pZP vaccine immunocontraception of African elephant (Loxodonta africana) cows: A review of 22 years of research

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Funding of the Veterinary Population Management Laboratory

• University of Pretoria
• HSUS and later HSI – financial support since 2003
• Technology Innovation Agency SA
Team/Collaborators

– **University of Pretoria**
  
  **Veterinary Population Management (vaccine production and research)**
  - Martin Schulman, Henk Bertschinger, Anne-Marie Human, Ofentse Mogoba
  - PhD students: C Joone, M Nolan and E Botha

  **Veterinary Tropical Diseases**
  - Jannie Crafford

– **HSI elephant contraception team**
  - Audrey Delsink, JJ van Altena, Teresa Telecky,

– **CSIR – Biosciences**
  - Michael Crampton, Maretha O’Kennedy, HC Stark, Robyn Roth, Ereck Chakauya, Tsepo Tsekoa

– **Utrecht University**
  - Tom Stout, Ben Colenbrander, Victor Rutten

• Many veterinarians for treatment of the elephants
• 34 Game Reserves
Elephant immunocontraception

- Two immuno-methods used
- Porcine zona pellucida (pZP) vaccine
  - Prepared from ovaries of slaughtered pigs
  - Final product formulated with Freund’s modified complete (primary) and Freund’s incomplete adjuvants
  - In 2003 started producing vaccine in our own laboratory
- GnRH vaccine (Improvac)
  - Used in bulls to control androgen-related aggression
  - Also works in cows
How does pZP work?

Behaviour

Oestradiol

Pheromone
• No Fertilization
• No pregnancy
• Oestrous cycle continues = 15 weeks in elephants
• But seasonal anoestrus common depending on rainfall and nutrition availability
Need for repeated treatment to boost anti-pZP antibody titres
Beginnings of elephant immunocontraception with pZP

- Study based on the work in horses by Liu, Kirkpatrick, Turner and others
- In 1995 contacted by Jay Kirkpatrick and Richard Fayrer-Hosken
  - Provide proof of concept for elephants
  - Follow up with a field trial in the Kruger National Park (KNP) 1995-1999

Proof provided in each study
Makalali Private Game Reserve
Flagship Immunocontraception project

- Makalali project initiated in 2000
- Tested
  - efficacy
  - safety
  - reversibility and
  - population effects
From 2002 to 2005 another 6 reserves joined the program

<table>
<thead>
<tr>
<th></th>
<th>Makalali&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Mabula</th>
<th>Phinda&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Shambala</th>
<th>Thornybush</th>
<th>Welgevonden</th>
<th>Kaingo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size (ha)</td>
<td>24 500</td>
<td>8 000</td>
<td>22 800</td>
<td>8 000</td>
<td>11 548</td>
<td>35 000</td>
<td>8 461</td>
</tr>
<tr>
<td>Population size (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1</td>
<td>47</td>
<td>11</td>
<td>92</td>
<td>10</td>
<td>35</td>
<td>117</td>
<td>9</td>
</tr>
<tr>
<td>Cows treated (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1</td>
<td>23</td>
<td>4</td>
<td>19</td>
<td>4</td>
<td>19</td>
<td>35</td>
<td>4</td>
</tr>
<tr>
<td>Age range of cows</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(years) Year 1</td>
<td>12-50</td>
<td>13-16</td>
<td>10-35</td>
<td>19-25</td>
<td>6-31</td>
<td>9-44</td>
<td>10-40</td>
</tr>
<tr>
<td>Cows (n) calved</td>
<td>No data</td>
<td>3</td>
<td>18</td>
<td>No data</td>
<td>11</td>
<td>25</td>
<td>No data</td>
</tr>
<tr>
<td>before treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimated mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>calving% before</td>
<td>21.7%</td>
<td>25.0%  (3)</td>
<td>21.0%  (6)</td>
<td>No data</td>
<td>16.7% (6)</td>
<td>20.6% (6)</td>
<td>No data</td>
</tr>
<tr>
<td>treatment (n years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Effects of vaccination on calving % of elephant cows in 7 game reserves

Cows normalised according to number of years in the program

<table>
<thead>
<tr>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
<th>Year 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of reserves</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Cows treated</td>
<td>108</td>
<td>108</td>
<td>108</td>
<td>107</td>
<td>98</td>
</tr>
<tr>
<td>Calves born</td>
<td>35</td>
<td>22</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Calving %</td>
<td>32.4%</td>
<td>20.4%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Side effects and safety

- Safety during pregnancy
  - 57 (52.7%) cows were pregnant at various stages during the first two years of vaccination
  - Gave birth to normal healthy calves thus demonstrating safety during pregnancy
  - 2 calves lost after birth due to injuries i.e. unrelated to contraception

- Contraceptive effect reached around time of first booster

<table>
<thead>
<tr>
<th>Trimester of gestation at time of primary vaccination</th>
<th>Number of calves</th>
<th>Conception in relation to primary vaccination</th>
<th>Number of calves</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td>18</td>
<td>Before</td>
<td>55</td>
</tr>
<tr>
<td>Second</td>
<td>20</td>
<td>Around the primary</td>
<td>1</td>
</tr>
<tr>
<td>Third</td>
<td>19</td>
<td>Primary and 1st booster</td>
<td>1</td>
</tr>
</tbody>
</table>

- Contraceptive effect reached around time of first booster
Additional game reserves join the program

• Eighteen private game reserves
• Seven provincial and one national park!

– Significant because SANARKS had initially been strongly opposed to use of immunocontraception in elephants

• Addo Elephant Park – two portions - excludes Main Camp (2013)
• Main camp to be initiated in 2020

– KZN parks
• Tembe Elephant Park (2007), Mkuze, Ithala, HiP and iSimangaliso Wetland Park (all 2015)

Today:
Total of \( \approx 1000 \) elephant cows being treated in 34 game reserves

iSimangaliso Wetland Park (all 2015)
New challenges posed by larger populations

- Populations too large for individual identification (40 – 160 cows)
- Terrain and habitat make darting of individuals more difficult
- To facilitate darting the matriarchs of individual herds are radio-collared
  - Herd numbers known - at least after the first round.
- Herd located and blanket darting applied
Use of mark and inject darts
Examples of larger populations

• Many reserves have not reached Year 3 of their respective programs
• Effect on calving rate not available yet

Three examples where results are available
• Tembe Elephant Park (2007)
  – Total population in 2007 = 200
• Addo Elephant Park (Sections 2013)
  – Total population in 2013 = 125-130
• Ithala to be presented by Pete Ruinard (2014)
Tembe calves born before and after contraception

- 2004 - 2007 10 to 14 calves annually
  - 2008 = 8 calves and 4 natural mortalities
  - 2009 = 10 calves and 2 mortalities
  - 2010 = 5 calves and 8 mortalities
  - 2011 = 3 calves and 9 mortalities
  ▶ net population increase of 3 elephants

- 2012 to 2016 3, 4, 4, 8 and 3 calves born respectively
Addo – calves born before and after (preliminary data)

• Population growth rate before start of program
  – Nyati 5% and
  – Kuzuko 2% per annum

• 2013 contraception commenced
  – ≈ 50 cows out of a total population of 125-130
  – Vaccinated three times in 2013
  – Followed by annual boosters

• 2016 zero calves born

• Benefit of 2 boosters in Year 1 vs cost
Effect of % contraception on population growth modelled by Bruce Page

- Mortality: 2.5%
- Calving interval: 4 years
- Conception rate: 1, 0.4, and 0.2
- r: 6.0, 4.0, and 2.4

Population size across years with different contraception levels.
Reversibility – cows calved

- Cows reversed
  - KNP study demonstrated short-term reversal in 3 cows treated for 1 year
  - Makalali
- **Connie** - vaccinated 2002-2005 (4 y) – calved November 2008: conceived after 19 m after last treatment
- **Smelly** - vaccinated 2000-2005 (6 y) – calved Dec/Jan 2008: conceived 18 months after last treatment
- **Toni** - vaccinated 2000-2011 (12 y) : died 2017 - **not** pregnant 60 m after last treatment but ovaries active
Reversibility – cows calved

• Larger populations – blanket treatment
  – Cows are missed (not located) during annual treatment sessions
  – Young cows start to cycle and conceive
  – Should result in a continual birth of calves

• Examples
  – Tembe

  Calves born: 3 in 2014; 5 in 2015; 8 in 2016