The future of Tropical Theileriosis control in Northern Africa

23th of April 2019, ILRI Nairobi

Presented by Mohamed Aziz DARGHOUTH (Ph.D, DVM, CES Medical Immunology)
Laboratory of Parasitology, National School of Veterinary Medicine (Sidi Thabet, Tunisia)
(darghouth@iresa.tn; mohamedaziz.darghouth@enmv.uma.tn; damaziz@yahoo.fr)
**Theileria annulata**  
Tropical Theileriosis (TT)

**Hyalomma vector ticks:**  
- *H. scupense*  
- *H. anatolicum*  
- *H. dromedarii*  
- *H. lusitanicum*
Three epidemiological patterns of transmission in North Africa

**Med-Climate:**
- *H. scupense*
- Indoors & summer disease
- Dominance of **low to moderate** infection pressures
- Potential vectors
  - *H. anatolicum*
  - *H. dromedarii*
  - *H. lusitanicum*

**Desert Climate:**
- *H. anatolicum*
- indoors/outdoors disease
- Transmission along the year
- Higher infection pressures
- Potential vectors
  - *H. dromedarii*
  - *H. scupense* (Soudan)

**Mauritania and Senegal Valley:**
- *H. dromedarii*
- indoors/outdoors disease (to confirm)
- Along the year?
Risks of emergence of new vectors under the effect of CC: example of *H. dromedarii* in Tunisia

Risks of emergence of *H. dromedarii* as a new vector

Competitive advantage to be highly adapted to aridity: extension by 2050 and adaptation to cattle? (scenario already observed in Mauritania)

*H. scupense* juveniles not adapted to dry conditions, retraction by 2050? LAST

---

H. *scupense*  
H. *dromedarii*
Risks of changing epidemiology under the effect of CC: example of *H. anatolicum*

Emergence risks for new vectors

*H. anatolicum* wild population (tick juveniles on small mammals) recorded in Morocco and Algeria (Ben Chikh Elfegoun et al., 2013, Laamri et al., 2012):

Possibility of adaptation to cattle in case of decreasing small mammals hosts populations with subsequent risks of expansion toward the East?
Importance of TT in Northern Africa

❖ **Smallholder cattle sector**
  - *low technicity and poor resources*

❖ **Financial impact**
  - *treatment cost (33 US $ /adult cow)*
  - *lethality post-treatment (10-12%)*
  - *abortion (approx. 30% pregnant cows, 70% of calf value)*
  - *long lasting milking drop (300l/30 days, Mbarek, 1994)*
  - *Effect on growth (Gharbi et al. 2006)*
  - *Carrier state on milk production and growth (Gharbi et al. 2005, 2006)*

❖ **Livelihood impact**
Control tools against TT: expectations of professionals (farmers and field veterinarians) and Society

- Easy to apply
  - Ideally one application/shot
  - Applicable on the whole herd (no restrictions of use)
- Financially affordable
- Safe to the animals
- Long lasting efficacy
- Neutral for Human and Environmental Health (EcoHealth)
- No emergence of resistance
- Efficacy perceived by farmers
### Mapping existing tools to expectations of professionals (farmers and field veterinarians) and Society

<table>
<thead>
<tr>
<th></th>
<th>Acaricides</th>
<th>Barns upgrading</th>
<th>Naphtoquinones</th>
<th>Live vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy to apply</td>
<td>+</td>
<td>+ (but once)</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Safe to cattle</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Efficacy</td>
<td>++ (if alone at best reduces risks)</td>
<td>+++</td>
<td>+</td>
<td>+++ (Med Climates) (+ Desert climates)</td>
</tr>
<tr>
<td>Duration efficacy</td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Financial affordability</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Neutral to Human &amp; Environment Health</td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Low Risks of emergence of resistance</td>
<td>+</td>
<td>+++ in Med-Climates (+ in Desert Climates)</td>
<td>++</td>
<td>+++</td>
</tr>
</tbody>
</table>

- **Competitive advantages**: Non competitive
- **Competitive in specific contexts**: Relatively competitive
- **Neutral to Human & Environment Health**: +
## Optimal attenuated vaccine features for Tunisia

<table>
<thead>
<tr>
<th>EPIDEMIOLOGICAL FEATURES</th>
<th>IMPLICATIONS FOR VACCINE ADAPTATION</th>
<th>OPTIMAL VACCINE PROFILE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Main targets: dairy purebred cows</td>
<td>High susceptibility to the parasite, lactating pregnant cows</td>
<td>Highly attenuated vaccine lines well tolerated by purebred lactating/pregnant cows: 0.2-0.26 % very mild reactions (&gt; 4000 cattle), cow vaccination till 6th month of pregnancy</td>
</tr>
<tr>
<td>2. Moderate infection pressure in the target contexts</td>
<td>Exposure of vaccinated cattle mainly to low- moderate natural challenges</td>
<td>Evidence of relative protection against lethal experimental challenge Evidence of good protection against sub-lethal moderate challenge 90% efficacy / fresh vaccine (2125 cattle)</td>
</tr>
<tr>
<td>3. Disease season: May-June to August</td>
<td>If vaccination in March April, protection cover the next TT season</td>
<td>Vaccine induced immunity should least at last 6 months Immunity till the next TT season (after 18 months): 77 to 73.5% efficacy (reduction of clinical cases)</td>
</tr>
<tr>
<td>4. Moderate to low prevalence of carrier cattle</td>
<td>No increase of carriers prevalence</td>
<td>No transmission to ticks</td>
</tr>
<tr>
<td>5. Smallholder farms &amp; widespread endemic regions</td>
<td>Small herds to vaccinate/ farm Delivery system without liquid N2</td>
<td>Packaging: 10 to 20 doses/vial Field delivery using liquid vaccine at ambient T°: viable cells up to days 6, efficacy of 82% (vaccine at day 0) &amp; 70% (vaccine at day 4)</td>
</tr>
</tbody>
</table>
New experimental control tools for the Tunisian context (Med-Climates)

- **Vaccination against H. scupense: Bm 86 ortholog “Hd 86”** (Ben said et al., 2012 and 2013; Galay et al., 2012)
  - Reduction of nymphs drop from cattle by 50%
  - No effect on adult ticks of *H. scupense* and *H. excavatum*

- **Association of live attenuated vaccines with a sporozoite of *T. annulata***
  - Significant improvement of protection with a tick stage SPAG1 against a lethal heterologous challenge (Darghouth et al., 2006)

- **Improving vaccine field delivery**
  - Development of a field delivery protocol based on liquid vaccine kept at ambient T°
Mapping new potential tools to expectations of professionals and Society

<table>
<thead>
<tr>
<th></th>
<th>MAP acaricides</th>
<th>Biological control of ticks</th>
<th>Sub-unit vaccine against disease</th>
<th>Hybrid vaccines (Cell Lines + rAg)</th>
<th>Anti-ticks and transmission blocking vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy to apply</td>
<td>+ (to improve)</td>
<td>++</td>
<td>+++++ if one shot</td>
<td>+++++ if one shot</td>
<td>+++++ if one shot</td>
</tr>
<tr>
<td>Safety to cattle</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Neutral to Human &amp; Environment Health</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Financial affordability</td>
<td>To investigate</td>
<td>To investigate</td>
<td>To investigate</td>
<td>To investigate</td>
<td>To investigate</td>
</tr>
<tr>
<td>Efficacy</td>
<td>To investigate</td>
<td>To investigate</td>
<td>+ &lt;&lt; live vaccine</td>
<td>+++++ (based on two experiments)</td>
<td>To investigate on the medium and long run</td>
</tr>
<tr>
<td>Duration efficacy</td>
<td>To investigate</td>
<td>To investigate</td>
<td>+</td>
<td>To investigate</td>
<td>To investigate</td>
</tr>
<tr>
<td>Acceptability</td>
<td>To investigate in relation to efficacy and cost</td>
<td>To investigate in relation to efficacy and cost</td>
<td>+</td>
<td>To investigate in relation to the frequency of boosts</td>
<td>To investigate if associated to anti-disease vaccines</td>
</tr>
</tbody>
</table>

Competitive advantages Additional investigations Non competitive
Perspectives

Investigate the relevance of “hybrid vaccines” against *T. annulata* (Adnen Menderes University, Free University of Berlin, Biotechnology Institute of Sidi Thabet and National Institute of Agronomy)

- Rational: efficacy of live attenuated vaccine improved when combined to SPAG and TaSP (Hussein et al. submitted).
- Select set of potentially most relevant antigens (sequences analysis)
- Analyse the putative antigenic diversity and immunogenicity of surface Ag (parasite-vectors-hosts-ecosystem)
- Select the best antigenic candidates for a hybrid vaccine experimental prototype

Improving vaccine field delivery (Looking for partners)

- Lyophilisation of eukaryotic cells?: technology watch, and economical assessment of technological components
Perspectives

**Better understanding of the vector biology** (Biotechnology Institute of Sidi Thabet and Institute Pasteur of Tunis)
- Modelling and simulating (ticks development parameters for *H. excavatum* and *H. scupense* in the lab)
- Ecological + management approaches for control: Effect the ticks physiology and reproduction and further analysis assessment by modelling (fungi, plant extracts, animal housing)

**Innovation platform using the One Health/EcoHealth approach** (component of the decennial strategic plan of the National Veterinary School)
- Advanced concept note: innovation to manage Animal health issues w/o affection Environment and Human Health
- Identification partners
- Strategy of fund raising to be developed

**Host resistance to ticks and TBD (local populations, exotic breeds)**
CONCLUSION

Valorising scientific outputs
Collective approaches with the end users
Prospecting sustainable solutions
Fostering technology and knowledge exchange and transfer
Collective Action:
Prof. M. Gharbi
Dr Moez Mhadhbi
Dr Souha Ben Abderazak
Dr Slimane Ben Miled
Dr Tarek Hajji

Thank You for your attention
Mean seasonnal dynamic of clinical cases for tropical theileriosis during 16 years in Tunisia, relationship with $T^\circ$ and hygrométrie (Fatnasy, 2008).