CELEBRATES SCIENCE

APRIL 2016
Top 5 Articles

Director: Prof Shabir Madhi

Article:


Impact Factor: 21.372

Summary:

Background Maternal group B streptococcus (GBS) serotype-specific capsular antibody concentrations are correlated with susceptibility to neonatal GBS invasive disease. Maternal immunisation against GBS during pregnancy might protect infants across the period of susceptibility to invasive disease, but no licensed vaccine exists. This study assessed the safety and immunogenicity of a CRM197-conjugated trivalent GBS vaccine in non-pregnant and pregnant women, and antibody transfer to their infants.

Methods We did a phase 1b/2, randomised, observer-blind single-centre study of an investigational trivalent GBS vaccine in healthy non-pregnant women (cohort 1), and a dose-ranging study in healthy pregnant women (cohort 2). The study was done at the Chris Hani Baragwanath Academic Hospital in Soweto, South Africa. Participants were healthy non-pregnant or pregnant (28-35 weeks' gestation) women aged 18-40 years. In cohort 1, non-pregnant women were randomly assigned (2:1) to receive the investigational vaccine (two injections, 1 month apart, of a 20 μg dose [of each serotype] of aluminium hydroxide-adjuvanted investigational vaccine) or placebo. In cohort 2, pregnant women were randomly assigned (1:1:1:1) to receive one injection at 28-35 weeks' gestation of 0-5 μg, 2-5 μg, 5-0 μg, or 20 μg of the non-adjuvanted investigational vaccine (for each serotype), or placebo. All study participants and study staff not involved with vaccine preparation were masked to the randomisation group. The vaccine contained an equal dose (0-5 μg, 2-5 μg, 5-0 μg, or 20 μg) of each of three glycoconjugates (serotypes Ia, Ib and III). Reactogenicity was monitored to day 7 and unsolicited adverse events (adverse events) and infant safety were recorded throughout the study. The primary outcomes were tolerability and GBS-specific antibody response (measured as geometric mean concentrations [GMCs] in μg/mL) following the two injections for cohort 1, and selection of one vaccine dose based on analysis of serotype-specific antibody responses at delivery (+72 h) for use in subsequent studies. These outcomes were assessed in participants or infants of participants who correctly received the study vaccine with no major protocol deviations, and provided evaluable serum samples at day 1 and the scheduled timepoints throughout the study. This study is registered with ClinicalTrials.gov, NCT01193920.

Findings: Between Oct 5, 2010, and Sept 21, 2011, we screened 75 non-pregnant and 417 pregnant healthy South African women. Of these, 60 non-pregnant women were enrolled in cohort 1 (40 randomly assigned to the GBS 20 μg group and 40 randomly assigned to the placebo group) and 320 pregnant women were enrolled in cohort 2 (80 in each of the four groups). Among the randomised groups of pregnant women, 33-40% experienced at least one local and 54-71% one systemic solicited adverse event, less than 4% of which were severe, and the rate did not differ by study group. Also, 2% of the pregnancies resulted in stillbirth and 3-5% of the liveborn babies died by 12 months age, none of these deaths were attributed to vaccination. There was one death in a GBS-vaccine recipient, which too was unrelated to vaccination. For cohort 1, serotype-specific antibody concentrations were significantly higher, as evident by no overlap of the 95% CIs of GMCs against all three serotypes in the vaccinated group than the placebo group. For cohort 2, pregnant women in all vaccine groups had significantly higher GMCs than did those in the placebo group at delivery (eg, GMCs against serotype Ia were 11 μg/mL [95% CI 7-0-18] for the GBS vaccine 0-5 μg group, 18 μg/mL [11-29] for the GBS vaccine 2-5 μg group, 22 μg/mL [13-35] for the GBS vaccine 5-0 μg group, and 0-64 μg/mL [0-42-0-98] for the placebo group) and at all measured timepoints. GMCs did not differ significantly between the vaccine doses at any of the measured timepoints (p<0.05).

Interpretation: The vaccine was well tolerated and induced capsular-specific antibody responses, in non-pregnant and pregnant women. Maternal vaccination led to higher GBS serotype-specific antibody concentrations in infants than did placebo, with both interventions resulting in similar safety profiles.
Summary:

Background: Homicide of children is a global problem. The under-5-y age group is the second largest homicide age group after 15-19 y olds, but has received little research attention. Understanding age and gender patterns is important for assisting with developing prevention interventions. Here we present an age and gender analysis of homicides among children under 5 y in South Africa from a national study that included a focus on neonaticide and infanticide.

Methods and Findings: A retrospective national cross-sectional study was conducted using a random sample of 38 medico-legal laboratories operating in 2009 to identify homicides of children under 5 y. Child data were abstracted from the mortuary files and autopsy reports, and both child and perpetrator data data were collected from police interviews. We erred towards applying a conservative definition of homicide and excluded sudden infant death syndrome cases. We estimated that 454 (95% CI 366, 541) children under the age of 5 y were killed in South Africa in 2009. More than half (53.2%; 95% CI 46.7%, 59.5%) were neonates (0-28 d), and 74.4% (95% CI 69.3%, 78.9%) were infants (under 1 y), giving a neonaticide rate of 19.6 per 100,000 live births and an infanticide rate of 28.4 per 100,000 live births. The majority of the neonates died in the early neonatal period (0-6 d), and abandonment accounted for 84.9% (95% CI 81.5%, 87.8%) of all the neonates killed. Distinct age and gender patterns were found, with significantly fewer boy children killed in rural settings compared to urban settings (odds ratio 0.6; 95% CI 0.4, 0.9; p = 0.015). Abuse-related killings and evidence of sexual assault were more common among older girls than in all other age and gender groups. Mothers were identified as the perpetrators in all of the neonaticides and were the most common perpetrators overall (71.0%; 95% CI 63.9%, 77.2%). Abandoned neonates were mainly term babies, with a mean gestational age of 38 wk. We did not have information on abandonment motives for all newborns and did not know if babies were abandoned with the intention that they would die or with the hope that they would be found alive. We therefore considered all abandoned babies as homicides.

Conclusions: Homicide of children is an extreme form or consequence of violence against children. This national study provides one of the first analyses of neonaticide and infanticide by age and gender and shows the failure of reproductive and mental health and social services to identify and help vulnerable mothers. Multi-sectoral prevention strategies are needed.
Article:
DOI: 10.1038/mt.2016.43.
Impact Factor: 6.938

Summary:
Background: User-friendly, rapid, inexpensive yet accurate TB diagnostic tools are urgently needed at points of care in resource-limited settings. We investigated host biomarkers detected in serum samples obtained from adults with signs and symptoms suggestive of TB at primary healthcare clinics in five African countries (Malawi, Namibia, South Africa, The Gambia and Uganda), for the diagnosis of TB disease.

Methods: We prospectively enrolled individuals presenting with symptoms warranting investigation for pulmonary TB, prior to assessment for TB disease. We evaluated 22 host protein biomarkers in stored serum samples using a multiplex cytokine platform. Using a pre-established diagnostic algorithm comprising of laboratory, clinical and radiological findings, participants were classified as either definite TB, probable TB, questionable TB status or non-pulmonary TB.

Results: Of the 716 participants enrolled, 185 were definite and 29 were probable TB cases, 6 had questionable TB disease status, whereas 487 had no evidence of TB. A seven-marker biosignature of C reactive protein, transthyretin, IFN-γ, complement factor H, apolipoprotein-A1, inducible protein 10 and serum amyloid A identified on a training sample set (n=491), diagnosed TB disease in the test set (n=210) with sensitivity of 93.8% (95% CI 84.0% to 98.0%), specificity of 73.3% (95% CI 65.2% to 80.1%), and positive and negative predictive values of 60.6% (95% CI 50.3% to 70.1%) and 96.4% (95% CI 90.5% to 98.8%), respectively, regardless of HIV infection status or study site.

Conclusions: We have identified a seven-marker host serum protein biosignature for the diagnosis of TB disease irrespective of HIV infection status or ethnicity in Africa. These results hold promise for the development of a field-friendly point-of-care screening test for pulmonary TB.
**Article:**


**Impact Factor:** 3.892

**Summary:**

We have undertaken an in-depth transcriptome analysis of adipogenesis in human adipose-derived stromal cells (ASCs) induced to differentiate into adipocytes in vitro. Gene expression was assessed on days 1, 7, 14 and 21 post-induction and genes differentially expressed numbered 128, 218, 253 and 240 respectively. Up-regulated genes were associated with blood vessel development, leukocyte migration, as well as tumor growth, invasion and metastasis. They also shared common pathways with certain obesity-related pathophysiological conditions. Down-regulated genes were enriched for immune response processes. KLF15, LMO3, FOXO1 and ZBTB16 transcription factors were up-regulated throughout the differentiation process. CEBPA, PPARG, ZNF117, MLXIPL, MMP3 and RORB were up-regulated only on days 14 and 21, which coincide with the maturation of adipocytes and could possibly serve as candidates for controlling fat accumulation and the size of mature adipocytes. In summary, we have identified genes that were up-regulated only on days 1 and 7 or days 14 and 21 that could serve as potential early and late-stage differentiation markers.
**Article:**


**Impact Factor:** 3.231

**Summary:**

**Background:** The diagnosis of drug-resistant tuberculosis (DR-TB) in children is challenging and treatment is associated with many adverse effects.

**Objective:** We aimed to assess if careful observation, without initiation of second-line treatment, is safe in asymptomatic children referred with 'culture-confirmed' DR-TB.

**Setting:** KwaZulu-Natal, South Africa-an area with high burdens of HIV, TB and DR-TB.

**Design, Intervention and Main Outcome Measures:** We performed an outcome review of children with 'culture-confirmed' DR-TB who were not initiated on second-line TB treatment, as they were asymptomatic with normal chest radiographs on examination at our specialist referral hospital. Children were followed up every other month for the first year, with a final outcome assessment at the end of the study.

**Results:** In total, 43 asymptomatic children with normal chest radiographs were reviewed. The median length of follow-up until final evaluation was 549 days (IQR 259-722 days); most (34; 83%) children were HIV uninfected. Resistance patterns included 9 (21%) monoresistant and 34 (79%) multidrug-resistant (MDR) strains. Fifteen children (35%) had been treated with first-line TB treatment, prior to presentation at our referral hospital. At the final evaluation, 34 (80%) children were well, 7 (16%) were lost to follow-up, 1 (2%) received MDR-TB treatment and 1 (2%) died of unknown causes. The child who received MDR-TB treatment developed new symptoms at the 12-month review and responded well to second-line treatment.

**Conclusions:** Bacteriological evaluation should not be performed in the absence of any clinical indication. If drug-resistant Mycobacterium tuberculosis is detected in an asymptomatic child with a normal chest radiograph, close observation may be an appropriate strategy, especially in settings where potential laboratory error and poor record keeping are constant challenges.
1. INTRAMURAL RESEARCH UNITS

Alcohol, Tobacco and Other Drug
Impact Factor: 2.519

Impact Factor: 2.010

Biomedical Research and Innovation Platform
Impact Factor: 3.155

Biostatistics
Impact Factor: 1.169

Burden of Disease
Impact Factor: 1.500

Impact Factor: 1.500

Impact Factor: 3.579
Centre for Tuberculosis


Environment and Health


Gender and Health

   DOI: 10.1371/journal.pmed.1002003
   Impact Factor: 13.585

   DOI: 10.1177/0886260516645818
   Impact Factor: 1.579

   DOI: 10.1016/j.socscimed.2016.04.005
   Impact Factor: 2.814

Health Systems

   DOI: 10.1136/archdischild-2015-310186
   Impact Factor: 3.231

   DOI: 10.1186/s13643-016-0230-8
   Impact Factor: None

   DOI: 10.1186/s12913-016-1274-0
   Impact Factor: 1.606

   DOI: 10.2105/AJPH.2016.303107
   Impact Factor: 4.138
HIV Prevention
   DOI: 10.1155/2016/8695146
   Impact Factor: None

   DOI: 10.1371/journal.pone.0153969
   Impact Factor: 3.057

MRC Office of AIDS
   DOI: 10.1186/s12889-016-2959-3
   Impact Factor: 2.209

Non-Communicable Disease
1. NCD Risk Factor Collaboration (NCD-RisC) [Kengne AP, Schutte AE]. Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19·2 million participants. Lancet. 2016 Apr 2; 387(10026): 1377-96. [Review]
   DOI: 10.1016/S0140-6736(16)30054-X
   Impact Factor: 44.002

   DOI: 10.1016/S0140-6736(16)00618-8
   Impact Factor: 44.002

   DOI: 10.18865/ed.26.2.171
   Impact Factor: 1.014

   DOI: 10.1016/j.plefa.2016.04.003
   Impact Factor: 3.155

   DOI: 10.1038/ijo.2016.65
   Impact Factor: 5.337

Impact Factor: 2.094


Impact Factor: 2.094

South African Cochrane Centre


Impact Factor: None


Impact Factor: 1.859


Impact Factor: 7.522
2. EXTRAMURAL RESEARCH UNITS

**Antiviral Gene Therapy**

   
   **Impact Factor:** 6.938

**Anxiety and Stress Disorders**

   
   **Impact Factor:** 3.689

   
   **Impact Factor:** 2.477


   **Impact Factor:** 5.847


   **Impact Factor:** 2.010

**Child and Adolescent Lung Health**


   **Impact Factor:** 2.148

**Developmental Pathways for Health**


   **Impact Factor:** 3.057
Impact Factor: 1.859

Impact Factor: 1.733

Impact Factor: 1.676

Impact Factor: 3.614

Drug Discovery and Development
Impact Factor: 4.177

Gynaecological Cancer Research Centre
Impact Factor: 3.200

Herbal Drugs
Impact Factor: 2.465

HIV/TB Pathogenesis and Treatment
Impact Factor: 2.148
Human Genetics
   DOI: 10.1186/s40169-016-0092-7
   **Impact Factor:** None

Maternal and Infant Health Care Strategies
   DOI: 10.7196/SAMJ. 2016.v106i5.10821
   **Impact Factor:** 1.500

Respiratory and Meningeal Pathogens
   DOI: 10.1016/S2213-2600(16)30042-X
   **Impact Factor:** 15.328
   DOI: 10.1016/S1473-3099(16)00152-3
   **Impact Factor:** 21.372
   DOI: 10.1371/journal.pone.0152524
   **Impact Factor:** 3.057

Rural Public Health and Health Transition
   DOI: 10.1016/j.socscimed.2016.04.002
   **Impact Factor:** 2.814

Stem Cell Research and Therapy
   DOI: 10.1016/j.scr.2016.04.011
   **Impact Factor:** 3.892
3. **GRANT FUNDED RESEARCH**

   DOI: 10.1016/j.bmc.2016.04.021
   Impact Factor: 2.923

   DOI: 10.1186/s13008-016-0019-0
   Impact Factor: 2.278

   DOI: 10.4172/2329-8790.1000240
   Impact Factor: None

   DOI: 10.1016/j.toxrep.2016.04.004.
   Impact Factor: None

   DOI: 10.1155/2016/5342082
   Impact Factor: 1.931

   DOI: 10.1016/j.jash.2016.04.001
   Impact Factor: 2.656

   DOI: 10.1016/j.jim.2016.04.006
   Impact Factor: 1.858

   DOI: 10.1016/j.bmc.2016.04.036
   Impact Factor: 2.923
Impact Factor: 3.057

4. CLOSED RESEARCH UNITS
Health Policy
Impact Factor: 1.283

Inter-University Cape Heart
Impact Factor: 2.881
5. RESEARCH UNITS WITH NO QUALIFYING PUBLICATIONS

Intramural
- MRC Office of Cancer
- MRC Office of Malaria
- MRC Office of Tuberculosis
- Primate
- Violence, Injury and Peace

Extramural
- Bioinformatics Capacity Development
- Common Epithelial Cancer
- Diarrhoeal Pathogens
- Health Policy
- Health Services to Systems
- Hypertension and Cardiovascular Disease
- Immunology of Infectious Disease
- Medical Imaging
- Microbial Water Quality Monitoring
- Molecular Mycobacteriology
- Prospective Gastrointestinal Cancer
- Receptor Biology
## 6. GRANTS AWARDED

### SAMRC LIST OF NEW CONTRACTS FOR APRIL 2016

<table>
<thead>
<tr>
<th>MRC Unit</th>
<th>Funder</th>
<th>Project Title/Description</th>
<th>Contract Value</th>
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<tbody>
<tr>
<td>Biomedical Research and Innovation Platform</td>
<td>National Research Foundation (NRF)</td>
<td>Effects of Rooibos on Microbiota and Prevention of Diabetes</td>
<td>Rand 545 000</td>
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<td>Biomedical Research and Innovation Platform</td>
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<td>Effects of Rooibos on Microbiota and Prevention of Diabetes</td>
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<td>Biomedical Research and Innovation Platform</td>
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<td>Incentive Funding for Rated Researches</td>
<td>Rand 74 000</td>
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<td>National Research Foundation (NRF)</td>
<td>Incentive Funding for Rated Researches</td>
<td>Rand 480 000</td>
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<td>Environment and Health</td>
<td>National Research Foundation (NRF)</td>
<td>Incentive Funding for Rated Researches</td>
<td>Rand 120 000</td>
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<td>HIV Prevention</td>
<td>National Research Foundation (NRF)</td>
<td>Incentive Funding for Rated Researches</td>
<td>Rand 120 000</td>
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<td>Non-Communicable Disease</td>
<td>The Academy of Medical Science</td>
<td>Academy of Medical Sciences-Newton Advanced Fellowship for the Application entitled&quot; Non-communicable disease risk in black South Africans: dissecting the role of glucocorticoides’</td>
<td>Rand 1 996 200</td>
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<td>SHIP</td>
<td>DST</td>
<td>Capacitating the MRC TTO to improve the management and commercialisation of health related publicity funded IP</td>
<td>Rand 999 650</td>
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<tr>
<td>South African Cochrane Centre</td>
<td>NDOH</td>
<td>Hosting and management of South African National Clinical Trials Register (SANCTR) in Pan African Clinical Trials Registry (PACTR) at the MRC</td>
<td>Rand 5 764 572</td>
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