An anti-tetanus vaccine

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**Neonatal tetanus**

- Maternal and neonatal tetanus is still a substantial but preventable cause of mortality in many developing countries.

- Case fatality from these diseases remains high and treatment is limited by scarcity of resources and effective drug treatments.

- The Maternal and Neonatal Tetanus Elimination Initiative, launched by WHO and its partners, has made substantial progress in eliminating maternal and neonatal tetanus.

- Sustained emphasis on improvement of vaccination coverage, birth hygiene, and surveillance, with specific approaches in high-risk areas, has meant that the incidence of the disease continues to fall.
By August 2015, 21 countries have still not reached the MNT elimination status.

http://www.who.int/immunization/diseases/MNTE_initiative/en/
MenAfriVac as an Antitetanus Vaccine

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MenAfriVac
devolved by the Serum Institute of India, Ltd.

MenAfriVac contains 10–33 µg of TT per dose or 3–9 Lf (limit of flocculation).
Using TT as a carrier protein became an attractive option for 4 reasons:

1. Conjugate vaccines using TT as a carrier protein had been successfully developed.

2. Both neonatal and non-neonatal tetanus were public health problems in sub-Saharan Africa.

3. Conjugate vaccines that were made with TT had shown an anti-tetanus serological response when tested.

4. Meningococcal conjugate vaccines using TT as a carrier protein enhance immune response to coadministered TT conjugated vaccines such as Hib.
Anti-TT IgG response following meningococcal CRM197 or TT conjugate vaccination

MCC-CRM = Meningitec or Menjugate
MCC-TT = NeisVac-C

Co-administration of meningococcal serogroup C conjugated to TT with DTaP/IPV/Hib-TT or DTwP/Hb-TT enhances Hib IgG responses

What have we learnt with regards to tetanus serology from the clinical trials of PsA-TT

- PsA-TT-001. Phase I in India. Healthy adults aged 18–35 years.

- PsA-TT-002. Healthy toddlers aged 12–23 months.

- PsA-TT-003 and 3a. Healthy Africans aged 2–10, 11–17, and 18–29 years and Indians aged 2–10 years.
PsA-TT-001. Anti–tetanus toxoid IgG GMCs for healthy adults aged 18–35 years following either PSA-TT, meningococcal ACWY polysaccharide vaccine, or TT vaccine.

PsA-TT-002. Anti–TT IgG GMCs for healthy toddlers aged 12–23 months following PsA-TT vaccine

Sites: Mali & the Gambia

PsA-TT-003 and PsA-TT-003a. Anti–TT IgG GMCs for healthy Africans aged 2–10, 11–17, and 18–29 years and Indians aged 2–10 years following vaccination with either PsA-TT vaccine or meningococcal ACWY polysaccharide vaccine.

African sites: Mali, Senegal, and the Gambia

Surveillance data for neonatal tetanus cases in meningitis belt countries was obtained from the WHO website.

Data were prepared listing NT cases and maternal TT2+ coverage from 2009 to 2013 for 3 categories of meningitis belt countries:

- Countries that had completed countrywide PsA-TT vaccination campaigns in 1- to 29-year-olds by 2012

- Countries with either partial coverage with PsA-TT or with campaigns still proceeding.

- Countries that had not yet begun PsA-TT campaigns.

http://apps.who.int/immunization_monitoring/globalsummary/timeseries/tsincidencetetanus.html
### Annual Reported Cases of Neonatal Tetanus and TT2 Coverage From 2009 to 2013 for Countries Completing Countrywide PsA-TT Campaigns in Persons Aged 1–29 Years

<table>
<thead>
<tr>
<th>Country</th>
<th>Year of PsA-TT campaign</th>
<th>2009</th>
<th></th>
<th>2010</th>
<th></th>
<th>2011</th>
<th></th>
<th>2012</th>
<th></th>
<th>2013</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>NT cases</td>
<td>% TT2 coverage</td>
<td>NT cases</td>
<td>% TT2 coverage</td>
<td>NT cases</td>
<td>% TT2 coverage</td>
<td>NT cases</td>
<td>% TT2 coverage</td>
<td>NT cases</td>
<td>% TT2 coverage</td>
</tr>
<tr>
<td>Burkina Faso</td>
<td>2010</td>
<td>6</td>
<td>85</td>
<td>2</td>
<td>85</td>
<td>2</td>
<td>88</td>
<td>1</td>
<td>88</td>
<td>0</td>
<td>88</td>
</tr>
<tr>
<td>Mali</td>
<td>2010/11</td>
<td>13</td>
<td>92</td>
<td>7</td>
<td>85</td>
<td>11</td>
<td>89</td>
<td>10</td>
<td>89</td>
<td>12</td>
<td>85</td>
</tr>
<tr>
<td>Niger</td>
<td>2010/11</td>
<td>14</td>
<td>84</td>
<td>13</td>
<td>84</td>
<td>11</td>
<td>84</td>
<td>3</td>
<td>84</td>
<td>1</td>
<td>81</td>
</tr>
<tr>
<td>Gambia</td>
<td>2011</td>
<td>0</td>
<td>91</td>
<td>0</td>
<td>91</td>
<td>2</td>
<td>91</td>
<td>0</td>
<td>92</td>
<td>0</td>
<td>82</td>
</tr>
<tr>
<td>Chad</td>
<td>2012</td>
<td>146</td>
<td>60</td>
<td>279</td>
<td>60</td>
<td>215</td>
<td>60</td>
<td>225</td>
<td>43</td>
<td>176</td>
<td>50</td>
</tr>
<tr>
<td>Senegal</td>
<td>2012</td>
<td>16</td>
<td>88</td>
<td>12</td>
<td>88</td>
<td>21</td>
<td>88</td>
<td>14</td>
<td>91</td>
<td>4</td>
<td>91</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>195</td>
<td>313</td>
<td>260</td>
<td>88</td>
<td>253</td>
<td>91</td>
<td>193</td>
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</tbody>
</table>

Cases of neonatal tetanus in 2013 declined in 5 of the 6 countries, with Mali being the sole exception.

Average annual cases of neonatal tetanus and TT2 coverage in Meningitis Belt countries that have introduced or have yet to introduce PsA-TT

<table>
<thead>
<tr>
<th>Campaign area</th>
<th>Average Annual Cases of NT</th>
<th>% TT2 Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campaigns in part of country‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>64</td>
<td>68</td>
</tr>
<tr>
<td>Campaigns covering all country*</td>
<td>260.2</td>
<td>194.5</td>
</tr>
</tbody>
</table>

When the average annual cases of neonatal tetanus in the 5 countries were compared before and after the PsA-TT campaigns, there was a 25% reduction in NT cases. Maternal TT2 coverage was unchanged.

† Côte d’Ivoire, Ethiopia, Mauritania, Democratic Republic of Congo, Guinea, Central African Republic.

‡ Cameroon, Togo, Benin, Ghana

* Burkina Faso, Mali, Niger, Gambia, Chad, Senegal

Seroprevalence studies in sub-Saharan Africa

- Immunity to tetanus among high school adolescents girls
  - Ibadan, Nigeria
  - June to August 2012
  - pre-MenAfriVac campaign
  - Used Tetanos Quick Stick (a immunochromatographic test)
  - ≥ 0.1 IU/mL

- Immunity to tetanus by age and sex in 1 to 29 year olds
  - Bamako, Mali
  - pre and post MenAfriVac campaign
  - used standardised bead based immunoassay
  - quantified assay
Immunity against tetanus among high school adolescents girls in Ibadan, Nigeria

Trend of age-specific seroprevalence of protective immunity against tetanus

38.1% positive overall
Private school 55.3%
Significantly higher than public school 34.6%.

No significant association between socio-economic class and level of tetanus Immunity.
Anti-TT IgG levels (IU/mL) by sex and age before and after a PsA-TT mass-vaccination campaign in Mali

All age groups evidenced statistically significant changes in the percentage with TT IgG levels ≥0.1 IU/mL 2 years after PsA-TT introduction.

Despite these increases, 2 years after PsA-TT introduction, 11.6% of participants still had TT IgG <0.1 IU/mL.
NT surveillance data from meningitis belt countries are interesting but incomplete.

In countries that have mounted national campaigns, there has been a decrease in reported cases of NT by 25%.

This has not been noted in countries that have not yet mounted campaigns or in countries that had partial campaigns.

NT is an underreported disease, and caution needs to be taken in over interpreting surveillance data.

Nonetheless, the information from countries that have completed PsA-TT campaigns is encouraging and is consistent with the tetanus serological data from the PsA-TT clinical trials in Africa.

Increasing immunity to tetanus in women of reproductive age doubtlessly happened at a result of the introduction of PsA-TT, but the extent to which this has translated to decreases in NT needs to be further quantified.
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