorithms guided by pre-specified criteria. Of 1005 children were included in this study, detailed analysis yielded 1,232 diagnoses; 22.6% of the children had multiple diagnoses, 62.2. had an acute respiratory infection, 13.3% had a systemic bacterial, viral or parasitic infection, 11.9% had a nasopharyngeal viral infection, 10.5% had malaria, 10.3% gastroenteritis, 5.9% urinary tract infection, 3.7% typhoid fever, 1.5% skin or mucosal infection and 0.2% meningitis. The cause of fever was undetermined in 3.2%. In total 70.5% of the children had a viral infection, 22.0% a bacterial infection and 10.9% parasitic disease. In an accompanying editorial Kathryn Maitland noted that once malaria and critical illness had been ruled-out, this study demonstrated that most febrile illnesses among children in outpatient settings can be treated conservatively without antibiotics.

Reference: D'Acremont V, et al. *N Engl J Med* 2014; 370: 809-17

Editorial: Maitland K. *N Engl J Med* 2014; 370: 875-77

Diagnosis of childhood TB and host gene expression

Tuberculosis is very difficult to diagnose in children. Existing tests including the recently developed Xpert MTB/RIF all have limitations. Consequently for most children strongly suspected of having TB on clinical and radiological grounds, the diagnosis of TB is never confirmed. In this multi-centre study, whole-blood gene expression signatures that distinguish TB from latent TB and/or other common childhood infection were identified in **South African** and **Malawian** paediatric cohorts with and without HIV infection. A 51-transcript signature distinguishing TB from other infections was converted into a TB risk score. In a **Kenyan** validation cohort the risk score showed a sensitivity of 82.9% and specificity of 83.6% for the diagnosis of culture-confirmed TB. Among children with cultures negative for *Mycobacterium tuberculosis* who were treated for TB (those with highly probable, probable, or possible cases of tuberculosis), the estimated sensitivity was 62.5 to 82.3%, 42.1 to 80.8%, and 35.3 to 79.6%, respectively, for different estimates of actual tuberculosis in the groups. In comparison, the sensitivity of the Xpert MTB/RIF assay for molecular detection of *M. tuberculosis* DNA in cases of culture-confirmed tuberculosis was 54.3% (95% CI, 37.1 to 68.6), and the sensitivity in highly probable, probable, or possible cases was an estimated 25.0 to 35.7%, 5.3 to 13.3%, and 0%, respectively; the specificity of the assay was 100%. Having shown that gene expression signatures may assist in distinguishing TB from other diseases, the next step in this research programme is to translate RNA expression (transcriptional) signatures into diagnostic tools that are appropriate for resource-poor communities. This is currently being explored.

Anderson ST, et al. N Engl J Med 2014; 370: 1712-1723

CONFERENCE & SOCIETY NEWS

6th International Workshop on HIV Pediatrics: This annual workshop takes place on 18 & 19 July 2014 in Melbourne, Australia. For more information consult the conference website: www.virology-education.com

South African Paediatric Association conference (SAPA 2014): This conference takes place from 11 – 14 September 2014 at the International Convention Centre, Cape Town and includes a pre-conference day-long workshop on paediatric ID entitled: current issues in paediatric ID. For more information including the complete preliminary programme visit the **c**onference website: www.sapacongress2014.co.za

2nd Southern African HIV Clinicians Society Conference: This conference takes place from 24 – 27 September 2014 in the International Convention Centre, Cape Town and covers both paediatric and adult HIV infection. For more information visit the Clinicians Society website: http://www.sahivsoc.org/

9th Respiratory Syncitial Virus Symposium: This conference takes place from 9 – 13 November 2014 in Stellenbosch, South Africa, and will be hosted by SASPID. For more information visit the conference website: www.RSV2014.co.za

4th Congress of the African Society for Immunodeficiencies (4th ASID): This conference takes place from 27 - 29 May 2015. For more information visit the ASID website: http://www.asid.ma/

45th Union World Conference on Lung Health: This conference takes place from 28 October to 1 November 2014 in Barcelona, Spain. For more information visit the conference website: http://www.theunion.org/what-we-do/conferences/world-conference-on-lung-health/45th-union-world-conference-on-lung-health

9th WSPID conference takes place from 18 – 21 November 2015 in Rio de Janeiro, Brazil. For more information visit the Paediatric Infectious Diseases Society website: http://www.pids.org/ AfPIDS will once more host a dedicated symposium at this conference, focussing on paediatric ID in Africa.

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