ROSLIN

The IDEAL Project

Infectious Diseases of East African Livestock

A Tale of Two *Theilerias*

An investigation into differential clinical outcomes following *Theileria* infection

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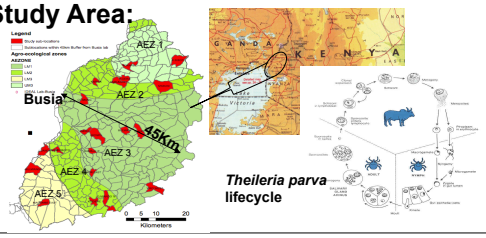
Background: 548 indigenous short horn zebu calves were recruited at birth from 20 sublocations (smallest Kenyan political land division) in Western Kenya, and followed for their first year of life. They remained in the homestead of birth, and were managed as their contemporaries, then being censored if poor health necessitated medical intervention. They received up to 11 5-weekly visits in which a detailed clinical examination was conducted and samples were collected. If death occurred a detailed post-mortem was conducted and further samples collected.

The aim of the project was to investigate the infectious disease burden and the dynamics of co-infection. This poster summarises the epidemiology of *Theileria parva* and discusses cofactors associated with death from this infection.

Research Question:

Why do calves living under apparently similar conditions have such different outcomes following infection? This study is a preliminary investigation of the complex relationship between host and *Theileria parva* as a first step to explaining why some calves prosper and some falter in this high infection pressure environment.

Study Area:



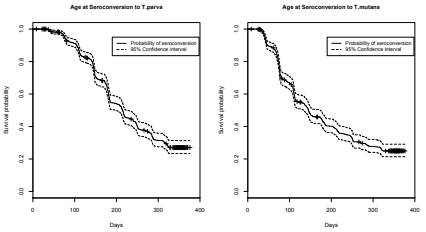
Theileria parva lifecycle

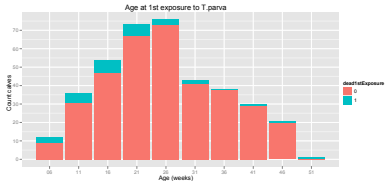
Theileria parva clinical signs:

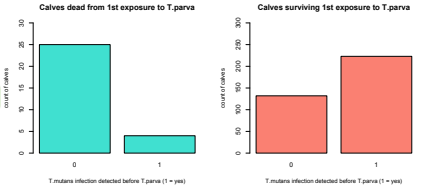
- Variable clinical outcome: subclinical to fatal infection
- Pyrexia (>40.5ºC)
- Lymph node hyperplasia
- Panleukopaenia
- Lymphoid depletion
- Immune depression
- Pulmonary oedema

Results:

Summary of *Theileria* in the cohort	
Median age at seroconversion to *T.parva* (survival plot to right)	213 days
Median age at seroconversion to *T.mutans* (survival plot to right)	170 days
Number of calves that had seroconverted to *T.parva* by their final visit or death.	361 (66%)
Number of calves that had seroconverted to *T.mutans* by their final visit or death.	381 (70%)
Overall death rate (7 non-infectious, 22 unknown suspected infectious, 58 known infectious cause)	87 (16%)
Total East Coast Fever (ECF) deaths	35 (6%)
ECF deaths on first infection with *T.parva* (no seroconversion)	29 (5% calves, 35% deaths)







Association with death following 1st *T.parva* infection:

Data set: All calves that died of first exposure to *T.parva* (29) or calves that survived to one year and seroconverted to *T.parva* (355).

UNIVARIATE ANALYSIS (Logistic regression)

	coef	se	z	p value	CI 2.5	CI 97.5	OR
(Intercept)	-1.61	0.39	-4.16	<0.001	-2.44	-0.91	0.20
Age (6-11 weeks)	REF	-	-	-	-	-	-
Age (16-21 weeks)	-0.56	0.48	-1.16	0.25	-1.50	0.43	0.57
Age (26-31 weeks)	-1.52	0.60	-2.53	0.01	-2.76	-0.36	0.22
Age (36-51 weeks)	-1.76	0.70	-2.50	0.01	-3.32	-0.46	0.17

	coef	se	z	p value	CI 2.5	CI 97.5	OR
(Intercept)	-1.66	0.22	-7.63	<0.001	-2.11	-1.25	0.19
T.mutans before *T.parva*	-2.36	0.55	-4.29	<0.001	-3.60	-1.38	0.10

MULTIVARIATE ANALYSIS (logistic regression)

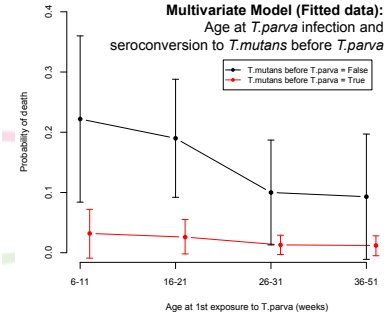
	coef	se	z	p value	CI 2.5	CI 97.5	OR
(Intercept)	-1.25	0.40	-3.13	<0.001	-2.11	-0.52	0.29
Age (6-11 weeks)	REF	-	-	-	-	-	-
Age (16-21 weeks)	-0.20	0.50	-0.39	0.70	-1.17	0.83	0.82
Age (26-31 weeks)	-0.94	0.62	-1.52	0.13	-2.22	0.25	0.39
Age (36-51 weeks)	-1.02	0.73	-1.41	0.16	-2.62	0.33	0.36
T.mutans before *T.parva*	-2.16	0.56	-3.86	<0.001	-3.42	-1.16	0.12

Controlling for age:

Case control method (conditional logistic regression): To manage the confounding between age and *Theileria mutans* seroconversion case control sets were formed from the data. ECF death cases were matched to controls that had survived to 1 year old and had seroconverted to *T.parva* 0-35 days after the death of the case (28 cases). One case died very close to one year old, and as calves required 2 consecutive high antibody titres to qualify for seroconversion there were no available survivors with a matching age.

28 acute ECF cases each with 3 controls matched by age at T.parva inf

	coef	se	z	pvalue	CI 2.5	CI 97.5	OR
T.mutans before *T.parva*	-1.52	0.67	-2.27	0.02	-2.84	-0.21	0.22



Summary:

Age at Infection: Overall, there was a highly significant decrease with age in the risk of death due to ECF on first exposure to *T. parva*. By 6-12 months of age the risk had fallen by approximately 80%. There was no significant difference in the risk between 0-3 and 3-6 month old calves, suggesting that maternal protection plays very little role in this disease.

Prior *T. mutans* exposure: Seroconversion to *T.mutans* prior to first *T.parva* infection was strongly associated with a decreased risk of death from East Coast Fever. This effect was seen both in a univariate analysis and a multivariate analysis including the age of first *T. parva* infection. However, because these 2 variables are highly correlated (*T. mutans* seroconversion being more likely in older calves) to avoid possible confounding we also matched a set of controls to the cases by age at first exposure to *T.parva*. The effect of *T.mutans* exposure remained in this analysis.

The work here suggests a possible protective effect from being infected with *T.mutans* prior to first exposure to *T.parva*. Future work will investigate this relationship further and explore possible mechanisms for the observed effect

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