Genetic Analysis of ELISA Scores for Paratuberculosis in Beef Cattle

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- Important Diseases
- Motivation
- Paratuberculosis
- UF Beef Cattle Research
- Results
- Next Steps

Important Diseases

- Foot and Mouth Disease
- Bovine leukemia
- Paratuberculosis
- Tuberculosis
- Mastitis
- Brucellosis
- Salmonellosis
- Trypanosomiasis
- Theileria
- Babesia
- Helminthosis
- Ticks

Motivation for Improving Disease Resistance

- Economic
  - Improve Productivity and Decrease Costs
- Changes in Resistance of Pathogens and Parasites
  - Bacteria Resistant to Antibiotics
  - Ticks Resistant to Acaricides
- Human Health Concerns
  - Transmission of Cattle ParaTBC to Humans

Paratuberculosis
(Johne's Disease)

- Chronic Progressive Disease of the Small Intestine of Ruminants (Cattle, Sheep, Goats)
- *Mycobacterium avium* subsp *paratuberculosis* *MAP*
- MAP may be related to Chron's Disease in Humans

Transmission

- Intrauterine infection
- Ingestion of contaminated feces on teats & hair
- Milk from infected dams

- Newborn calves are the MOST susceptible
- Susceptibility decreases with age

Subclinical Signs

Lower milk production
Lower growth
Lower feed efficiency
Higher susceptibility to other diseases

Subclinical stage can last for many years

Infected animals shed bacteria through feces

Clinical Symptoms

Frequently appear under stressful conditions

Diarrhea
Poor body condition
Lower milk production
Unresponsive to treatment
Weight loss even with normal appetite

Emaciation and Death

Economic Losses Due to Paratuberculosis

US Livestock Industry
US$1,500 million per year

Premature culling
Reduced availability of replacements
Decreased milk production
Reduced growth and feed efficiency

Increased susceptibility to other diseases
Increased veterinary costs
Loss of market value

Stages of Paratuberculosis

Stage IV
Final Phase (1)

Stage III
First Clinical Signs (2)

Stage II
Silent Carrier (3)

Stage I
Initial Infection (4)

Diagnosis

Agar Gel Immunodiffusion
(AGID; 1 day)

Enzyme-Linked Immunosorbent Assay
(ELISA; 1 day)

Fecal Culture
(12-16 weeks)

Polymerase Chain Reaction - DNA Test
(1day)

UF Beef Cattle Research

ELISA
ELISA + Fecal Culture
Most Common Diagnostic Procedures

Angus-Brahman Multibreed Herd
ELISA
Low ability to detect infected animals (50%)
High ability to detect non-infected animals (99%)

Goal and Objective

Improve effectiveness of ELISA as a tool in prevention and control programs of paratuberculosis in beef cattle

Identify and Evaluate Genetic and Environmental Factors Related to MAP ELISA Scores

ELISA S/P Ratios

Blood Sample -> Serum
IDEXX Antibody Test kit -> immunoglobulins
Spectrophotometer -> Color (Optical Density)

Optical Density (OD) is proportional to amount of antibodies in a serum sample

S = OD Sample – OD Negative Control

P = OD Positive Control – OD Negative Control

ELISA Scores

0 = s/p ratios (0.0 to 0.09) -> negative

1 = s/p ratios (0.10 to 0.24) -> suspect

2 = s/p ratios (0.25 to 0.39) -> weak positive

3 = s/p ratios (0.40 to 0.99) -> positive

4 = s/p ratios (0.99 to 10.0) -> strong positive

Data

UF Angus-Brahman Multibreed Herd
2003 to 2004
238 Cows
352 ELISA Scores (1.5 per cow)
(late May blood samples)

Cow Condition Score (late May)
Cow Days Pregnant (mid August)
Cow Days in Lactation (late May)
Cow weights (late November and late May)
Calf weights (birth and late May)

Number of Cows

	Breed Group of Sire						
BGDam	A	75 A	Br	50A	25A	B	All
A	23	3	7	6	7	5	51
75 A	5	6	7	7	8	8	41
Br	9	2	12	3	3	4	33
50A	14	4	8	5	6	8	45
25A	7	7	3	4	5	8	34
B	4	1	4	0	2	23	34
All	62	23	41	25	31	56	238

Cow ELISA Scores

	Breed Group of Sire						
BGDam	A	75 A	Br	50A	25A	B	All
A	34	5	10	7	11	7	74
75 A	8	9	11	11	12	10	61
Br	16	3	16	6	4	5	50
50A	23	7	13	9	11	13	76
25A	9	10	5	5	5	11	45
B	7	2	6	0	3	28	46
All	97	36	61	38	46	74	352

Mixed Model – Part 1

Cow ELISA Score

Year (2003, 2004)
Age of dam (3, 4, 5 and older)

Brahman breed [Regression on prob(B)]

Heterosis [Regression on prob(A/B)]

Mixed Model – Part 2

Cow weight change from November to May

Cow days in lactation until May

Cow condition score in May

Cow days pregnant in August

Calf birth weight

Calf preweaning gain until May

Mixed Model – Part 3

Cow random effect
Cows Unrelated
Mean Zero; Common Variance

Residual
Uncorrelated
Mean Zero; Common Variance

Results

Breed Group Combination Means

Estimates of Fixed Effects

Repeatability Estimate

Graphs of Mean Predicted ELISA Scores

Means Cow ELISA Scores

	Breed Group of Sire						
BGDam	A	75 A	Br	50A	25A	B	All
A	0.62	0.80	1.00	0.86	0.55	1.43	0.77
75 A	0.50	0.89	1.00	0.36	0.58	1.20	0.74
Br	0.50	1.00	1.00	0.50	0.75	0.80	0.74
50A	0.91	0.86	0.77	0.22	1.36	1.08	0.89
25A	0.67	1.00	0.86	0.80	2.40	1.82	1.29
B	0.71	3.00	1.20	-	1.00	1.29	1.24
All	0.67	1.03	0.97	0.50	1.00	1.30	0.91

Year Effects

Effect	Estimate	SE	P > |t|
Year 2003	1.86	0.66	0.006
Year 2004	1.34	0.66	0.045

Significant …
No surprise here …

Cow Age Effects

Effect	Estimate	SE	P > |t|
(3 - 5) yr old Cows	-0.13	0.14	0.338
(4 – 5) yr old Cows	0.13	0.14	0.346

Cows infected mostly later in life

Speed of progress too variable within ages

Sensitivity of ELISA too low to separate ages

Dataset too small to differentiate ages

Genetic Group Effects

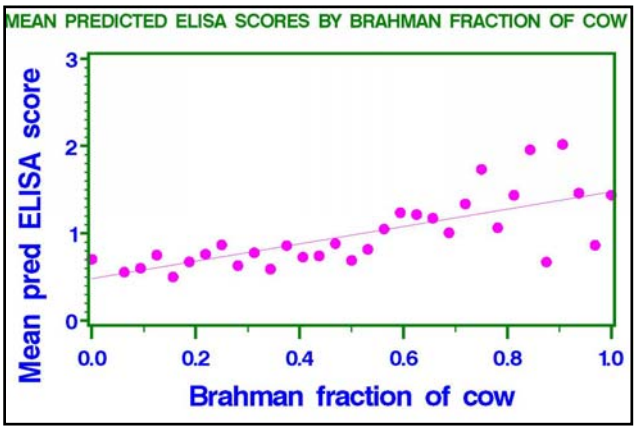
Effect	Estimate	SE	P > |t|
(B – A) Breed Cow	0.59	0.24	0.017
Maternal Heterosis	0.05	0.28	0.846

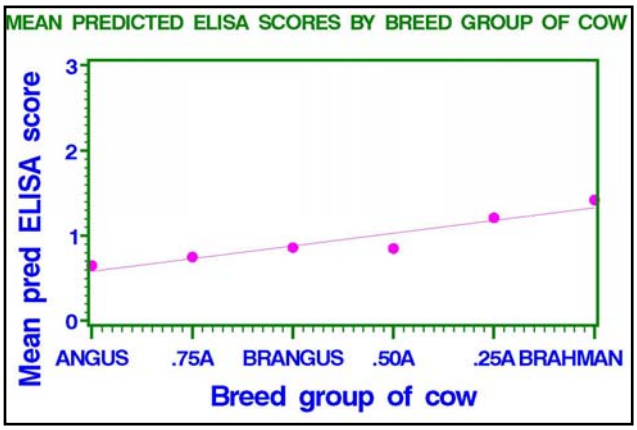
High % Brahman Cows -> more susceptible

High % Brahman Cows -> more resistant

Eating Behavior High %B ≠ Low %B Cows

Antibody Response High %B ≠ Low %B Cows



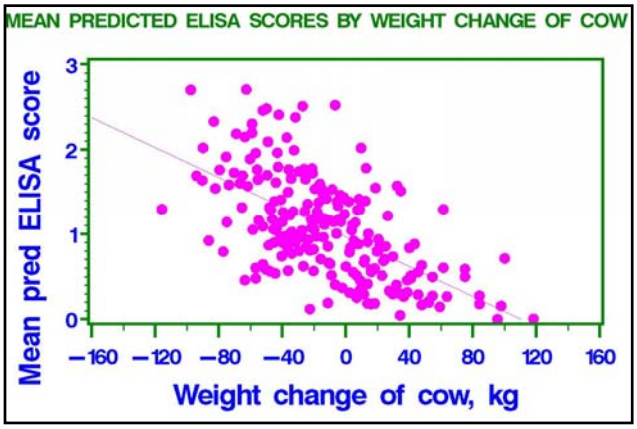


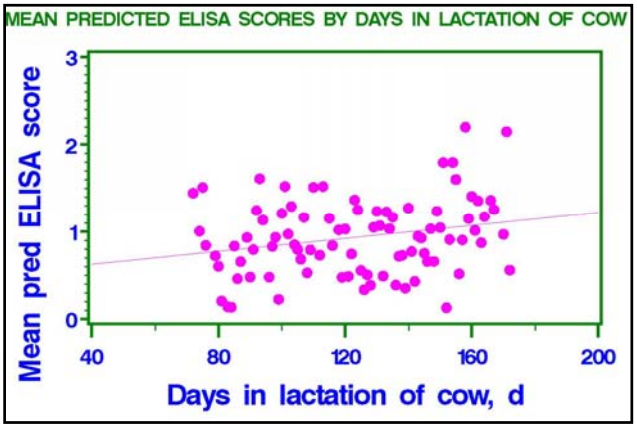
Cow Regression Effects 1

Effect	Estimate	SE	P > |t|
Cow WT Change	-0.006	0.002	0.002
Days in Lactation	0.009	0.003	0.021

Higher ELISA Scores
=> Less Gain if Positive WT Change
=> More Loss if Negative WT Change

Increased Antibody Response as Resources Allocated to Milk Production Decreased



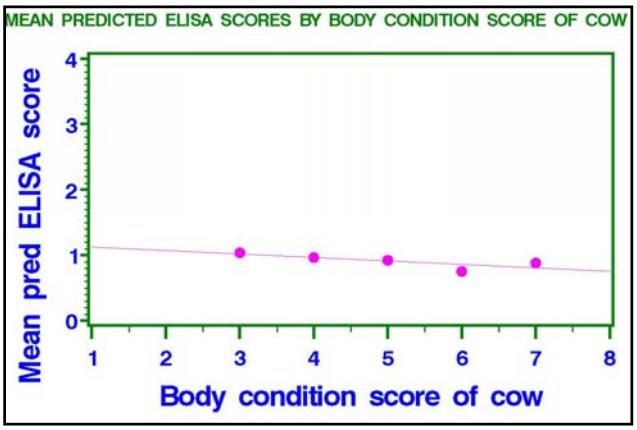


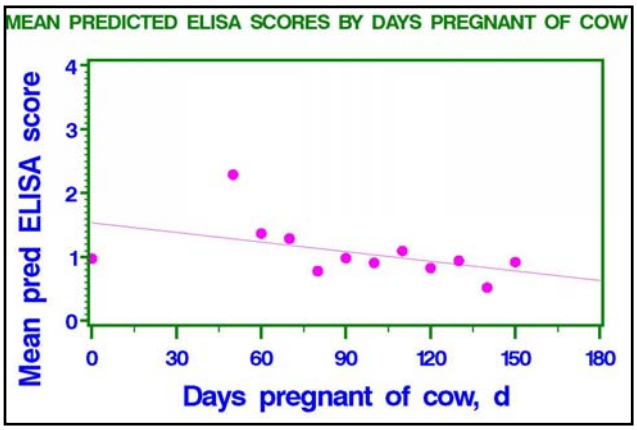
Cow Regression Effects 2

Effect	Estimate	SE	P > |t|
Condition Score	-0.049	0.077	0.522
Days Pregnant	0.000	0.001	0.982

Cond Score -> Low Sensitivity to Subclinical MAP
Small Decreasing Trend for Predicted ELISA Scores

ELISA During First Third of Pregnancy
=> Expected Small Effect on ELISA Scores
Decreasing Trend for Predicted ELISA Scores

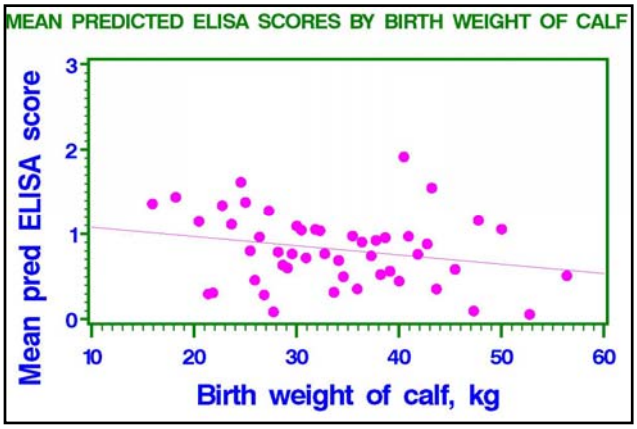


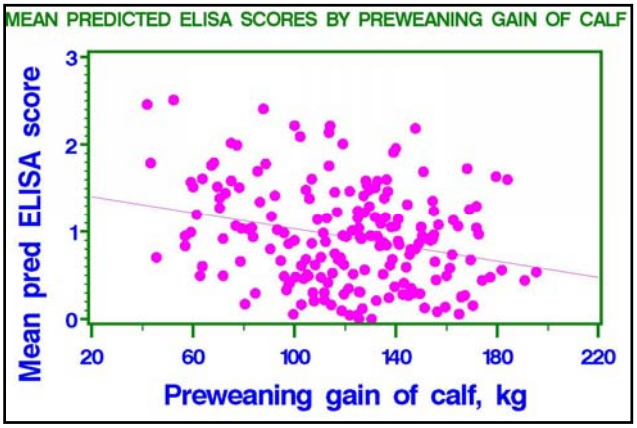


Calf Regression Effects

Effect	Estimate	SE	P > |t|
Birth Weight	-0.022	0.010	0.035
Preweaning Gain	-0.009	0.003	0.001

Cows with Higher ELISA Scores
=> Lower Calf Birth Weights
=> Lower Calf Preweaning Gains
=> Lower Milk Production?





Random Effects

Cow Variance = 0.34 ± 0.11
Residual = 0.65 ± 0.09

Repeatability Ratio = 0.34 ± 0.01

Sizable Variation Among Cow ELISA Scores

ELISA Scores Repeatable Within Cows Across Years

Conclusions

Measurable Breed Effect
High % Brahman ≠ High % Angus

High ELISA Scores
Lower Cow Weights
Lower Calf Birth Weights
Lower Calf Preweaning Gains
Lower Milk Production?

Implications

Although ELISA has
Low Sensitivity (50%; Infected Animals)
High Specificity (99%; Non-infected Animals)

There appears to be significant negative impact of subclinical paratuberculosis on production traits of dams and calves in beef cattle

Applications

Improve Control and Eradication Measures

Help Diagnosis During Subclinical Stages

Decrease Prevalence of MAP in Infected Herds

Current Control Measures Angus-Brahman Herd

Reduction of Exposure to Fecal Infection
Use of hay rings and special water containers

Separation of pre-partum cows by age and paratuberculosis status

ELISA and DNA testing of Cows with Clinical Symptoms

More Specific Cow Groups

Use breed group of dam, dam weight changes, calf WT and calf gains to create cow groups

Prepartum Cows
Age × Breed Group × ELISA Score

Postweaning Cows
Age × Breed Group × ELISA Score × Preweaning Calf Growth

Next Steps

Analyze Angus-Brahman data from a production trait perspective
Gestation Length
Cow Weight Maintenance
Calf Birth WT, Prewean Gain, Postwean Gain
Carcass Traits

Reevaluate Angus-Brahman herd with more data (serological, bacteriological, DNA) from future years