Africa's response to childhood infection

The AfSPID BULLETIN

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EDITOR'S COMMENT

Dear Colleagues

Welcome to the 14th edition of the AfSPID Bulletin.

COVID-19 infection which had been at the frontline of scientific and social media since March 11, 2020, when it was declared a pandemic appears to be giving way to other previously enlisted players in the field of infections. There is no doubt that the development of the vaccine has played a major role in preventing, containing, and breaking the transmission of SARS-CoV-2 but the period of effectiveness is yet to be fully determined. The new variants of SARS-CoV-2 have added further complexity to the virus.

The other issues still requiring attention with the novel coronavirus include equity and acceptance of the vaccine. As the COVID-19 vaccine roll out continues, Africa appears to be lagging in its distribution with very low vaccination rates being recorded in most of the countries.[1] Strategies to tackle vaccine hesitancy must be put in place as well as surveillance and appropriate documentation of adverse events.[2] Safety concerns about the new vaccines should be adequately addressed. Ultimately, to improve access across the continent, COVID-19 vaccine production technology may need to be transferred to Africa.

In this edition of the bulletin, Lindsay Petersen discusses the impact of COVID-19 in pregnant and lactating women with its implication for their offspring. COVID-19 vaccination appears to offer protection as current evidence shows that unvaccinated pregnant and lactating women are at increased risk of severe infection with associated maternal, foetal, and neonatal risks. The recent authorisation of Pfizer's COVID-19 vaccine for children as young as five years could be an important step towards the road to elimination of the virus.

Before the advent of COVID-19 infection, the epidemiology of many infectious diseases had changed over time following the introduction of life-saving vaccines against their causative agents. The risk factors and management of bacterial meningitis and rubella are featured here to draw attention to the fact that cases of these infections are still reported with devastating consequences in sub-Saharan Africa as the vaccines are yet to be included in the national immunization schedules of most of the countries.

Brian Eley sheds light on a clinical trial that suggests significant disruption in the transmission of dengue virus infection with the deployment of *Wolbachia* bacteria in *Aedes aegypti* mosquitoes. He reflects that such clinical trials are also needed to test the efficacy in the control of other arboviruses such as zika, chikungunya and yellow fever.

I hope you will find these and other contributions in this edition of the bulletin interesting.

Regina Oladokun, deputy editor

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SOCIETY NEWS

APPOINTMENT OF NEW EDITORIAL BOARD MEMBERS

We welcome seven colleagues to the editorial board.

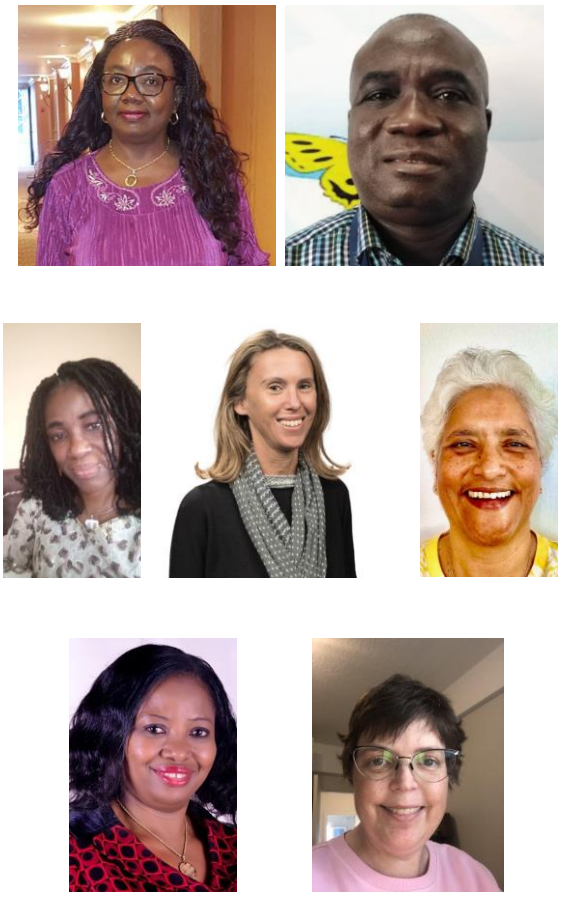

Figure 1: New editorial board members: Prof Ebelechuku Francesca Ugochukwu (top row, left), Dr Anthony Enimil (top row, right), Prof Ayebo Evawere Sadoh (middle row, left), Dr Lisa Frigati (middle row, centre) Dr Paula Vaz (middle row, right), Prof Ebunoluwa Aderonke Adejuyigbe (bottom row, left) and Dr Elizabeth Prentice (bottom row, right)

Ebelechuku Francesca Ugochukwu, MB.BS, FWACP, is a consultant paediatrician at the Nnamdi Azikiwe University Teaching Hospital, Nnewi, and a professor of Paediatrics at the Nnamdi Azikiwe University, Awka, Nigeria. She completed her undergraduate medical degree at the University of Nigeria in 1986. She has a Fellowship of the West African College of Physicians. She was trained in 2003 by the Centers for Disease Control and Prevention in conjunction with the University of Maryland Institute of Human Virology and Baylor College of Medicine, Texas Children's Hospital USA in the use of antiretroviral drugs for the treatment of Pediatric AIDS and the prevention of mother to child transmission of HIV and associated complications. She has since worked predominantly with children affected and infected with HIV/AIDS. She is currently the Head /Coordinator of HIV Care Services at the Nnamdi Azikiwe University Teaching Hospital.

Anthony Enimil is a consultant paediatric infectious diseases specialist at the Komfo Anokye Teaching Hospital (KATH) in Ghana and a senior lecturer at the School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.
He is a fellow of the West African College of Physicians and a fellow of the Ghana College of Physicians and Surgeons.

He completed his subspecialty training in paediatric infectious diseases at the Red Cross War Memorial Children's Hospital in 2020.

He heads the Paediatric Infectious Diseases Unit of KATH. He is a technical working group member of the National AIDS Control and National Immunization Programmes. He is the National Childhood TB focal person and chairs the Afro WHO child TB working group.

His research interests include pharmacokinetics of antiretrovirals and anti-TB medications in HIV/TB co-infected paediatric patients. He has several publications in this field. He also has an interest in disclosure and stigma in adolescents and young adults living with HIV.

He has a special interest in antimicrobial stewardship/resistance and serves as KATH's institutional focal person for the Open University /Fleming Antimicrobial resistance programme.

Ayebo Sadoh is a professor of Pediatric Infectious Diseases and Child Health. She graduated from the School of Medicine, University of Benin in 1988. She had her residency training in pediatrics in the University of Benin Teaching Hospital and obtained a fellowship of the West African College of Physicians in Paediatrics in 1997. In 2012 she received a masters degree in public health. In 2014, as part of further professional development in the subspecialty of paediatric infectious diseases, she completed a three-month observership in paediatric infectious diseases at the University of Nebraska Medical Center and Children's Hospital and Medical Center, Omaha, Nebraska,

She worked as a consultant paediatrician in Federal Medical Centre Abeokuta, Nigeria where she was also Head of Department of Paediatrics from 1998 to 2005. She then moved to the University of Benin, Benin City in 2006 where she currently works in the Institute of Child Health, while also teaching paediatrics in the University of Benin Medical School. She is also an Honorary Consultant to the University of Benin Teaching Hospital where she is the Head of the Paediatric Infectious Diseases Unit.

Prof Sadoh has been Director of the Institute of Child Health (2014 to 2017) and has served in various committees such as the committee for the development of the Paediatric Infectious Diseases Curriculum of the West African College, Committees of the National Tuberculosis, Leprosy, and Buruli Ulcer control Programme to review training manuals

and develop standard operating procedures and guidelines as well as the National Covid-19 Vaccine Coordinating Committee.

Her research interests are in Vaccinology, Vaccine preventable diseases and Community Paediatrics. She has authored and co-authored many journal publications in paediatrics and child health. She is currently the deputy editor of Annals of Biomedical Sciences, a journal of the Medical and Dental Consultants of Nigeria, Benin chapter.

Lisa Frigati, is a trained paediatrician and paediatric infectious diseases sub-specialist. She completed her PhD in 2021. She is currently employed as a paediatrician at Tygerberg Hospital and Stellenbosch University, in Cape Town South Africa where she leads the outpatient paediatric HIV clinical service and outreach clinics. She also provides care for inpatients admitted to the paediatric infectious diseases ward, performs antibiotic stewardship ward rounds and relevant infection prevention control activities, consults on patients in connected disciplines. She is a senior lecturer in the department of paediatrics. Her major research and scientific interests include paediatric infectious diseases, paediatric HIV, paediatric TB, adolescent HIV, and tropical infections. Her research publications reflect these interests.

Paula M. S. Vaz is a paediatrician trained in Mozambique and France. Dr Vaz received her MD from Eduardo Mondlane University School of Medicine (1987) in Mozambique, Diploma in Mother and Child Health from Necker Faculty of Medicine (1994) in Paris, France, specialized in paediatrics in Mozambique in 1996, a University Diploma in Children and Adolescents Psychopathology from University Paris XI in Paris (2002), France and her PhD in Biomedical Sciences from the Karolinska Institute (2010) in Stockholm, Sweden. In addition, she trained in HIV/AIDS at Necker Hospital during 2001 and 2002.

She serves in her current role as Fundação Ariel's Executive Director, an affiliate of the Elizabeth Glaser Pediatric AIDS Foundation, since its inception in 2011 as a Mozambican non-governmental organization dedicated to the fight against pediatric AIDS.

Prior to Fundação Ariel, Dr Vaz was the national coordinator of pediatric AIDS treatment for the Ministry of Health, where she directed the nationwide scale-up of paediatric AIDS services. She also worked with the Maputo Central Hospital where she established the first pediatric day hospital in Mozambique and held the position of Deputy Dean of the School of Medicine at Eduardo Mondlane University. She is also a former Chef de Clinique assistant at Necker Faculty in Paris.

She has also published papers and conducted clinical and operational research. She participated in the WHO Paediatric Working Group for the HIV Guidelines and is currently part of the EPIICAL team. She has been collaborating with Eduardo Mondlane University serving as a tutor for MPH and PhD students and being part of the jury for paediatrics, MPH and MSc exams.

Her main interests are Paediatric HIV/AIDS, TB and child and adolescent mental health issues.

Ebunoluwa Aderonke Adejuyigbe obtained her medical degree from the Obafemi Awolowo University (OAU) in 1987. She is a fellow of the National Postgraduate Medical College of Nigeria having completed her residency training in Paediatrics at the Obafemi Awolowo University Teaching Hospital Complex (OAUTHJC), Ile-Ife, Nigeria. She became a Professor of Paediatrics and Child Health in 2007. Her work experience includes Head of the Department of Paediatrics (2010 – 2012), Dean of the Medical School (2012 – 2016), member of the Management Board of the OAUTHC (2013 – 2015), member of the OAUTHC Ethical and Research Committee (2005 – 2017) and of which she later became the chair (2009 to 2017). She was the President of the Medical Women Association of Nigeria, Osun State Chapter from 2005 to 2008 and member of the National HIV taskforce. She is currently the President of the Nigerian Society of Paediatric Infectious Diseases, Co-Chair of the National Child Health Technical Working Committee and Board member of the StopTB Nigeria. She is also a member of various international committees including the UNICEF Expert Advisory Group (Survive, Thrive and Transform: Inpatient Care for Every Small and Sick Newborn), World Health Organization (WHO) convened Staged KMC Working Group, WHO Expert Committee on Postnatal Care (2012), WHO Guideline Development Committee on skin and oral infections in HIV- infected children and adults (2013) and Breastfeeding Counselling (2017) She is a recipient of several grants and a Principal Investigator of several studies including the WHO multi-country African Neonatal Sepsis Trial (AFRINEST), WHO Antenatal Corticosteroid for the improvement of outcome in preterm (ACTIONS Trials) ,WHO Immediate Kangaroo Mother Care and IKMC Neurodevelopmental follow up studies and Growth Failure in the Under 6 months. She is a member of the Data Safety Management Board of the study on "Evaluation of a heterologous, two-dose preventive Ebola vaccine for effectiveness and safety in the Democratic Republic of the Congo (DRC-EB-001), and DSMB Chairperson of NACOVID Clinical Trial involving the use of Nitazoxanide plus Atazanavir / Ritonavir for the treatment of COVID-19. She is also a recipient of the prestigious Washington DC-based International Women Leadership Forum Fellowship. Her research interests include newborn disorders and infectious diseases especially neonatal sepsis and Paediatric HIV. She is widely published. She has served as member of several journals including the Nigerian Journal of Paediatrics and Ife Journal of Science and Technology.

Elizabeth Prentice completed her studies in Clinical Microbiology at WITS University in 2011. She worked in the TB National Priority Programme and as a technical advisor at the National Department of Health in the Communicable Disease Directorate. For the past 4 years she has been working as a medical microbiologist at the NHLS Microbiology Laboratory at Groote Schuur Hospital, prior to which she worked at Ampath National Reference Laboratory in Pretoria. Her main interests are communicable disease control and antibiotic resistance.

INTRODUCTION OF PEER REVIEW

In accordance with a decision taken at the 2nd Editorial board meeting, peer review of submitted papers is being progressively introduced. As of this edition, all commentaries, reviews, research papers, case reports and medical images have been subjected to peer review. A peer review policy is under development.

SUMMARY OF AfSPID 2ND ANNUAL GENERAL MEETING

The 2nd annual general meeting of AfSPID was conducted via MS Teams on 25 August 2021 at 14h00 South African Standard Time.

Attendees: The meeting was chaired by Mark Cotton (MC) (AfSPID president) and attended by 30 members.

Meeting summary

1. **Welcome - MC (president)**

- Mark Cotton (MC) welcomed everyone to the 2nd AGM and gave everyone an opportunity to introduce attendees briefly.
- MC gave an overview of the establishment and history of the society in 2012.
  - Introduction to EXCO
  - Constitution (Elections every 4 years and hoping to achieve this from this AGM)
  - Bank Account
  - Travelled to Kenya (Kenyan Paediatric Association) to introduce the new society in 2019 (self-funded).

2. **AfSPID Bulletin – Brian Eley (BE)**

- Overview of newsletter – 13 editions to date. Aim for 3 editions per year.
- Archived on FIDSSA and WSPID websites.
- Introductions of the Editorial Board Members which is well represented throughout Africa.
- Twitter account to promote the newsletter: December 2020 – @afspid
- Structure of newsletter and future planning.
- Paula Vaz suggested herself available for Portuguese translations. Brian Eley (BE) will send invitation to join the editorial board.
- Prof Ebun Adejuyigbe volunteered to join the newsletter as a Nigerian representative and encouraged moving forward with a journal instead of a newsletter.

3. **AfSPID on Twitter – Tinsae Alemayehu (TA)**

- Account co-managers: TA (Ethiopia) and Olubukola Idoko (Gambia).
- Overview of twitter account opened December 2020 – 167 followers cross the whole world (35 countries including 14 from Africa).
- TA explained the contents, cases on account. David Moore enquired about the ethical guidelines when tweeting cases of which TA reassured that only already published cases are tweeted.

4. **WSPID Update– Mark Cotton**

- MC will step down as WSPID President in January 2022.
- BE will be next AfSPID Board representative on WSPID. Amha Mekasha will serve for another 2 years.
- BE and Helena Rabie are the AfSPID representatives on the WSPID International Scientific Committee and BE the AfSPID representative on the WSPID Education Committee – need to fill these important positions. Nominees and volunteers are needed. Nominations to be send to MC and the Exco for consideration. BE gave an overview of the functions and responsibilities of the positions. Victor Musiime (Uganda) will replace BE on the WSPID International Scientific Committee and Regina Oladokun (Nigeria) will replace BE on the WSPID Educational Committee in February 2022.
- Young WSPID - Harsha Lochan (HL) and TA are our representatives. HL gave an overview of our involvement.
- MC suggested that anyone that are young and eager should join by contacting HL or TA.

- **Blue Book 5th edition**
  - i) MC gave and overview and call for volunteers to assist with writing the new edition.
  - ii) There are 126 Chapters and inviting original authors to re-visit and inviting co-authors.
  - iii) Copies of book will be made available for distribution – more information to follow.

- **WSPID webinar programme**
  - i) Had 6 webinars to date. Can be downloaded from WSPID Education portal.
  - ii) Had a request for AfSPID webinar (Nov/Dec) – up for discussion. Need speakers, topics, etc.
  - iii) Antimicrobial resistance working group 2019 in Manilla; PIDJ Supplement – Susan Coffin, et. al.
  - iv) Mohammad Issack (Microbiologist from Mauritius) gave feedback. MC will prepare summary to send to group.

5. **New office bearers**

- MC referred to constitution which explained the nomination for new Executive members. MC suggested expansion of Exco and roles were explained. Terms are for 4 years although we have not been adhering. Anyone interested in roles outlined in constitution can submit a nominations to Natasha Pipers at samuels@sun.ac.za. Self-nominations are welcome.
- Roles available: President, 2 Vice-Presidents, Secretary, Treasurer, Representatives for West, East, North and Southern African countries.

6. **Conferences**

- 2022 virtual conference – AfSPID Session – MC will forward information slides.
- 2023 – Durban, SA

7. **Conclusion**

- MC thanked everyone for your valuable contribution and effort to AFSPID.

SUMMARY OF 2nd EDITORIAL BOARD MEETING OF THE AfSPID BULLETIN

The second meeting of the editorial board of the AfSPID Bulletin was held on 4 October 2021.

Attendees: Brian Eley (chair), Regina Oladokun, Ombeva Malande, Tinsae Alemayehu, Olukukola Idoko, Babatunde Ogunbosi, Harsha Lochan, Heloise Buys, Adegoke Falade, Mark Cotton, Victor Musiime, Charles Hammond, Charles Wiysonge, Tisungane Mvalo, Ebelechuku Ugochukwu, Anthony Enimil, Ayebo Sadoh, Lisa Frigati, Paula Vaz, Ebunoluwa Adejuyigbe & Elizabeth Prentice

Apologies: Rudzani Muloiwa, Joycelyn Dame, Norbertta Washaya, Hafsah Tootla

Meeting summary:

1. Review of response to action points arising from the 1st editorial board meeting that was held on 27 November 2020:
   a. Expansion of editorial board: Since the 1st editorial board meeting the membership has increased from 8 members including editor & deputy editor representing six countries to 26 members, including editor, deputy editor, six associate editors representing 10 African countries (this includes the 7 new members that will be formally introduced in the November/December 2021 edition of the newsletter).

b. The structure of the newsletter was revised. The following amended structure was used throughout 2021:
    i. Table of contents
    ii. Editor's note
    iii. Society news
    iv. Commentaries and reviews
    v. Research
    vi. Case reports & medical images
    vii. Publication watch
    viii. Information on the newsletter

    Furthermore, notices of forthcoming events were discontinued in the July 2021 edition. Forthcoming events will in future be published on the AfSPID twitter account.

c. Author instructions were updated in accordance with discussion at the 1st editorial board meeting. Guidance for writing case reports and medical images were included and guidance on formatting research papers updated.
d. Newsletter frequency: the frequency of 3 editions per annum was maintained throughout 2020 and 2021
e. Circulation estimation, based on a survey undertaken at the beginning of 2021, the estimated circulation of the newsletter is ± 2400.

2. Steps in launching a journal.
    a. Key steps that should be followed in launching a new journal were reviewed. The aims of this review were (1) to highlight interventions that should be adopted to strengthen our newsletter, and (2) to initiate a discussion on whether we should convert our newsletter to a journal.
    b. The discussion that followed was in favour of converting the newsletter to a journal. At least seven board members commented; all were in favour of upgrading the newsletter to a journal
    c. The editor indicated that several improvements and changes are needed before this objective can be realized. During the next 6-8 months an attempt will be made to complete/implement all or many of these changes. The first steps are to ensure that most of board members are in favour and to obtain the approval of the AfSPID EXCO.

3. Development of the newsletter during the next year
    a. Confirm that most board members are in favour of converting the newsletter to a journal
    b. Approach the AfSPID EXCO for approval to convert the newsletter to a journal
    c. Draft a mission statement; revise the aims and scope
    d. Continue expanding the editorial board, focussing (1) on African countries with limited / no representation and (2) diversifying the skill set of the editorial board
    e. Copy editing & proofreading functions: Two board members have offered to assist with these functions, Regina Oladokun and Lisa Frigati
    f. Develop a peer review procedure for the newsletter
    g. Arrange a webinar on the peer review procedure for editorial board members: a few of the senior members of the editorial board who have in depth experience of the peer review process will be approached to conduct a webinar for all board members
    h. Registration and International Standard Serial Number
    i. Additional measures:
        a. Consider what publishing licenses to offer authors
        b. Consider a plagiarism policy and practice guidelines for the newsletter
        c. Review best practice guidelines on ethical publishing and implement relevant measures
    j. Arrange discussion with online hosting companies, including AJOL and AOSIS, about hosting the newsletter/journal
    k. Aim to increase frequency to 4 editions per annum in 2023 or 2024

4. New sections
    a. There was support for starting a dedicated section on vaccinology / vaccines. Several editorial board members expressed interest in participating in this section of the journal, notably, Charles Wiysonge, Ombeva Malande, Ayebo Sadoh and Olukukola Idoko. The editor will communicate with these members regarding the appointment of associate editors for this new section of the newsletter and if necessary inviting additional academics with expertise in vaccinology to join the editorial board.
    b. There was support for the development of a section on laboratory issues. Recently, two microbiologists joined the editorial board. The editor will have a discussion with these two board members regarding co-opting additional board members with laboratory expertise to build a dedicated laboratory section. One additional microbiologist was suggested for this section.
    c. An additional proposal was for a dedicated section on antimicrobial stewardship and resistance.

5. Revised editorial board responsibilities
    a. Editorial board members
        i. Advise the editor on matters concerning the development of the newsletter
        ii. Write or commission (from one/two of their students / registrars / research associates / colleagues) a minimum of one/two article(s) per year

iii. Assist with advertising the newsletter and circulating the newsletter to colleagues & students. Keep a record of the number of individuals to whom they circulate the newsletter, for future circulation surveys
iv. Assist the editor to find new editorial board members
v. Participate in the peer review process

b. Associate editors
i. In addition to the above, take responsibility for an entire section of the newsletter

Next editorial board meeting: Annual meetings of the editorial board will continue. The date for the next annual meeting will be finalised 2-3 months before the next annual meeting.

If the AfSPID EXCO supports converting the newsletter to a journal there may be a need for several *ad hoc* meetings during the next 12 months to discuss key steps.

ACTIVITIES OF THE AfSPID TWITTER PAGE, @afspid

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The AfSPID twitter account (@afspid) that was opened by Tinsae Alemayehu and Olubukola Idoko in December 2020, is gaining in popularity.

Twitter is a microblogging site with around 330 million users all over the world. Messages are limited to 280 characters or less. Users are encouraged to keep messages or **tweets** short and simple and "to the point" because most users use Twitter for learning updates and news. Users can also send private messages with other twitter accounts. Posts or tweets are retweeted (shared by readers with their friends or **followers)** leading to messages getting further amplified and reaching thousands more people around the world (beyond your actual number of followers). It's an open and dynamic platform where one can follow anyone resulting in a high engagement rate. Twitter account names or **usernames** are preceded by @ and followed by the name chosen (e.g. @afspid). The reach of tweets is further enhanced using **a hashtag (#)**. Hashtags (such as key words at the end of research abstracts) link and group similar tweets to encourage conversations. When one types in a hashtag, one receives tweets on that topic from anywhere and by anyone thereby making the addition of hashtags to your tweets an important tool to enhance your message.

Followers of the @afspid twitter feed include paediatric ID specialists and fellows, paediatricians, paediatricians practicing other subspecialties like pulmonology or rheumatology, microbiologists, researchers of many walks of the medical field, medical students etc. Apart from individual followers, institutions for infectious diseases research and care e.g. World Society for Pediatric Infectious Diseases (WSPID), International Society of Infectious Diseases (ISID), European Society of Clinical Microbiology and Infectious Diseases (ESCMID), Latin American Society of Pediatric Infectious Diseases (SLIPE), The Australian and New Zealand Paediatric Infectious Diseases Group (ANZPID), the Australasian Society for Infectious Diseases (ASIDANZ), the Pediatric Infectious Diseases Society (PIDS), the St. George's AMR research team and PENTA Child Health Research Network, Infectious diseases and microbiology fellowship programs of Washington University and Baylor College; journals like the Transplant Infectious Diseases Journal, Pediatric Infectious Diseases Journal (PIDJ), Journal of Pediatric Infectious Diseases (JPIDS), Journal of Pediatrics; societies from non-infectious diseases disciplines like the African Society for Immunodeficiencies (ASID), the Pediatric Society of the African league against Rheumatism (PAFLAR), International Kawasaki Disease Symposium and the Pediatric Association of Gambia are some other followers of the AfSPID twitter posts.

The AfSPID twitter account is being used to increase the visibility of the AfSPID Bulletin, make announcements of meetings, webinars and promote future academic events, draw attention to case reports and medical images published in the AfSPID Bulletin (eleven cases so far), highlight recent publications relevant to paediatric infectious diseases practice and publish notices of new disease outbreaks. As of 4 November 2021, @afspid had 261 followers based in 46 countries, Figure 1.

Figure 1: Distribution of countries where followers of the @afspid twitter account are based

Twitter and other social media platforms are accessible and influential modes of communication concerning medical care, research and education. They reach a wide audience, force you to be concise, offer options for discussions and link photos, videos and references. The reader of the tweets can also have them translated into many languages. It is limited by character limits of 280 characters (if you choose not to expand your messages include links, pictures or follow-up tweets as a thread).

The AfSPID twitter account can be further enriched by diversifying posts and members from many countries. Journal clubs and other medical education platforms can be added to improve the communication experience.

COMMENTARIES & REVIEWS

UPDATE ON ACUTE BACTERIAL MENINGITIS IN CHILDREN

Margaret Hammond[1], Charles K. Hammond[2]*

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Introduction

Acute bacterial meningitis is a severe life-threatening infectious disease of the membranes lining the brain with an associated high morbidity and mortality.[1,2] It affects all age groups, causing up to 15 million infections worldwide. Young children and the elderly are the most commonly affected.[1] Globally, the epidemiology of bacterial meningitis has changed considerably over the past few decades following the introduction of conjugated vaccines against the most common etiologic agents. However, cases are still reported with the highest incidence occurring in children in sub-Saharan Africa.[3]

Traditionally, laboratory diagnosis of bacterial meningitis relies on the identification of the offending agents through examination of the cerebrospinal fluid (CSF) obtained from lumbar puncture. Recent advances in the diagnostic workup have resulted in more rapid identification of the causative bacteria.[4,5] In 2016, the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) published a comprehensive guideline on the diagnosis and treatment of community-acquired bacterial meningitis in hospitals, providing up-to-date scientific evidence for best medical practice.[6] No such comprehensive evidence-based guidelines exist for resource-limited settings. This review highlights the key points of the ESCMID guideline and discusses the challenges for diagnosis and treatment faced in resource-limited settings including sub-Saharan Africa.

Epidemiology

The causative organisms of community-acquired acute bacterial meningitis vary according to age and immune status. Most cases are caused by group B streptococcus (*Streptococcus agalactiae*), *Escherichia coli*, *Listeria monocytogenes*, *Haemophilus influenzae* type B, *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Staphylococcus aureus*.[1,3–6]

In neonates, it is typically caused by *Streptococcus agalactiae* (group B Streptococcus) and *E. coli.*[1,6] Group B Streptococcus (GBS) colonizes the birth canal and infects the newborn during delivery. Recent studies have examined, with mixed outcomes, the effect of prophylactic intrapartum antibiotics and maternal vaccination on vaginal colonization by GBS and whether these interventions impact the incidence of GBS meningitis in neonates.[2]

E. coli is the next most important cause of neonatal meningitis. In various studies performed in four European countries, it accounted for 21% of cases seen.[6]

After the neonatal period, the common meningeal pathogens are *Streptococcus pneumonia*, *Neisseria meningitidis* and *Haemophilus influenzae*, accounting for more than 77% of cases.[1,3] *S. pneumoniae* remains the most common cause of community-acquired bacterial meningitis in children in developing countries despite the introduction of various polyvalent pneumococcal vaccines. Various studies have reported a decrease in the incidence of pneumococcal meningitis in children in well-resourced countries following vaccination, although not all serotypes are included in the vaccines.[1] In some resource-limited countries, pneumococcal vaccines are not fully rolled out leading to high morbidity and mortality from pneumococcal meningitis. The case fatality rate of pneumococcal meningitis is 10-20% in high-income countries and 30-40% in resource-limited countries, with a global estimate of 0.7 to 1.0 million deaths annually among children less than 5 years of age.[1,4]

Haemophilus influenzae affects children under 6 years with peak incidence between 6 to 12 months of age. Although there are several serotypes, type B accounts for >90% of *H. influenzae* meningitis.[4] Following the introduction of *H. influenzae* type B conjugate vaccines, *H. influenzae* now accounts for only 7% of cases of bacterial meningitis.[1] In the United States, H. influenzae meningitis is now seen primarily in children who are not immunized.[5]

Neisseria meningitidis often causes meningitis in epidemics. In several resource-limited countries including many parts of sub-Saharan Africa, major epidemics are caused primarily by serogroup A, although epidemics from other serogroups have been reported. The attack rates during these epidemics can approach 1% of the population.[1,4] To prevent transmission from a patient to close contacts, chemoprophylaxis with ciprofloxacin, ceftriaxone or rifampicin is recommended.[4,6] Meningococcal polysaccharide vaccines to specific populations are recommended for prevention of outbreaks. The introduction of a serogroup A meningococcal conjugate vaccine in the African meningitis belt has been a remarkable success. The rollout started in Burkina Faso which saw a drastic reduction in the incidence of serogroup A meningitis cases and a fall in carriage of serogroup A from 0.39% to 0%. In Chad, a similar reduction in carriage was seen from 0.75% to 0.02%, conferring an important additional benefit of herd immunity.[7] Currently, many African countries working together with the WHO, have introduced the meningococcal A conjugate vaccine into childhood immunization programmes as part of the WHO global road map to defeat meningitis by 2030.[8]

Listeria monocytogenes causes about 9% of acute bacterial meningitis worldwide, with highest incidence in infants, the elderly and the immunosuppressed such as individuals with malignancies or post-transplantation. Outbreaks can develop from eating salami, raw vegetables, seafoods, unpasteurized milk or homemade goat cheese. The mortality rate is up to 30% but may be elevated in patients with pre-existing comorbidities.[4]

Staphylococcus aureus is a major cause of hospital-acquired meningitis, accounting for about 5% of cases in children with a mortality rate of about 30%. *S. aureus* meningitis occurs due to post-operative complication or via hematogenous spread in hospitalized children.[4] Methicillin-resistant strains are increasingly becoming important in hospital-acquired *S. aureus* meningitis.[9]

Risk factors

Maternal risk factors for acute bacterial meningitis in neonates include chorioamnionitis, endometritis, group B Streptococcal colonization, and prolonged duration of intrauterine monitoring exceeding 12 hours. Host risk factors in neonate and infants include prematurity, low birth weight, traumatic delivery, fetal hypoxia, urinary tract abnormalities, dermal sinus tract of the spine, galactosaemia, Down syndrome and congenital heart diseases.[4]

In older children, the risk factors for acute bacterial meningitis include poor socio-economic background, malnutrition, day care attendance, asplenia, primary immunodeficiency, HIV infection, sickle cell anaemia, recent or current respiratory tract infection, recent exposure to a case of meningococcal or *Haemophilus influenzae* meningitis, CSF leakage, intracranial shunts, penetrating head trauma, dermal sinus of the spine, cochlear implants and lack of immunization.[4]

The risk for invasive infections, including meningitis is increased in immunocompromised states such as HIV infection, diabetes mellitus, asplenia, cancer and immunosuppressive therapy. HIV-infected children have a higher risk of invasive pneumococcal infections. Highly active anti-retroviral therapy (HAART) reduces this risk but leaves it still higher than for children without HIV infection. The most common pathogen in immunocompromised children is *S. pneumoniae*, but other pathogens such *as L. monocytogenes, E. coli, Salmonella* species and *S. aureus* are also frequently encountered.[1]

The most common risk factor for recurrent bacterial meningitis in children is congenital anatomical defects. Other risk factors include head trauma, CSF leakage, and immunodeficiencies resulting from HIV infection, asplenism and complement component deficiencies.[1]

Clinical features

The symptoms and signs of bacterial meningitis in children depend on the age of the child, the duration of illness and the immune status of the host.[5] In neonates and infants, the classical features may be subtle and non-specific, and may include temperature instability (hypothermia or fever), lethargy, sleepiness, jitteriness, irritability, poor feeding, vomiting, diarrhoea, respiratory distress, bulging fontanelles, hypotonia, seizures and impaired consciousness. Older children may report headaches, neck pain, photophobia, nausea, back pain and confusion in addition to fever, vomiting, irritability, seizures and altered mental status.[4–6]

Classical signs of meningeal irritation seen in bacterial meningitis include neck stiffness, Kernig's sign and Brudzinski's sign. Focal neurological findings and signs of raised intracranial pressure may also be elicited. However, these signs may be absent in younger children and the immunocompromised. Cushing's triad, comprising systemic hypertension, bradycardia and respiratory depression, is often a late sign.[5] It is important to note than there is no clinical sign of bacterial meningitis that is present in all patients.[6]

Diagnostic workup

Examination and culture of the cerebrospinal fluid (CSF) obtained from lumbar puncture (LP) is the key to the diagnosis of bacterial meningitis. LP is quite invasive and should be performed only after carefully ruling out contraindications such as cardiopulmonary instability, bleeding tendencies, localized infection of the skin of the lower back, ongoing seizures, and signs of raised intracranial pressure. In well-resourced centres, a CT scan of the brain is done to evaluate the possibility of increased intracranial pressure before performing a LP.[4–6] In centres where CT scans are not available, clinical characteristics can be used to identify patients with increased intracranial pressure and thus increased risk of brain herniation.[6]

The following CSF parameters should be determined for patients with acute bacterial meningitis:

- CSF opening pressure: this is usually increased to 200-500 mmH_20 in older children. In infants and younger children, the opening pressure may be lower.
- CSF appearance: this is usually cloudy but may be clear.
- CSF leukocyte (WBC) count: this is typically elevated to 1000-3000/mm^3. However, in the immunosuppressed child, the WBC count may be lower. Also, in neonatal meningitis, the CSF leukocyte count is frequently normal or slightly elevated.[6]
- WBC differential: predominantly neutrophils (polymorphonuclear leukocytes).
- CSF glucose concentration: this is usually reduced to <40mg/dL. It is best to compare the CSF glucose to the serum level at the time of the LP. The normal CSF glucose is about two-thirds the serum level.
- CSF protein concentration: usually elevated above the upper limit of 0.4 g/L.
- CSF lactate: this is usually raised in bacterial meningitis. Studies have shown that CSF lactate has a better diagnostic accuracy than leukocyte count. It is however less specific as it cannot differentiate bacterial meningitis from other CNS diseases such as encephalitis and seizures.[6]
- Gram stain: a positive Gram stain depends on the concentration of bacteria in the CSF. The average positivity rate is >75%. Cytospin centrifugation increases the chances of detecting organisms in Gram-stained CSF.[5]
- Culture and antibiotic sensitivity: this also depends on the concentration of bacteria in the CSF and whether the patient has previously received antibiotics. In such children, an increased WBC count and protein concentration are sufficient to establish the diagnosis.[4,5]

Other alternative diagnostic tests include latex agglutination which detects bacterial antigens in the CSF. Newer techniques such as multiplex polymerase chain reaction (PCR) on the CSF are now widely used in well-resourced countries to provide a faster and more accurate diagnosis of bacterial meningitis.[4–6]

Serum inflammatory markers may help differentiate between bacterial and viral meningitis. In children with meningitis, elevated C-reactive protein and pro-calcitonin are associated with bacterial infections.[6] However, in situations where there is coexisting pneumonia or sepsis, these inflammatory markers have little value for the diagnosis of bacterial meningitis.[1,6]

Blood cultures may detect the causative organism if CSF cultures are negative or not available. Blood culture positivity rate is different for each causative organism. It is reported to be about 75% for pneumococcal meningitis, 50-90% for *H. influenzae* meningitis and 40-60% for meningococcal meningitis.[1] The yield of blood cultures decreases if the patient is pre-treated with antibiotics.[1,6] The ESCMID guideline recommends performing blood cultures in patients with suspected bacterial meningitis before the first dose of antibiotics are administered.[6]

Neuroimaging may be helpful in identifying complications such as cerebral infarcts, subdural empyema, intracranial abscess, and hydrocephalus. Where resource availability permits, it is also recommended to perform cranial imaging before an LP in patients with focal neurologic deficit,

severely altered mental status (Glasgow coma score <10), new-onset seizures, or severely immunocompromised state. In patients lacking these characteristics, cranial imaging before an LP is not recommended.[6]

Antimicrobial treatment

Performing a LP to obtain CSF for diagnostic work-up should not delay the start of antibiotics. It is strongly recommended to start antibiotics as soon as possible in patients with acute bacterial meningitis.[10] The ESCMID guideline recommends that time from clinical suspicion to antibiotics administration should not exceed 1 hour. Whenever the LP is delayed, empirical treatment should be started on clinical suspicion, even if the diagnosis has not been established.[6]

Empirical treatment in neonates should include a penicillin plus cefotaxime or an aminoglycoside. In older children, the ESCMID recommends cefotaxime or ceftriaxone plus vancomycin or rifampicin.[6]

The specific antibiotic treatment in bacterial meningitis is based on antimicrobial susceptibility testing. After identification of the pathogen through culture and antibiotic sensitivity testing, the antibiotic treatment can be optimized. The duration of antibiotic treatment depends on the culture isolate. *For S. pneumoniae*, the treatment is typically for 10-14 days. For meningococcal meningitis, the patient should be treated with antibiotics for 7 days. Where *L. monocytogenes* is isolated, the treatment should be for at least 21 days. Patients with *H. influenzae* meningitis should receive 7-10 days treatment with antibiotics.[1] In neonates with group B *Streptococcus* meningitis, it is recommended to treat for 14-21 days, while those with Gram negative isolates should be treated for a minimum of 21 days.[11]

For *S. aureus* meningitis, the optimal duration of treatment varies and should be based on the simultaneous treatment of both the CNS and the primary infection such as endocarditis, skin and soft tissue infection, and epidural abscess, as well as removal of infected shunts and intracranial devices. Where an infected shunt is removed, placement of a new shunt should be followed by continuation of antibiotic therapy for at least 14 days.[9]

The recommended treatment for patients in whom no pathogen can be detected should be according to the empiric regimen for a minimum duration of 2 weeks.[6] Table 1 below summarizes the common antibiotic treatment and duration for various CSF isolates.

Table 1: Specific antibiotic therapy for bacterial meningitis based on bacterial isolate from the CSF[9–11]

CSF isolate	Standard therapy	Minimum duration of treatment
Streptococcus pneumoniae	Penicillin G or ampicillin 3rd generation cephalosporin (cefotaxime or ceftriaxone) Vancomycin (plus 3rd generation cephalosporin)	10-14 days
Haemophilus influenzae	Ampicillin 3rd generation cephalosporin Meropenem (plus 3rd generation cephalosporin)	7-10 days
Neisseria meningitidis	Penicillin G or ampicillin 3rd generation cephalosporin	7 days
Listeria monocytogenes	Ampicillin or penicillin G	21 days
Streptococcus agalactiae	Ampicillin or penicillin G (aminoglycoside or cefotaxime may be added)	14-21 days
Gram negative organisms in neonates	Aminoglycoside (ampicillin, cefotaxime or ceftazidime may be added)	21 days
Staphylococcus aureus Methicillin sensitive Methicillin resistant	 Naficillin or oxacillin or cloxacillin Vancomycin (trimethoprim/sulfamethoxazole or rifampicin may be added)	Varies (based on successful treatment of primary source or removal of intracranial implant)
No pathogen isolated	Empirical treatment	2 weeks minimum

Adjunctive treatment

The outcome of bacterial meningitis is related to the severity of inflammation in the subarachnoid space. Thus, immunomodulation of the inflammatory response with corticosteroids influences the neurologic outcome in survivors such as hearing loss, aphasia, ataxia, paresis and cognitive impairment, especially in those in whom the causative agent is either *S. pneumoniae* or *H. influenzae*.[4] Dexamethasone is the most widely used corticosteroid in children with bacterial meningitis beyond the neonatal age group. It is recommended that the treatment with dexamethasone should be started with the first dose of antibiotics or within 4 hours of starting antibiotics. Expert opinion suggests that dexamethasone should be stopped if the patient is discovered not to have bacterial meningitis or if the causative organism is found to be a species other than *S. pneumoniae* or *H. influenzae,* although some experts advise that adjunctive corticosteroid should be continued irrespective of the causative bacterium.[4,6]

Other adjunctive treatments with proven benefits in bacterial meningitis include acetaminophen and antiepileptic treatment. Acetaminophen has been considered to improve the inflammatory response and decrease fever. However, in a randomized control trial in Malawian children, no beneficial effect was observed.[12] Antiepileptic treatment should be used in children with prolonged or recurrent seizures.

The use of osmotic agents such as glycerol, mannitol and hypertonic saline in children with bacterial meningitis remains controversial with some authors suggesting no potential beneficial effect.[6]

Nursing management consists of effective delivery of antibiotic therapy, fluid management and supportive care.[13]

Prophylaxis

There is a very high risk of meningococcal disease in individual who are close contacts of persons with meningococcal meningitis. This risk may be averted by taking prophylactic antibiotics. The ESCMID guideline strongly recommends that close contacts of patients with

meningococcal meningitis receive prophylactic antibiotics consisting of either ceftriaxone, ciprofloxacin or rifampicin.[6] Close contacts are defined as household contacts, child care centre contacts and anyone directly exposed to oral secretions of the patient.

Vaccination

Many cases and deaths from bacterial meningitis can be prevented through vaccination. In the past 20 years, there has been significant progress in reducing the incidence of meningitis globally. Although the burden of bacterial meningitis is greatest in the meningitis belt of sub-Saharan Africa, it remains a threat in all countries worldwide. The WHO recommended vaccination programmes against some of the bacterial agents are yet to be introduced in many countries. In 2017, stakeholders from governments, health organizations, academia and civil society called for a global vision action to "defeat meningitis by 2030". The WHO is coordinating this action and has developed a roadmap to that effect. This initiative seeks, among other goals, to make vaccines more widely available.[8]

The goals of the WHO Defeating Meningitis by 2030 roadmap are

1. To eliminate bacterial meningitis epidemics
2. To reduce cases of vaccine-preventable bacterial meningitis by 50% and deaths by 70%, and
3. To reduce disability and improve quality of life after meningitis due to any cause.[8]

To achieve these goals, there are enhanced efforts to encourage all recommended immunizations and promote high levels of vaccine coverage for bacterial meningitis at national levels. Conjugate vaccines have been introduced into childhood immunization programmes of many low- and middle-income countries and have dramatically reduced the burden of meningitis caused by *N. meningitidis*, *S. pneumoniae* and *H. influenzae* type b, but their global uptake needs to be enhanced.[7,8]

Complications

Common complications of acute bacterial meningitis in neonates include sepsis, seizures, and hydrocephalus. Patients with sepsis should be evaluated for other foci of infections such as pneumonia and endocarditis and treated according to guidelines for the management of sepsis.

Seizures may be clinical or subclinical. If not clinically evident, EEG should be done to detect subclinical seizures and antiepileptic treatment provided accordingly. Neonates with meningitis should have transcranial ultrasound or cranial MRI to rule out hydrocephalus. If detected, external ventricular drain or shunt can be placed.[6]

Older children and adults with bacterial meningitis may also suffer seizures and hydrocephalus. In addition, other common complications are stroke (both ischaemic and haemorrhagic), subdural empyema, abscess, sinus thrombosis and hearing loss. Neuroimaging can help to identify ischaemic infarcts, bleeds, empyema, abscess, or sinus thrombosis. Patients with haemorrhagic stroke, empyema or abscess are managed surgically. All children with bacterial meningitis should have hearing assessment to evaluate for hearing loss. Hearing loss needs to be detected early during the disease course in order to ensure appropriate referral and early treatment.[6]

After recovery, children may suffer neuropsychologic sequelae. such as poor cognitive abilities and school failures. Such children will benefit from neuropsychology evaluation and appropriate rehabilitation.[6]

Conclusion

Acute bacterial meningitis is a serious neurologic illness with significant morbidity and mortality if not treated promptly and adequately. The etiologic agents vary with different age groups and are influenced by host risk factors and immune status. The classical presentations in patients with bacterial meningitis are fever, neck stiffness, headache, and altered mental status. However, in neonates and young children, the presentation may be subtle requiring a high index of suspicion. CSF microscopy, chemistry, Gram stain and culture remains the best approach to confirming the diagnosis, though new technologies are being deployed in well-resourced centres. When bacterial meningitis is suspected, antibiotic treatment should be started as soon as possible for better outcomes. The use of adjuvant corticosteroids has been shown to be helpful in specific clinical situations.

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IMPACT OF COVID-19 IN PREGNANT AND LACTATING WOMEN AND THE IMPLICATIONS FOR THEIR OFFSPRING

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Introduction

The coronavirus disease 2019 outbreak is the first pandemic of the century, which has led to major impacts on health systems, society mobility and the economy. In December 2020 the Centers for Diseases Control and Prevention (CDC) included pregnancy as one of the high-risk medical conditions in phase 1c of their COVID-19 vaccine allocations, along with cancer, chronic kidney disease, diabetes, chronic obstructive pulmonary disease, heart disease, immunosuppression, and obesity. Increasing numbers of pregnant women with COVID-19 are being reported globally, with more than 73,600 infections and 80 maternal deaths in the United States alone as of 1 March 2021.[1] Pregnant women and their neonates are considered vulnerable populations for COVID-19 infection, with significantly greater morbidity and mortality risks.[2] Although pregnant women do not seem to contract this infection more frequently than the general population, they are at risk factor for severe COVID-19 disease. Data from large studies have demonstrated that approximately 8–11% of pregnant women with COVID-19 require hospitalization and between 2–4% require admission to an intensive care unit.[3]

Mother to child transmission

Less than 2% of neonates born to SARS-CoV-2-infected women test SARS-CoV-2 positive within 24 hours of birth. Postnatal transmission appears to be responsible for most of the SARS-CoV-2 infections documented in neonates. Mother-to-foetus (in utero or transplacental) transmission is a rare event.[4] Routes and mechanisms of transmission that have been reported are:

1) *In utero* transmission: possible, but rare and more likely to occur with severe maternal disease. The angiotensin converting enzyme type 2 receptors required for SARS-CoV-2 cellular entry have been identified on placental cells. These receptors are also found in foetal lung and tissues enabling foetal infection. SARS-CoV-2 causes vascular damage and placenta findings of infected mothers show vascular malperfusion and ischemic injury.

2) Intrapartum transmission: SARS-CoV-2 is more frequently detected in faeces than vaginal swabs of infected women. Faecal contamination of the vaginal canal during labour can cause transmission during vaginal birth.

3) Post-natal transmission: is responsible for the majority of neonatal infections through exposure to an infected mother or caregiver. SARS-CoV2 has not been detected in breast milk. Thus, breastfeeding should be promoted as studies have found that SARS-CoV-2 IgG, IgM, IgA can be detected in breast milk.[5,6]

The World Health Organization (WHO) recently convened an expert consultation at which consensus definitions were developed for (i) *in utero* transmission, (ii) *in utero* transmission with foetal demise, (iii) intrapartum transmission and (iv) early postnatal (>48 hours to 28 days) transmission. This is an important guide for neonatologists, paediatricians, and paediatric infectious diseases sub-specialists as it should assist us in investigating and classifying neonatal SARSCoV-2 infections that we encounter in clinical practice.[7]

Impact of COVID-19 on pregnancy and newborn health

The CDC, American College of Obstetricians and Gynecologists (ACOG), the Society for Maternal-Fetal Medicine (SMFM), and other women's health organizations have acknowledged and included pregnancy as a risk factor for severe COVID-19 illness.

A systematic review published in March 2021 demonstrated that SARS-CoV-2 infection in pregnant women compared to their non pregnant counterparts was associated with an increased risk of pre-eclampsia, ICU admission, ventilation, emergency c/s-and prolonged hospital stay for the mom and increased risk of preterm birth, still birth, low birth weight, NICU admission for the neonate.[8] Pregnant patients with co-morbidities such as obesity and diabetes are at increased risk of severe disease associated with perinatal morbidity and mortality compared to the general population.[9,10] Findings from a national cohort study published in England demonstrated an increased risk of adverse maternal and perinatal outcomes in women who tested positive at the time of birth and they were twice as likely to have foetal death and preterm delivery.[9]

Vaccination in pregnant and lactating women

Initial guidance from governments and professional organizations, advised against the COVID-19 vaccination for pregnant and breastfeeding woman. This, combined with the exclusion of pregnant and lactating women from clinical trials, has led to reluctance of pregnant and lactating women to take up the vaccine offer. Although this advice has been refuted , it has left its mark among these women, and has not yet been replaced by the latest recommendations. [3]The ACOG recommends that pregnant and lactating individuals have access to COVID-19 vaccines. Furthermore, prior advice circulated shortly after the start of the COVID-19 outbreak including: 1) that pregnancy should be avoided for 2–3 months after vaccination, 2) that pregnant women should not be vaccinated until the end of pregnancy, and 3) that women should avoid vaccination during lactation has been refuted by recent research findings.[11]

On the 29 January 2021 the WHO stated that there was no specific reason to believe that COVID-19 vaccines expose pregnant women to more risks than benefits.[12]

The ACOG recommended in December 2020 that 1) COVID-19 vaccination should not be withheld from pregnant women meeting criteria for vaccination, (2) pregnant women should be free to make their own decision and (3) access of pregnant women to vaccination should be facilitated by removing unnecessary barriers.[11]

The International Federation of Gynaecology and Obstetrics (FIGO) published its position in early March 2021 stating that there are no risks that outweigh the potential benefits of vaccination for pregnant women. Therefore, FIGO supports offering COVID-19 vaccination to pregnant and breastfeeding women.[3] Data collected from the VSAFE pregnancy registry from 14 December 2020 to 28 February 2021 showed similar incidences of adverse pregnancy and neonatal outcomes when compared to the pregnant population prior to COVID-19.[13]

The WHO recommends exclusive breastfeeding for the first 6 months of life, followed by continued breastfeeding with appropriate complementary foods until or beyond the age of 2 years. Breastfeeding should always be promoted and supported unless exceptional circumstances are present. Breast is best, even in the presence of maternal SARS-CoV-2 infection and the associated risk of infection to the newborn, is not a reason to discontinue breastfeeding. Recent studies have shown that SARS-CoV-2 antibodies cross into breastmilk after maternal COVID-19 vaccination with the possibility of passive immunity and protection to breastfed infants.[6]

The theoretical risks regarding the vaccination's safety does not outweigh the potential benefits of receiving the vaccine. For this reason, all the guidance currently agrees that COVID-19 vaccination is recommended for pregnant

and breastfeeding women who meet the criteria for vaccination. The ACOG recommends mRNA vaccines (manufactured by Pfizer or Moderna) for pregnant and postpartum women.[3]

Antibody transfer and neonatal protection

With many women asking whether the vaccine will protect their unborn children, recent studies have reported that the transfer of anti–SARS-CoV-2 antibodies to the foetus is significantly impaired during the third trimester, however a large cohort of patients infected between 15 and 30 weeks of gestation generated both maternal and cord blood anti–COVID-19 antibodies. These observations suggest that there is a lag in antibody transfer across the placenta in late gestation.

Furthermore, a study undertaken in Israel found that the Pfizer-BioNTech COVID-19 mRNA vaccine elicits a rapid rise in IgG titres and results in effective transfer across the placenta, exceeding the titres observed in pregnant women with third trimester SARS-CoV-2 infection.

These data support the effectiveness of COVID-19 mRNA vaccines during pregnancy.

In addition to transplacental acquired defence, specific anti-SARS-CoV-2 antibodies cross into maternal breastmilk, potentially building another line of defence for breastfed infants. Antenatal immunization therefore provides maternal and neonatal protection at highly vulnerable life stages. [2]

Conclusion

To date there is no evidence that contraindicates COVID-19 vaccination in pregnant and lactating women. While ongoing studies and trials address the knowledge gaps about COVID-19 in pregnancy and lactation, pregnant and lactating women should be encouraged and supported to protect themselves and their offspring through vaccination, as current evidence shows that the unvaccinated pregnant and lactating women remain at heightened risk of severe COVID-19 with associated maternal, foetal and neonatal risks. Clinicians need to be aware of these adverse outcomes and adopt effective strategies to reduce maternal and foetal risks.

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RUBELLA AND THE DEVASTATING EFFECTS OF CONGENITAL RUBELLA SYNDROME

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Abstract

Rubella virus is a vaccine preventable disease that is endemic in many countries worldwide. We appraised the prevalence and risk factors for rubella and considered the effects of congenital rubella syndrome (CRS) in children. A systematic review of relevant literature was carried out according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA). Articles were searched for through PubMed, Medline, EMBASE, Scopus, Google Scholar, web of Science, and Index Medicus. Rubella and CRS are endemic in African as well as the South-East Asian region. The current global vaccination coverage of rubella was estimated to be 70%. However, many countries in African and South-East Asia are yet to include rubella vaccination in their national immunization schedules. Mauritius and Seychelles are exceptions in Africa, while Sri Lanka and Maldives in the South-East Asian region have implemented this regimen. Globally, only the Americas has successfully eradicated rubella. It is still endemic in many African countries with devastating effects among infants and pregnant women. Cases are unabated and several children continue to suffer the consequences of CRS. Concerted efforts are needed to create awareness and galvanize support to control the incidence of rubella and CRS.

Keywords: Rubella virus; Congenital Rubella Syndrome; Africa.

Introduction

Rubella is derived from a Latin word meaning "little red". It is a medical condition caused by the rubella virus, a member of the genus *rubivirus*, family Togaviridae.[1] It is an enveloped virus which is spherical, 50-60nm in diameter and contains a positive single-stranded RNA genome that is 9.8kb in length. Five proteins are encoded in the viral genome which includes two non-structural proteins (p90 and p150) and three structural proteins [glycoproteins E1, E2 and the Capsid protein (C)].[2] Only one serotype of rubella is known but many genotypes circulate globally. This implies that naturally acquired infection or vaccination confers immunity against recurrent acute infections. The wild-type and vaccine strains of rubella can be distinguished immunologically using assays that measure avidity of how serum produced against one strain can react with the other strain (Neutralization assays).[3] Twelve genotypes (1B, 1C, 1D, 1E, 1F, 1G, 1H, 1I, 1J, 2A, 2B and 2C) and one provisional genotype (1A) of rubella have been identified.[4]

Rubella was first described in the mid-eighteenth century and is also known as German measles or three-day measles.[5] The first clinical description of rubella was made by German physician and chemist, Friedrich Hoffman in 1740. This was confirmed by de Bergen in 1752 and later by Orlow in 1758.[6] The fact that three Germans were involved with the description of Rubella led to the common name "German measles".[7] Congenital rubella syndrome (CRS) is a series of manifestations that occur in a developing foetus. CRS can occur in a developing foetus of a pregnant woman who has contracted rubella, usually in the first trimester.[1] In 1941, Australian ophthalmologist Norman McAlister Gregg successfully described the relationship between CRS and cataracts.[8] The major complication of rubella is the teratogenic effects when pregnant women contract the disease, especially in the early stage of gestation. The virus can be transmitted to the foetus through the placenta, and is capable of causing congenital defects, abortions, and stillbirth.[9] Despite various vaccination campaigns, rubella has been reported to cause congenital defects and is a cause of prenatal disability in resource limited countries. However, large numbers of rubella cases and CRS remain undiscovered in developing countries.[10] This study reviewed the incidence and geographical distribution, risk factors, transmission, elimination strategies and vaccination campaigns for rubella and CRS.

Transmission of rubella virus

Rubella is globally spread with humans being the only reservoir of the virus, transmitted by respiratory droplets either directly or through contact with contaminated surfaces (close contact is required).[11] The virus can be transmitted to the foetus through the placenta and is capable of causing congenital defects, abortions, and stillbirths.[9] Virus shedding by infected persons is mostly through nasal and throat secretions.[12] An infected person remains contagious for one to two weeks before the onset of rash, until about one or two weeks after the rash disappears. Congenitally infected neonates can shed the virus for many months after birth.[13]

Congenital rubella syndrome

Rubella virus causes CRS in the newborn, this is the most severe complication of rubella. CRS follows intrauterine infection by the virus and this comprises cardiac, cerebral, ophthalmic and auditory defects. CRS occurs when the virus in the pregnant woman affects the developing foetus in the first three months of pregnancy.[4] The foetal defects of CRS are teratogenic because of direct viral damage of infected cells. Regardless of the mechanism, any injury affecting the foetus during the phase of organogenesis in the first trimester results in congenital organ defects.[15] The risk of vertical transmission to the foetus, and likelihood of developing CRS is determined by the gestational age at the time of maternal infection.[16] The pathogenesis of CRS begins with maternal viraemia in which vertical transmission of the virus from mother to the foetus occurs following placental infection. All organs are infected by the virus however, the response of these organs to the virus depends on the stage of foetal maturation.[17] Chronic infection of CRS in infants can persist for months to years. Infants may shed the virus through urine, blood, eye, nasal or throat secretions, and cerebrospinal fluid thereby facilitating viral transmission to susceptible persons.[11] There are two mechanisms of viral induced foetal damage. First, cell death through mitotic disruption and apoptosis. Second, endothelial damage of small blood vessels resulting in poor organ development.[18]

If infection occurs less than 28 days before conception, the infant has a 43% chance of being affected. If the infection occurs 0–12 weeks after conception, chances increase to 51%. If infection occurs 13–26 weeks after conception, the chance is 23% of the infant being affected by the disease. However, infants are not usually affected if the virus is contracted during the third trimester, or 26–40 weeks after conception.[19] Age of pregnancy and chances of developing organ defects are summarized in the Table 1.

Table 1: Age of pregnancy and chances of organ anomalies[1]

Age of pregnancy	Chances of Organ Anomalies
1-8 weeks	Cardiac defects and hearing impairment, other CRS anomalies (80%)
9-12 weeks	Hearing impairment and features of CRS (50%)
13-16 weeks	CRS anomalies (30%), hearing loss is prominent than others
>20 weeks	Changes of foetal damage are minimal or none

In considering the outcome of CRS, focus is on period (weeks) of pregnancy when maternal exposure to rubella virus occurred. Risk is higher if exposure occurs during the first trimester, or if there is no history of maternal immunization or past infection. Also, evidence of intrauterine growth retardation during pregnancy may impact negatively on CRS.[14] A classic triad distinguishes CRS from other congenital conditions, namely (1) sensorineural deafness (58% of patients), (2) congenital heart disease especially pulmonary stenosis and patent ductus arteriosus (50% of patients) and (3) eye abnormalities especially pigmentary retinopathy, cataract and microphthalmia (43% of patients).[1] Other manifestations include spleen, liver, or bone marrow abnormalities some of which may disappear shortly after birth. In addition, intellectual disability, microcephaly, eye defects, low birth weight, and thrombocytopenic purpura can occur[19] Characteristic ''blueberry muffin spots'' (purple to dark-blue macules, papules, or nodules representing extramedullary haematopoiesis) are associated with CRS.[20]

In the laboratory, rubella can be diagnosed by virus isolation, by detection of IgG antibodies at 3, 6 and 12 months of age, by identification of rubella specific hemagglutination inhibition antibodies after 9 months of age, or by demonstration of rubella specific IgM antibodies. IgM is produced by the foetus and does not cross the placenta hence this is indicative of rubella. False negative results for IgM were found in 20% of infected infants before 1 month of age. If they have clinically consistent signs but test negative after birth, infants should be retested at 1 month. In the case of a false-positive result, this may be a result of rheumatoid factor, other viral infections such as Epstein Barr virus and parvovirus, or heterophile antibodies.[14] Complete blood count may reveal leucopenia and thrombocytopenia used to monitor the course of thrombocytopenia, Liver function tests such as total and direct bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transpeptidase (GGT) levels may reveal hepatic injury in disseminated rubella infection, especially in neonates.[21]

Distribution and spread of rubella

The burden of rubella is global and in African countries children under the age of 15 years are commonly affected. Susceptibility to rubella is known to occur in adults as well.[22] Rubella is a vaccine-preventable disease, yet still claims an estimate of 568 lives (mostly children) worldwide each day and it is a leading cause of preventable birth defects. In 2001, the CDC established the Measles and Rubella Initiative (MRI), a global partnership working towards a measles and rubella free world.[14] Since the isolation of the virus in 1962, it has become a global problem. The severity of rubella reduced markedly in 1969 after the discovery of the rubella vaccine but minor epidemics occur every 10 years while pandemics occur every 30 years.[23] During the 1962-1965 worldwide epidemic, an estimated 12.5 million rubella cases occurred in the United States, resulting in 20,000 cases of CRS.[24] A total of 100,000 cases of CRS occur yearly.[25] In the African region, it is estimated that 38,712 cases occurred in 2010, while the global estimate was 105,391, representing 36.7% of the global burden. In 2013, the incidence of CRS was estimated to be 69/100,000 live births in Democratic Republic of the Congo corresponding to 2,886 infants (95% CI 342, 6395) born with CRS per year.[26] The number of reported cases is high in countries where routine rubella immunization is unavailable or was recently introduced. In 1990, a total of 65,591 cases of rubella was reported in Mexico[27] China is the top on the list of countries with the highest rubella cases in the world.[27] As of 2020, there were 2,202 cases that accounts for 21.6% of the world's rubella cases. Among the top 5 countries are Mozambique, India, Democratic Republic of the Congo, and Nigeria which account for 65.5% (Tables. 2). According to the Uganda Demographic and Health Survey key indicators report of 2017, 25% of adolescents between 15-19 years had begun childbearing and most of them were at risk of rubella and CRS.[27] One study in Abia State, Nigeria showed an incidence of new rubella infections of 6.81/1,000,000 population in 2007 which decreased to 2.28/1,000,000 in 2009, but soared to 6.34/1,000,000 in 2011.[28]

Table 2: Countries with the highest rates of rubella from 1999-2019

Year	Nigeria	SA	DRC	China	MOZ
1999	Nil	Nil	Nil	Nil	Nil
2000	Nil	541	Nil	Nil	Nil
2001	Nil	Nil	Nil	Nil	Nil
2002	Nil	208	Nil	Nil	Nil
2003	Nil	2089	Nil	Nil	Nil
2004	Nil	612	Nil	24015	Nil
2005	Nil	428	Nil	25446	Nil
2006	Nil	Nil	207	37137	Nil
2007	466	1072	Nil	74746	Nil
2008	422	Nil	969	120354	166
2009	234	2975	110	69860	69
2010	450	Nil	130	43117	70
2011	3691	3266	318	65549	143
2012	239	2298	1860	40156	428
2013	88	103	1704	17580	127
2014	102	10	864	11793	210
2015	419	54	464	81333	Nil
2016	503	819	204	4535	Nil
2017	543	1876	Nil	1605	102
2018	4772	1213	287	3930	117
2019	1644	1370	561	32539	74

SA = South Africa; DRC = Democratic Republic of Congo; MOZ = Mozambique

Several countries in Africa have conducted rubella seroprevalence surveys. However, none has established routine surveillance for CRS despite the fact that there is paucity of data on this in the continent.[29] Serological studies done across Nigeria have shown that rubella is endemic in Nigeria.[30] Despite the devastating consequences of this condition and the high prevalence in many African countries, screening and vaccination of women and children is neither part of antenatal schedule nor among the diseases targeted for vaccination in routine immunization in many African countries.[31]

Vaccination coverage

Rubella among infants can be prevented by vaccination. In the USA, vaccination focuses on children between 12-15 months of age, and children 4-6 years old. Immunity of women childbearing age is determined and those of childbearing age are vaccinated to prevent vertical transmission.[32] Rubella vaccine is a live-attenuated, lyophilized and exists as monovalent (rubella only), bivalent (measles-rubella combination [MR]) or trivalent measles-mumps-rubella combination [MMR].[33] In the United States, the rubella vaccination programme targeted children to reduce the spread of the infection as well as to protect pregnant women. As a result, rates of CRS decreased by about half. However, disease incidence in individuals above the age of 15 years did not fall rapidly, and it became clear that much of the transmission was from adult to adult. Thus, in 1979 greater efforts were placed on vaccination of adolescent girls and adult women.[34] Emphasis was placed on CRS being the most severe complication of rubella infection, with the aim of eradicating CRS rather than eradicating rubella.[35] From 1996 to 2009, only two countries in Africa (Mauritius and Seychelles) had introduced rubella vaccine however, all countries in the Americas and European region had introduced the rubella vaccine in their national immunization schedule in 2009.[36]

The World Health Organization recommends that (1) countries considering the introduction of rubella vaccination should have achieved ≥80% coverage with the first dose of the measles vaccine, (2) MR vaccination strategy should

commence with an MR vaccination campaign targeting both sexes and a wide age range (e.g. 9 months to 15 years), (3) the vaccination campaign should be immediately followed by the introduction of either the MR or MMR vaccine into routine immunisation programme in a 2-dose schedule, and (4) the first dose of the routine immunisation schedule can be delivered at 9 or 12 months of age.[37] Of the 46 countries in the WHO African Region, 17 (37%) had estimated first-dose measles-containing vaccine coverage of 80% in 2009.[33,38] More so, 15 additional countries carried out vaccination campaigns for rubella before its introduction in the routine vaccination schedule (Botswana, Burkina Faso, Cameroon, Cape Verde, Gambia and Ghana, Kenya, Namibia, Rwanda, São Tomé and Principe, Senegal, Swaziland, Tanzania, Zambia and Zimbabwe). At the end of 2017, the vaccine was used in 162 countries with a global coverage of 52%.[39] After 13 years, there was no significant change in the number of countries administering rubella vaccine in Africa and South-East Asia hence the high incidence of rubella and CRS. In 1996, only 2 countries commenced administration of rubella vaccine in Africa, 2 in South-East Asia, 10 in the Western Pacific, 21 in the Americas, 9 in Eastern Mediterranean and 39 in Europe. In 2009, the number of countries in Africa was unchanged, with 4 countries in South-East Asia, 35 in the Americas, 15 in Eastern Mediterranean, 37 in Western Pacific and 53 in Europe.[36]

Table 3: Cases of rubella and congenital rubella syndrome (CRS) in the United States of America, 1969-2007

Year	Number of cases	Number of deaths	CRS incidence*
1969	57686	29	31
1970	56552	31	77
1971	45086	20	68
1972	25507	14	42
1973	27804	16	35
1974	11917	15	45
1975	16652	21	30
1976	12491	12	30
1977	20395	17	23
1978	18269	10	30
1979	11795	1	62
1980	3904	1	50
1981	2077	5	19
1982	2325	4	7
1983	970	3	22
1984	752	1	5
1985	630	1	0
1986	551	1	5
1987	306	0	5
1988	225	1	6
1989	396	4	3
1990	1125	8	11
1991	1401	1	47
1992	160	1	11
1993	192	0	5
1994	227	0	7
1995	128	1	6
1996	238	0	4
1997	181	0	5
1998	364	0	7
1999	267	0	9
2000	176	0	9
2001	23	2	3
2002	18	Nil	1
2003	7	Nil	1
2004	10	Nil	0
2005	11	Nil	1
2006	11	Nil	1
2007	12	Nil	0

- Per 10,000 live births

In 2015, the WHO Region of the Americas became the first in the world to be declared free of endemic transmission of rubella. This reduced the incidence of rubella and CRS in the USA is shown in Table 3. The number of countries using rubella vaccines in their national programme continues to increase. In 2018, 168 out of 194 countries had introduced rubella vaccines and global coverage was estimated at 69%. Reported rubella cases declined by 97%, from 670 894 cases in 102 countries in 2000 to 14 621 cases in 151 countries in 2018. CRS rates are highest in the WHO African and South-East Asian regions where vaccination coverage is lowest (Table 4). By the end of 2020, the rubella vaccine was introduced in 172 member states of the WHO and the global coverage was estimated at 70%.[40] Few countries in the African and South-East Asian regions currently include rubella-containing vaccination in their national immunization schedule.[41] According to WHO, the Maldives and Sri Lanka remain the only countries in the South-East Asian region to have successfully eliminated rubella.[40]

Table 4a: Twenty-year trend of the burden of rubella cases in WHO-AFRO, -PAHO and -EMRO regions, 1999-2019

Year	Africa (AFRO)	Americas (PAHO)	Eastern Mediterranean (EMRO)
1999	51	58755	5775
2000	865	39228	3122
2001	1572	24614	1328
2002	2265	14644	569
2003	4835	1203	510
2004	4452	3101	8368
2005	2868	5296	14967
2006	2457	2990	3685
2007	3993	13243	12071
2008	16297	4534	2363
2009	17422	18	2030
2010	2754	17	1398
2011	16190	8	2749
2012	10850	15	1681
2013	13739	11	3904
2014	7402	10	2945
2015	5302	5	1885
2016	4157	2	1981
2017	6166	7	931
2018	11787	2	1622
2019	6027	25	2603

Table 4b: Twenty-year trend of the number of cases of rubella cases in WHO-South-East Asia, -EURO, and -Western Pacific regions, 1999-2019

Year	South-East Asia	Europe (EURO)	Western Pacific
1999	5093	804567	875
2000	1165	621039	5475
2001	983	800469	7366
2002	1187	617860	3222
2003	1475	304390	5002
2004	1231	263964	27097
2005	9834	206359	28659
2006	4135	193923	42912
2007	14073	67927	85194
2008	7436	23912	126487
2009	17208	11623	73077
2010	15275	10551	45966
2011	9810	9677	76022

2012	6877	30579	44275
2013	10434	39391	33677
2014	9690	653	12814
2015	6515	655	9398
2016	10361	1471	5446
2017	4386	842	4061
2018	4533	800	7262
2019	4537	671	35273

Eradication of rubella

In earlier times, rubella eradication would have seemed far-fetched, but several factors have now shown that rubella can be eradicated globally. Rubella affects humans only and is transmitted by only humans therefore controlling CRS cases automatically controls the reservoirs. There are effective vaccines and accurate diagnostic tests available.[35] Vaccination plays an important role in eradication and if vaccination coverage is less than 80%, an increase in CRS is possible.[42] In 2010, the WHO Strategic Advisory Group of Experts on Immunization concluded that rubella-measles vaccination and surveillance for fever and rash was effective in the control of rubella and the prevention of CRS.[40] To monitor the effects of rubella and CRS eradication, proper surveillance of rubella and CRS is key. If surveillance for CRS is present, rubella vaccination can be administered to infants with a booster dose administered at a later stage of childhood, however, vaccination of infants without associated vaccination of adults may not likely eradicate rubella.[35] WHO defines rubella elimination as "the absence of endemic rubella transmission in a defined geographical area for ≥12 months and the absence of CRS cases associated with endemic transmission in the presence of a well-performing surveillance system".[40] The Global Measles and Rubella Strategic Plan 2012-2020 period observed a significant reduction in the measles and rubella disease burden, an increase in the introduction of a second dose of rubella vaccines, and improvements in surveillance. However, despite the significant progress made, the regional measles and rubella elimination targets for 2020 were not met and emerging challenges are cause for growing concern. One of the major goals of any eradication campaign should involve closing the immunity gap between children and adults as well as reflect the fact that all six WHO regions have established or expressed a commitment to achieving regional elimination of measles and rubella.[40]

Conclusion

Rubella is preventable but many African countries have not included the rubella vaccine in their national immunization schedules, and this has hampered eradication strategies on the continent. Countries in Africa with high burden of rubella have paucity of prevalence and incidence data of the disease. In countries that experience winter and spring, rubella occurs most commonly during such periods. It is transmitted directly by respiratory droplets or by contact with contaminated surfaces. The virus can also be transmitted to the foetus through the placenta and may cause abortions, and stillbirths. Rubella can cause CRS in the newborn, this being the most severe complication of rubella. CRS follows intrauterine infection by the virus and causes cardiac, cerebral, ophthalmic, and auditory defects. Despite an effective control measure, vaccination is not entirely accepted, or generally deployed and this is worsened by poverty and population growth. Although, it has been eradicated in the United States, most parts of the world are still grappling with this childhood disease. Therefore, concerted efforts are needed by countries worldwide to eradicate rubella.

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CASE REPORTS & MEDICAL IMAGES

A CASE OF A FOUR-YEAR-OLD WITH HELMINTHIASIS COMPLICATED BY INTESTINAL OBSTRUCTION AND ATRIAL TRIGEMINY

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Abstract

A child presented with a 4-day history of abdominal pain and distension, constipation, and bilious vomiting. The diagnosis of intestinal obstruction secondary to multiple worm boluses in the intestinal lumen was established during laparotomy. Intraoperatively, he suffered a cardiac arrest which was preceded by an episode of near-fatal arrhythmia. The arrythmia was thought to be a complication of eosinophilic myocarditis which had hitherto not been widely documented in children with heavy worm infestation. As children bear a significant burden of helminthiasis, there is a need to intensify public deworming programmes.

Background:

Ascaris Lumbricoides is a common cause of parasitic infection in humans. More than one quarter of the world's population is affected.[1] In resource-limited countries, while malaria, respiratory tract infections, measles and diarrhoea are leading causes of morbidity and mortality, helminthiasis, a significant public health challenge, contributes to the morbidity experienced by children. Intestinal helminthiasis increases the risk of malnutrition, poor growth and heavy infestation.[2] Intestinal obstruction is a known complication of helminthiasis. *A. lumbricoides* has also been reported to produce a neurotoxin that causes spasticity increasing the risk of obstruction.[3] There may also be parasite induced eosinophilia which is most common in children[1].

We describe a child with intestinal obstruction secondary to ascariasis who experienced cardiac problems possibly induced by eosinophilic myocarditis.

Case report

A 2-year-old boy presented to the children's emergency ward with a 4-day history of abdominal pain associated with constipation and bile-stained vomiting. He experienced increasing abdominal distention before presentation. The patient had passed roundworms per rectum two days before the illness began, for which the mother gave levamisole that had been purchased over the counter. The patient did not vomit worms at any time. At presentation, he was acutely ill, pale, and dehydrated. His pulse rate was 110/minute and regular. He had normal heart sounds. His abdomen was distended, a mass with an irregular surface was palpated in the suprapubic region and a digital rectal examination revealed an empty rectum. A diagnosis of mechanical intestinal obstruction secondary to possible helminthiasis was made. Plain abdominal radiographs showed dilated loops of bowel with multiple air-fluid levels. Full blood count showed a total white blood cell count of 5,290 cells/mm^3 (Neutrophils – 39%, Lymphocytes – 51% and Eosinophils - 6%. The haemoglobin concentration was 8.6g/dl, while the serum electrolytes and blood urea were within normal limits. The chest radiograph revealed no features of pneumonia or pneumonitis. Pre-operative echocardiography showed a structurally normal heart with good cardiac function. He had intravenous fluid hydration, nasogastric decompression, intravenous ceftriaxone, and metronidazole and was worked up for emergency exploratory laparotomy.

At surgery, distended loops of the small bowel and a single perforation of 1cm in diameter in the ileum located 60cm from the ileocaecal junction were present. Multiple worm boluses were present in the intestinal lumen at different segments between the duodenojejunal junction and the rectum. The bowel appeared relatively healthy-looking. The ascaris worms in the jejunum and ileum were milked distally

and evacuated through the ileal perforation, and a sigmoidostomy was made to extricate the worms in the colon. The ascaris worms are shown in Figure 1.

Figure 1: Intestinal ascaris extracted during laparotomy

The ileal perforation and sigmoid colon incision were repaired, and the wound closed in layers. Intraoperatively, the patient had an episode of cardiac arrest associated with hypotension and was successfully resuscitated. He recovered fully from the anaesthesia and was transferred to the ward. In the immediate postoperative period, his pulse rate became regularly irregular, with heart rates ranging between 70 and 100/minute over the first 48 hours after surgery. ECG revealed sinus rhythm, heart rate of 83 beats per minute with P waves of normal morphology but there was atrial trigeminy, Figure 2. The QRS axis was +70°, QRS complexes occurred in couplets. The dominant QRS wave in leads V1 and V2 was the S wave while in V5 and V6 was the R wave in keeping with LV dominance as expected for age and the T wave axis was 32° which were both normal for age. The atrial trigeminy resolved after the administration of IV Hydrocortisone. He was also treated with albendazole. He made satisfactory clinical progress, the wound healed satisfactorily, and he was discharged home six days post-surgery. At follow up, his heart rate was 120/minute with a regular rhythm.

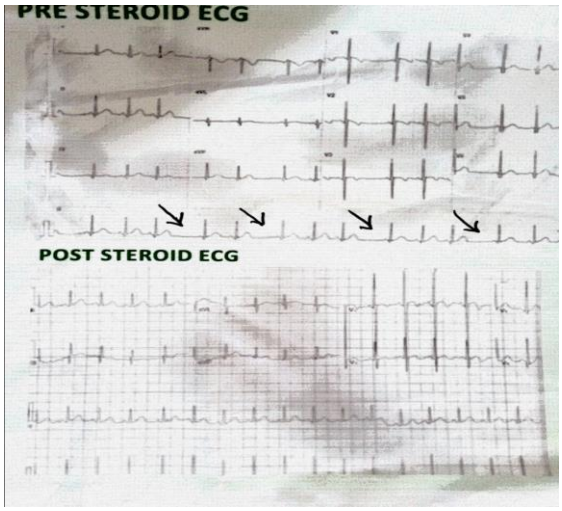

Figure 2: ECG showing atrial trigeminy (arrows)

Discussion

Intestinal obstruction caused by intestinal ascariasis is often diagnosed at laparotomy. It is recommended that in areas endemic for *A. lumbricoides*, any child manifesting acute abdominal symptoms consistent with intestinal obstruction or perforation should be evaluated for ascariasis.[1] Children between the ages of 3 and 5 years are more prone to obstruction because of the reduced internal diameter of their intestines and the ileocecal valve.[3] *A. lumbricoides* produces a neurotoxin that causes spasticity increasing the risk of obstruction.[3,4]

Complications of helminthiasis are not limited to intestinal obstruction. Others include eosinophilic pneumonia, anaemia, malnutrition, pancreatitis and cognitive impairment.[5] One of the rarely reported complications of helminthiasis is myocardial involvement. A few cases of myocarditis have been reported in adults.[6] The definitive diagnosis of ascariasis with myocardial involvement rests on evidence of parasite and of cardiac dysfunction. ECG findings may be non-specific with negative T-waves.[7] Myocarditis has rarely been reported in children. Possible causes of arrhythmia in this child include cardiac hypoxia occurring during the cardiac arrest, electrolyte derangement and myocarditis secondary to eosinophilia. In this report, the possibility of the arrythmia being due to eosinophilic myocarditis is reviewed. Serum sodium, potassium, calcium, and glucose values were within normal limits.

Though, myocarditis in patients with ascariasis is usually associated with hypereosinophilia, it may be absent in helminthic infections that are well contained within the tissues or are solely intraluminal within the intestinal tract.[8] Mild eosinophilia in this child who had solely intraluminal ascariasis may therefore not be an abnormal finding. There have also been similar reports in adults in whom eosinophilia was absent.[6,9] In the report by Sugiyama *et al*, eosinophilic myocarditis was supported by a myocardial biopsy.

With regards to prevention of the infestation, in areas of high prevalence, school deworming programmes may be beneficial in the short term but because of reinfection, which is inevitable in such settings, improved sanitation and sustained economic growth are most effective for parasite control in the long-term.[1] It is to be noted that most mass treatment strategies target school-aged children, though pre-school aged children have a similar infestation rate and burden compared to school-aged children.[10]

There is a need to intensify public deworming exercises in children since they bear a significant burden of helminthiasis. This case report highlights the need to broaden the deworming strategy to include preschool aged children as they are also prone to developing complications from heavy helminthic infestation.

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PUBLICATION WATCH

EFFICACY OF WOLBACHIA-INFECTED MOSQUITO DEPLOYMENTS FOR THE CONTROL OF DENGUE

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Dengue is a major public health challenge throughout tropical and sub-tropical regions. According to recent estimates close to 400 million dengue infections occur annually; 96 million of these infections manifest clinically. Furthermore, 0.5 million dengue infections require hospitalisation and dengue causes 20,000 deaths every year. Vaccine development has thus far only been partially successful.[1]

Various vector control methods have been developed to reduce the burden of mosquito-borne viral infections.[2] One such method is *Wolbachia* transmission disruption, aimed at controlling *Aedes aegypti* mosquito transmission of arboviruses to humans.[2-4] *Wolbachia,* obligate intracellular bacteria, can be introduced into *Aedes aegypti* mosquitoes by stable trans-infection. Once infected, the mosquitoes are less likely to transmit arboviruses to humans because *Wolbachia* infection disrupts arboviral replication and transmission by (1) manipulating the autophagy system thus reducing the nutritional resources needed for viral growth, (2) immune-priming that allows the mosquito to defend itself against arboviruses, (3) induction of phenol oxidase production resulting in increased melanin production which has antipathogenic properties, (4) controlling arboviral infection via the microRNA (miRNA)-dependent immune pathway, and (5) reduction in the fitness of *Aedes* mosquitoes leading to a decline in the mosquito population. Because *Wolbachia* is maternally transmitted to the mosquito offspring it is maintained in the mosquito population.[3]

The publication in focus described the findings of an open-labelled, cluster-randomized trial that evaluated the efficacy of releasing *Aedes aegypti* mosquitoes infected with a specific strain of *Wolbachia pipientis* on the incidence of virologically confirmed dengue infection in Yogyakarta province, Indonesia. The trial location comprised 12 intervention clusters and 12 control clusters. Each intervention cluster received between 9 and 14 mosquito releases. The incidence of symptomatic, virologically confirmed dengue infection was significantly lower among participants who resided in the intervention clusters, representing a protective efficacy of 77.1% for hospitalisation for virologically confirmed dengue. Infection was also significantly lower in populations living in the intervention clusters and the proportion of participants with virologically confirmed dengue infection in 11 of the 12 intervention clusters was lower than among people living in the control clusters.[5]

These findings suggest that this vector control method can contribute substantially to reducing the burden of human dengue virus infection. The control method has already been implemented in some Asian countries. Similar, high quality clinical trials are needed to determine whether this control method can also be used for reducing the burden of human infections caused by other arboviruses such as zika, chikungunya and yellow fever.

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