NATIONAL SCHOOL OF VETERINARY MEDECINE,
SIDI THABET, TUNISIA

The future of Tropical Theileriosis control in Northern Africa

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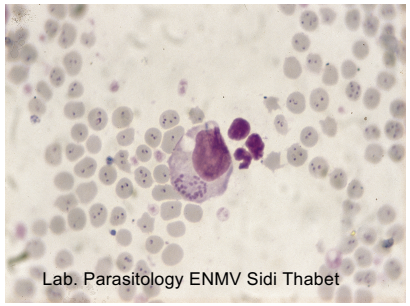
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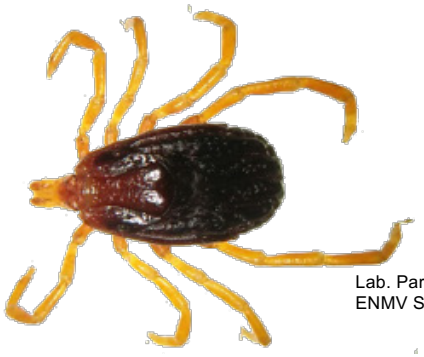
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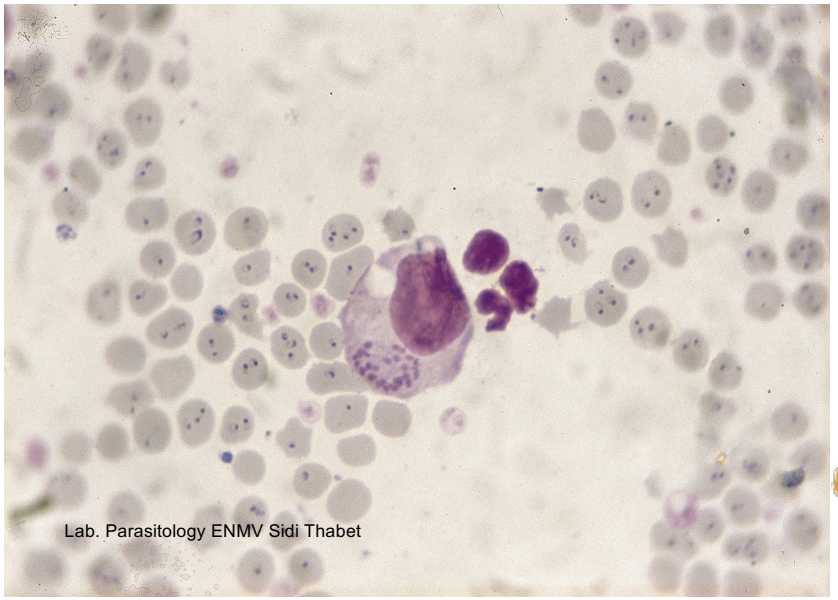


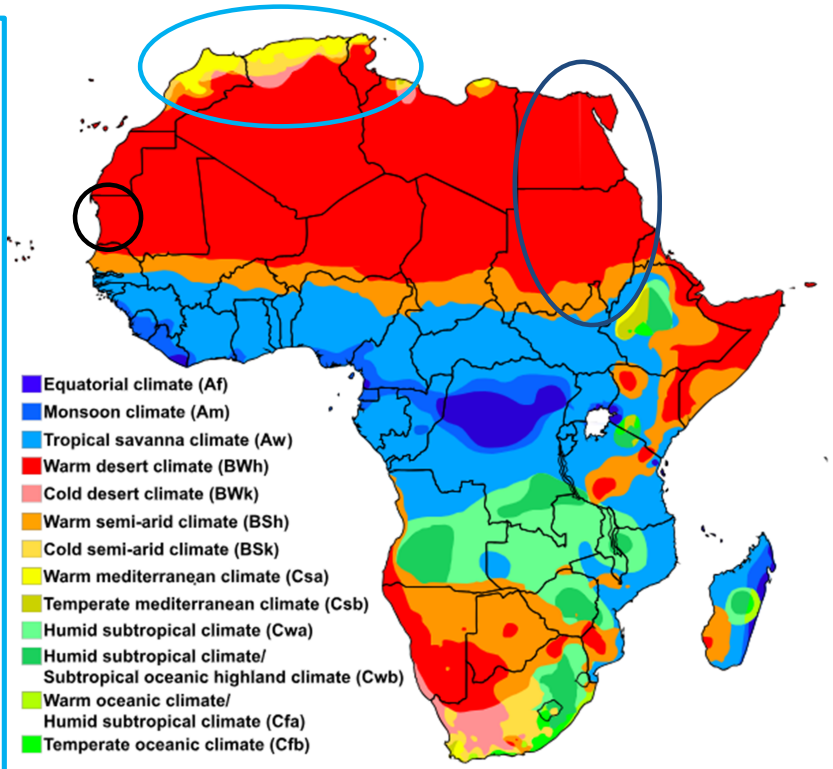
Theileria annulata
Tropical Theileriosis (TT)

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

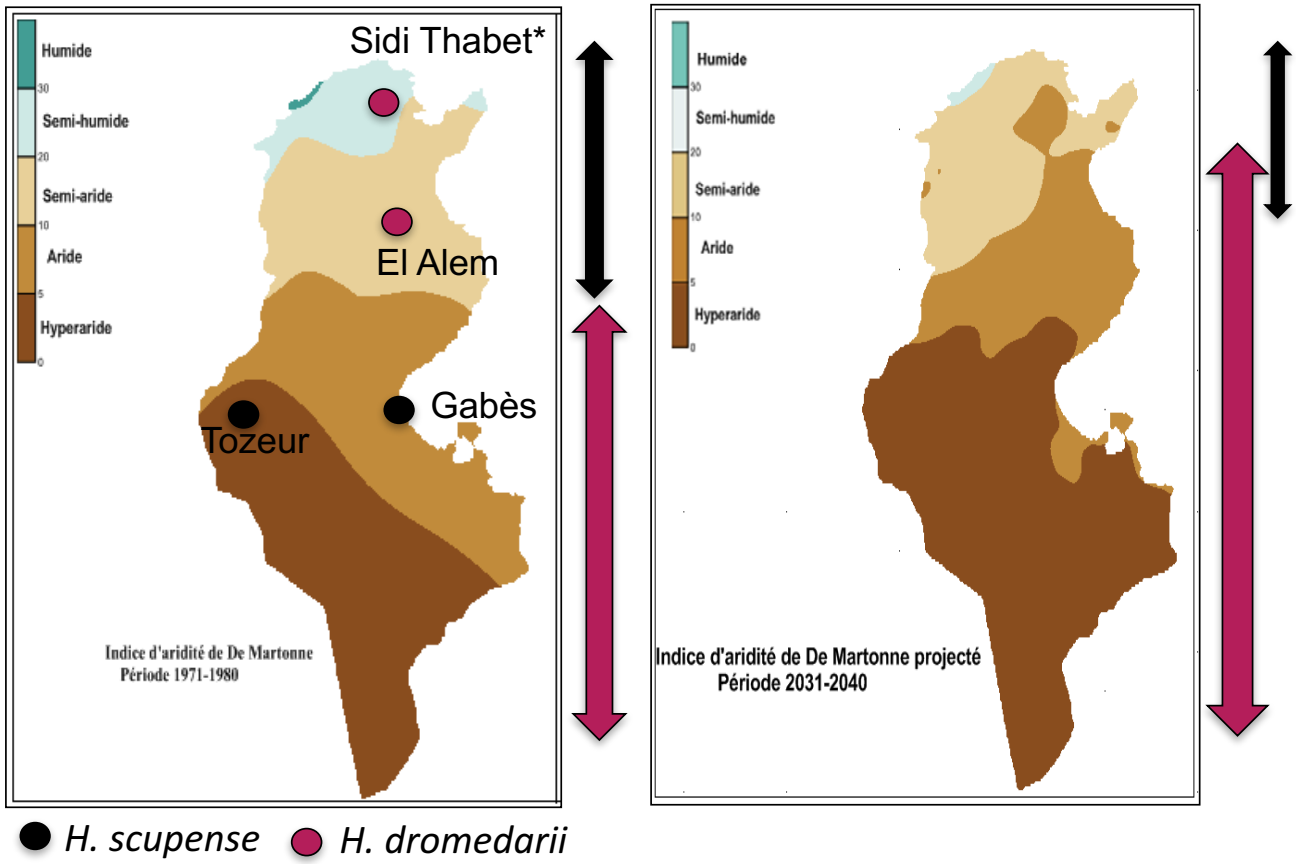


Mauritania and Senegal Valley:
- *H. dromedarii*
- indoors/outdoors disease (to confirm)
- Along the year?

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

H. dromedarii
H. scupense (Soudan)

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 higly 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**

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

	Acaricides	Barns upgrading	Naphtoquinones	Live vaccines
Easy to apply	+	+ (but once)	++++	++++
Safe to cattle	++	++++	++++	+++
Efficacy	++ (if alone at best reduces risks)	++++	+	+++ (Med Climates) (+ Desert climates)
Duration efficacy	+	++++	+	+++
Financial affordability	++	+	++	++++
Neutral to Human & Environment Health	+	++++	+	++++
Low Risks of emergence of resistance	+	+++ in Med-Climates (+ in Desert Climates)	++	+++

Competitive advantages

Competitive in specific contexts

Relatively competitive

Non competitive

Optimal attenuated vaccine features for Tunisia

EPIDEMIOLOGICAL FEATURES	IMPLICATIONS FOR VACCINE ADAPTATION	*OPTIMAL VACCINE PROFILE*
1. Main targets : dairy pure bred cows	High **susceptibility** to the parasite, lactating **pregnant cows**	*Highly attenuated vaccine lines* ***well tolerated by purebred lactating/pregnant cows:*** ***0.2-0.26 % very mild reactions (> 4000 cattle), cow vaccination till 6th month of pregnancy***
2. Moderate infection pressure in the target contexts	Exposure of vaccinated cattle mainly to **low- moderate natural challenges**	*Evidence of* ***relative protection against lethal experimental*** *challenge* *Evidence of* ***good protection against sub-lethal moderate challenge*** ***90% efficacy / fresh vaccine (2125 cattle)***
3. Disease season: May-June to August	If vaccination in March April, protection cover the **next TT season**	*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)***
4. Moderate to low prevalence of carrier cattle	No increase of carriers prevalence	***No transmission*** *to ticks*
5. Smallholder farms & widespread endemic regions	**Small herds** to vaccinate/ farm Delivery system **without liquid N2**	*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) & 70% (vaccine at day 4)***

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

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

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

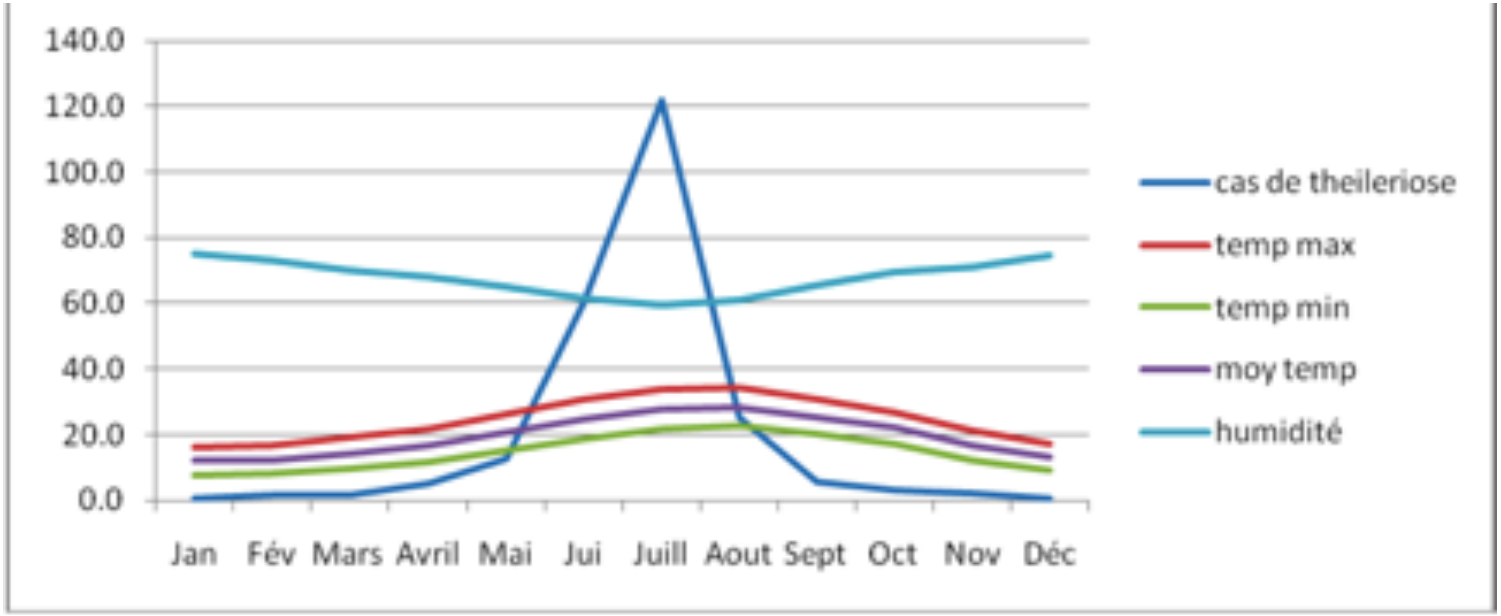
Collective approaches with the end users

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° and hygrométrie (Fatnasy, 2008).