Technical updates on Voluntary Medical Male Circumcision: device methods, tetanus-toxoid containing vaccination

Julia Samuelson, WHO Department of HIV/AIDS
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WHO Prequalification status on devices for adolescent and adult male circumcision for HIV prevention

• ShangRing: prequalified to 13 years and older
  – METHOD CHANGES pending data review: age to 10 years, topical anaesthetic cream, no flip technique, fewer device sizes.
    • Anticipated Q2 2017

• PrePex: prequalified to 13 years and older
  – NEW RISK and MANAGEMENT
    • use only with evidence of sufficient protection through vaccination or provision of doses(s) as needed.
    • tetanus --30 fold increased risk compared to conventional surgical
  – CHANGES REQUESTED: pending review, age to 10 under review
  – NEW METHOD: foreskin removal at Day 0
    • Requires series of studies and data per Framework for Clinical Evaluation

• UniCirc: no full submission on PQ
Tetanus and *Clostridium tetani*

- Causes spastic paralysis – suffering requiring intensive care
  - Often fatal in low resource setting (40-70%)
- Caused by neurotoxin produced by *Clostridium tetani*
- Spores widespread in nature: dust, soil, faeces
  - Spores can survive extreme conditions such as
    - Boiling for 10-15 minutes
    - Disinfectants such as alcohol, phenol or formalin
  - Spores killed by iodine, bleach, H$_2$O$_2$, extreme heat
- Vegetative bacteria thrive in anaerobic conditions
- Any break in the skin can serve as entry point
- Effective cheap vaccine. Not communicable so no herd immunity.
- Incubation period average ~7 days
Annual VMMCs in East and Southern Africa by method and reported tetanus cases by year (n = 16) (cases identified through VMMC programmes)

Over 12 million men reached in 14 countries

By MMC method:
• 96% -- with conventional surgical methods
• < 200,000 with PrePex

= 1 tetanus case after conventional surgery
= 1 tetanus case after elastic collar compression
### Epidemiology: Tetanus incidence and incidence rate ratio by circumcision method, 2014 – June 2016

<table>
<thead>
<tr>
<th>Countries</th>
<th>Elastic collar compression device cases/circs</th>
<th>Incidence per 100,000 (95% CI)</th>
<th>Surgery cases/circs</th>
<th>Incidence per 100,000 (95% CI)</th>
<th>Incidence rate ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kenya, Rwanda, Uganda and the United Republic of Tanzania</td>
<td>6 / 113,662</td>
<td>5.28 (1.94, 11.5)</td>
<td>6 / 3,717,338</td>
<td>0.161 (0.059, 0.351)</td>
<td>32.7 (8.74, 122)</td>
</tr>
<tr>
<td>Rwanda and Uganda only</td>
<td>6 / 110,800</td>
<td>5.45 (1.99, 11.8)</td>
<td>3 / 1,986,443</td>
<td>0.151 (0.031, 0.441)</td>
<td>35.9 (7.66, 222)</td>
</tr>
</tbody>
</table>

Countries included based on reports of Tetanus case by June 2016; Zimbabwe case not included but IRR remains similar
Biological plausibility on greater risk of tetanus with elastic collar compression method

• All cases were generalized and fit association criteria A or B
• Potential contamination before and while wearing
  – Spores widespread in environment
• Germination of spores and multiplication
  – Anaerobic environment, necrotic tissue with PrePex
    • Inherent method difference
  – Incubation 1 -112 days – all cases 9-12 days post placement
  – Presence of flagella
    • migration possible
• Toxin entry possible:
  – microabrasions, bleeding at removal, granulation tissue friable
Tetanus toxoid-containing vaccination and sero protection
Global and regional diphtheria-tetanus-pertussis 3 (DTP) immunization coverage, 1980–2013, and VMMC age cohort examples

In 2015 age 30 year: 30%

In 2015 age 20 year: 55%

In 2015 age 10 years: 60% coverage
Summary of hospital studies of non-neonatal tetanus in sub-Saharan Africa published 2003-2014

- 71% males, 32.7 years
Aristotle described tetanus.

First Tetanus toxoid vaccine in 1924.

WHO: Tetanus toxoid containing vaccination for general population in addition to maternal and infant schedules in 2006.

VMMC for men in high HIV prevalence settings in 2016.

WHO: Tetanus toxoid containing vaccination for general population in addition to maternal and infant schedules in 2006.

1-2 countries with post-infant booster dose policy.
Some key points

• Exponential expansion of medical male circumcision services to men in 5 years

• Gender differential on tetanus protection –
  • men not reached systematically with TTCV vaccination –
    policy and practice of boosters limited or lacking

• VMMC is safe with low numbers of adverse events despite large numbers of circumcisions performed in resource limited settings
  • tetanus rare after VMMC, but risk exists with wound and is preventable

• Risk differs by method so risk mitigation will differ
WHO Advice - July and September 2016

• For conventional surgical methods in which the foreskin was removed at the time of the surgery, no modification to the 2015 consultation advice on vaccination:

• Ministries of health were advised to develop and phase-in effective and practical delivery strategies for providing tetanus vaccination in the context of their programmes (VMMC and vaccination).
  • strategies depend on the country’s TTCV schedule and practices, and its tetanus burden.
  • unless an individual has documented evidence of received of a full five-dose TTCV series, it is advised that a single TTCV dose be administered before or at the time of circumcision.
WHO Advice: July and September 2016
TTCV Differential Mitigation

• Circumcision with a device method where the foreskin is left in situ and removed several days after application should be undertaken only if the client is adequately protected against tetanus by immunization with tetanus-toxoid-containing vaccine (TTCV):
  • two TTCV doses at least 4 weeks apart, with the second dose at least 2 weeks before device placement; or
  • if received three infant doses, or one dose during adolescence or adulthood, a TTCV booster at least 2 weeks before device placement (a booster at the time of placement provides only limited protection as it takes 7–14 days for antibodies to rise to protective levels); or
  • a series of five doses of TTCV.
July and September 2016 reports

• **A clean care approach** for all circumcision methods:
  • Encourage personal cleanliness, asking the client to wash his genital area, including under the foreskin, before circumcision and encouraging him to wear clean undergarments.
  • Follow standard surgical protocols on skin preparation

• **Enhance individual and community education** on clean wound care
  • clear and understandable instructions on wound care and genital hygiene
  • clean or sterile dressings to use at home
  • when to return to the health-care facility for post-procedure care
  • educate on benefits of vaccination against tetanus and educate on dangers of applying substances that may contain *Clostridium tetani* (e.g. animal dung poultices or herbal remedies).
Tetanus toxoid-containing vaccination recommendation

WER NO 6., Feb 2017, WHO SAGE recommendations and advocacy for TTCV for adolescent boys

- Inputs from VMMC and gender difference
- 6 doses – 3 primary doses plus 3 booster doses (12-23 mo, 4-7 y, 9-15 y)
- 5 doses if start any time after infancy
  - Adolescents. 9 – 15 years. Aligned with HPV.
    - Pre-adolescent and adolescent boosters are also programmatically feasible and align with the human papillomavirus immunization schedule (girls 9 – 14 years)
- Catch up boosters: military, synergies with adolescent VMMC, method specific
- Provide vaccination cards
- Preferably Td
- Cost 0.10 USD per dose
- Other prevention efforts needed:
  - community education on clean wound care
- Collaborate with MoEd

PRIMARY PREVENTION

Girls 9–13
HPV vaccination
Girls and boys, as appropriate
- Health information and warnings about tobacco use*
- Sexuality education tailored to age and culture
- Condom promotion/provision for those engaged in sexual activity
- Male circumcision

* Includes general health information and awareness about risks associated with tobacco use, including the consequences for health and well-being.
Potential issues on implementation

• Resources - Stock of vaccine available? Funding?

• Safety monitoring strengthening within national programmes -- reporting tetanus and other adverse events. Only Uganda reports non-neonatal tetanus

• Immediate and longer term method perspectives:
  – Maintain high quality essential surgical skills for other interventions
  – Will method choice make difference to accelerate for 15 – 29 yo through 2020
  – Adolescents - younger adolescents need another method as not eligible for ECC method
  – ShangRing of interest?
Thank You