



Managing the Risk of Salmonellosis

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Disease and Productivity

- Fundamentals of Production
 - Cow comfort (Environment, pathogen exposure)
 - Nutrition
 - Reproduction
- Determinants of Host Pathogen Interactions
 - Host immunity (Environment, nutrition ...)
 - Pathogen dose and virulence (Environment)

Host Immunity

Pathogen Dose / Virulence

Health

Disease



Risk Management in the Production Cycle

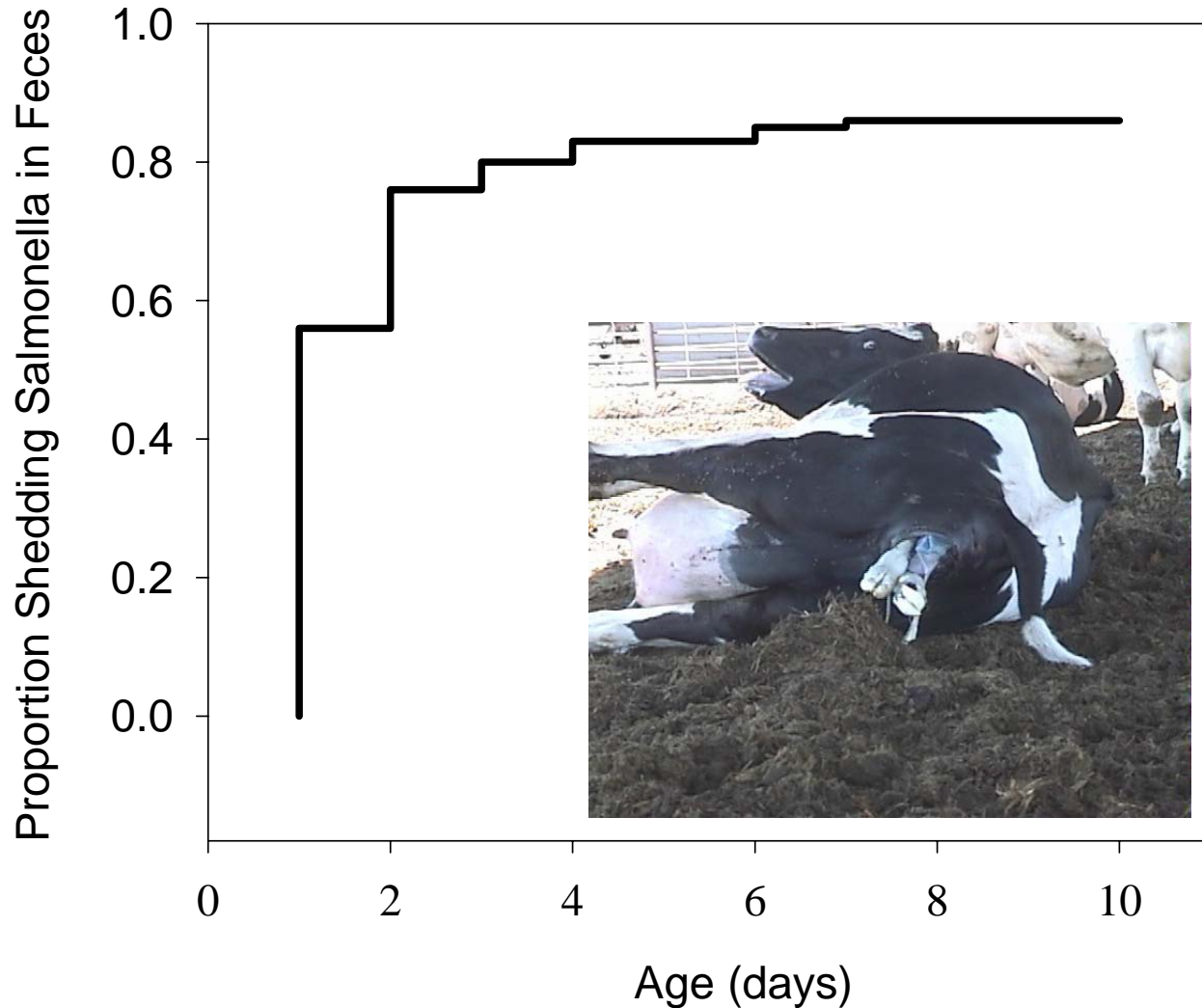




Birth - Calf Risk

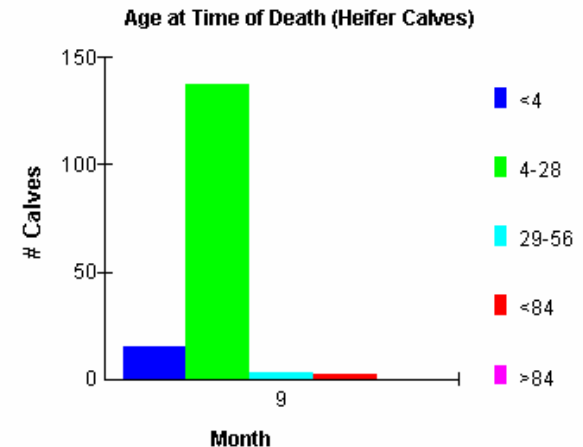
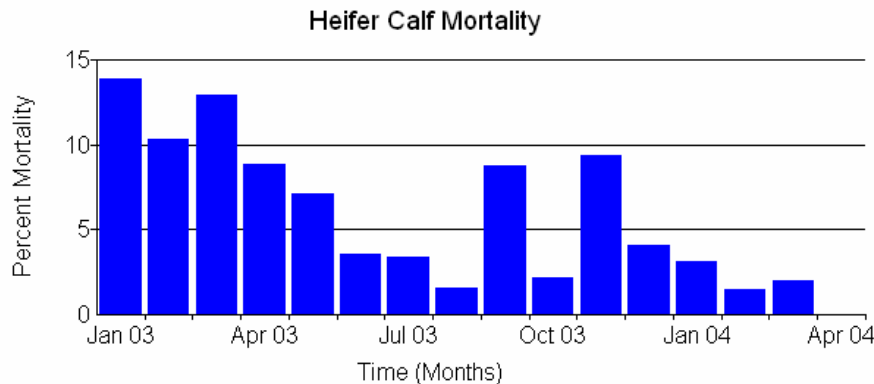
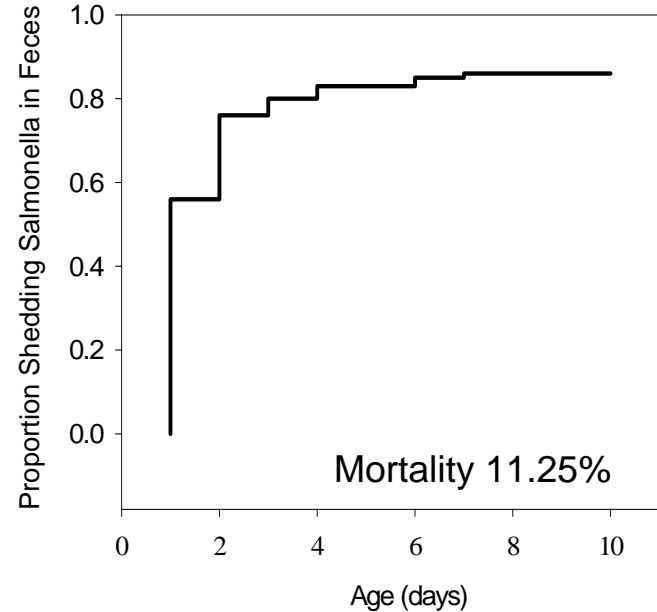
- Host immunity
 - Immunological naivety
 - Failure of passive transfer
 - Dystocia – hypoxia
 - Colostrum volume, timing of harvest and administration, microbial quality.
 - Environmental stress
- Pathogen exposure
 - Environmental
 - Other animals
 - Feed
 - Equipment
 - Personnel
- Pathogen Relevance
 - *Salmonella spp.*
 - Rotavirus
 - Coronavirus
 - Cryptosporidia
 - Enterotoxigenic *E. coli*
 - Enteropathogenic *E. coli*
 - *Mycobacterium paratuberculosis*
 - *Mycoplasma spp.*
 - Etc.....

Cumulative Proportion of Calves Shedding Salmonella



Challenge Dose, Virulence, Host Immunity interactions

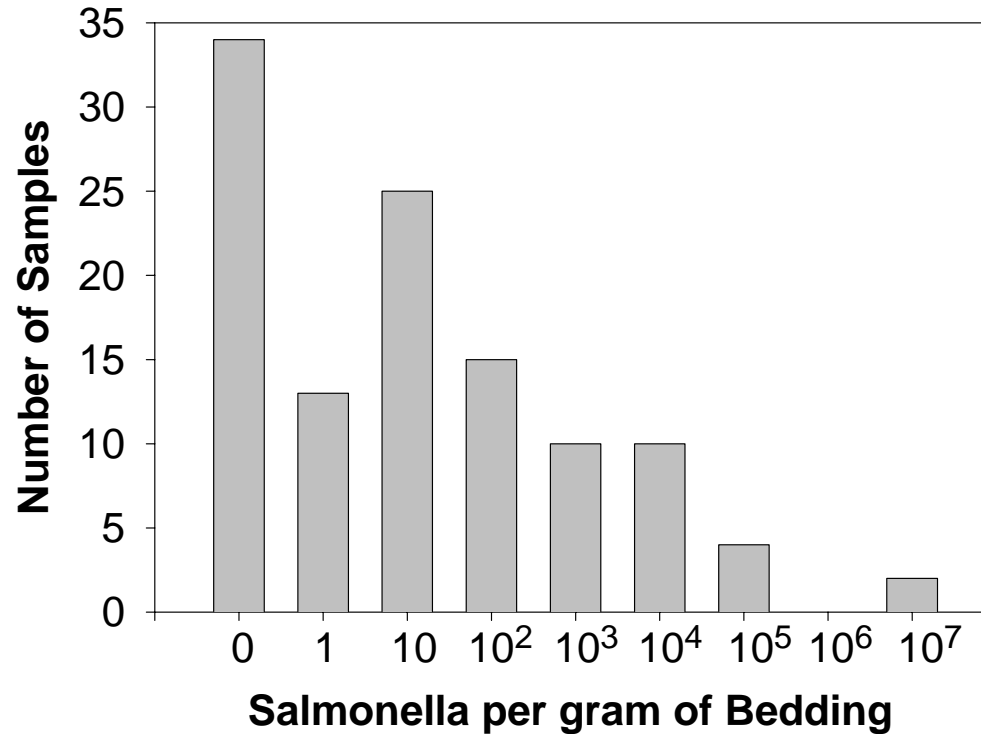
- Shedding may not equate with disease



Environment



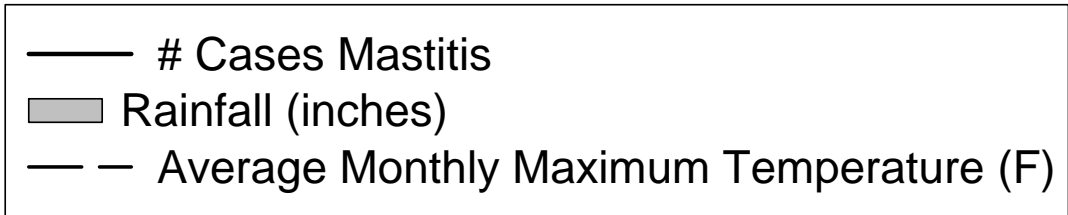
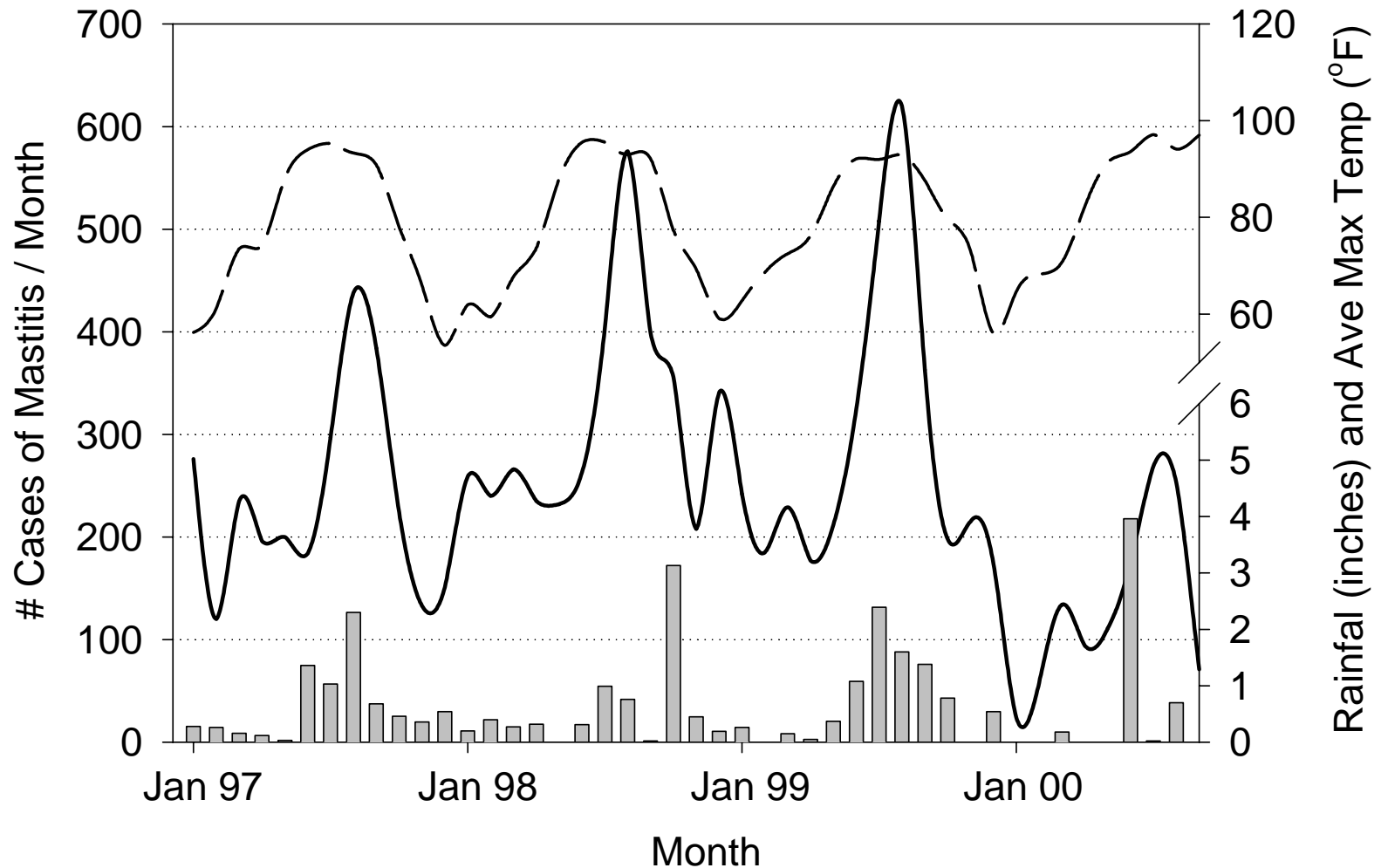
Histogram, Number of Salmonella per Gram of Bedding



Temperature and moisture

	Temperature °C		
Dry Matter Content (%)	4	20	37
92	68	6.8	3.2
70	146	31	68
40	681	3.1×10^7	1.4×10^7

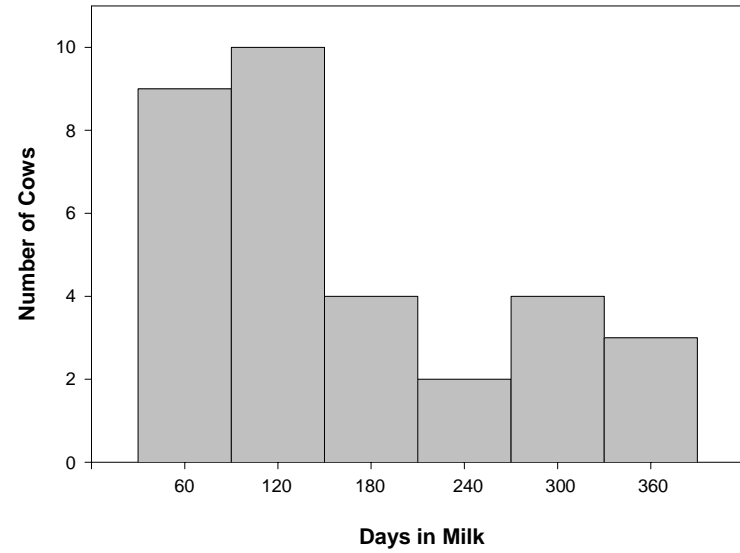
Mastitis and Environmental Conditions



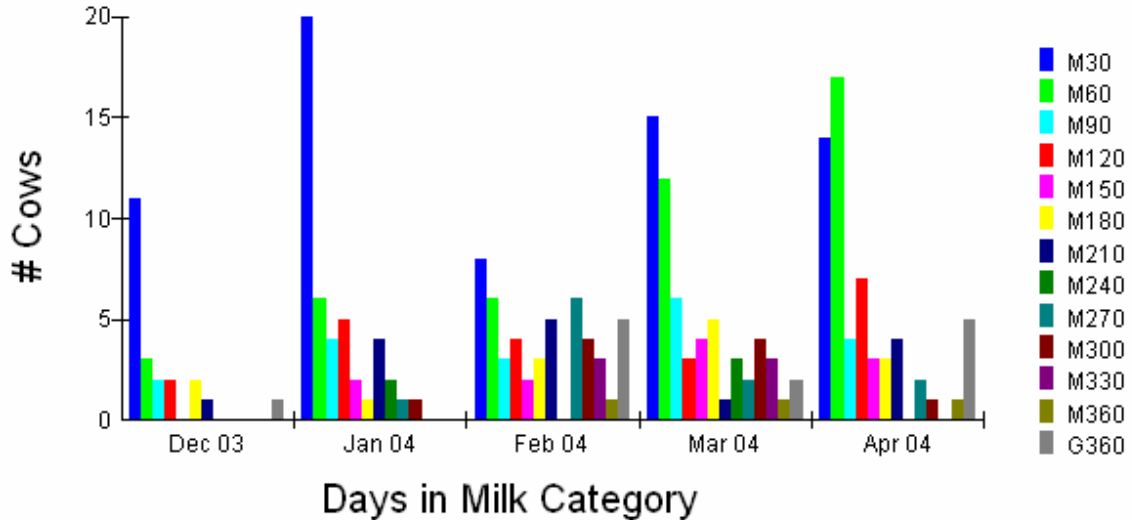
Environmental management



Histogram of Days From Parturition to Salmonella Mastitis



Clinical Mastitis Events by DIM



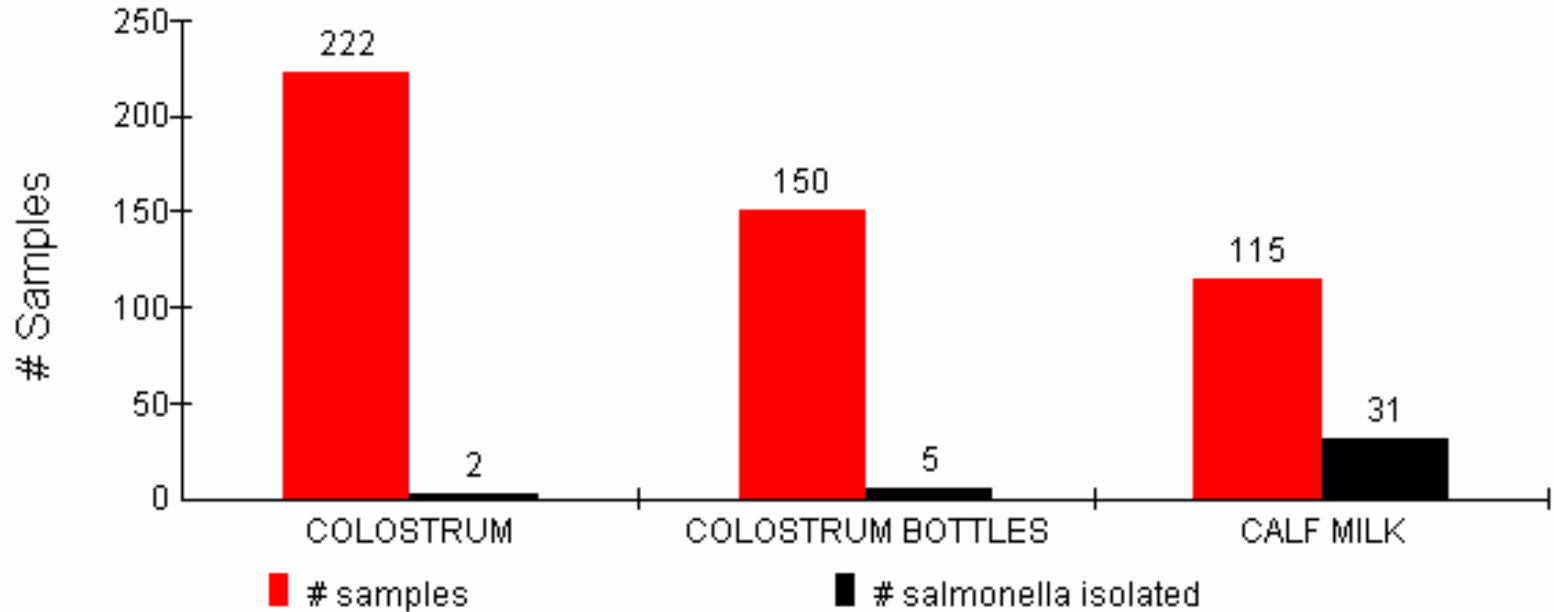
Individual Cow Sampling

- Colostrum 2 / 200
- Cows and heifers 2 - 21 DIM 0 / 200
- Mid lactation cows 0 / 200
- Heifers mid lactation 2 / 200
- Mastitis 11 / 200
- OK Mastitis pending withholding 3 / 200



Colostrum and Calf Milk Quality

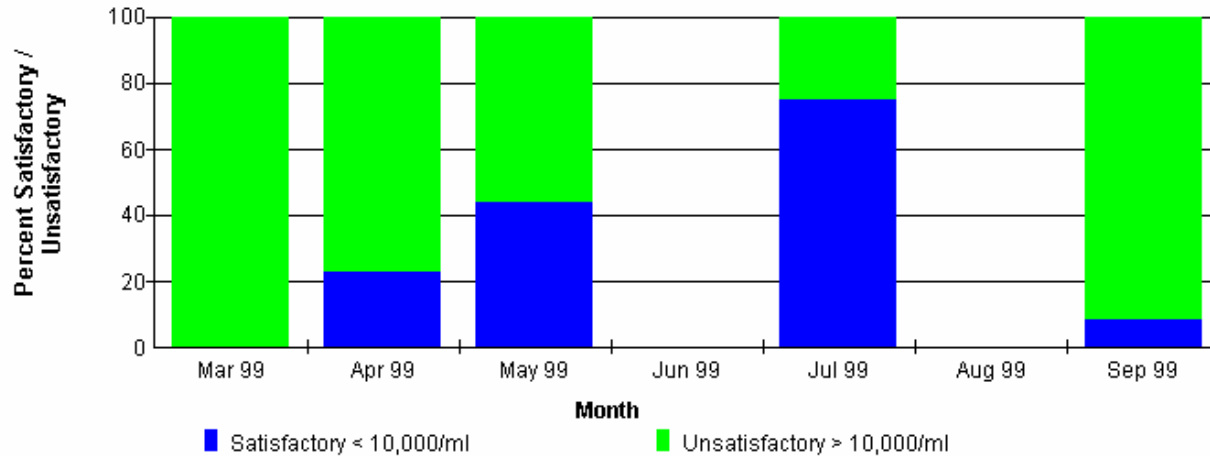
Salmonella Isolates from Potential Calf Milk Sources



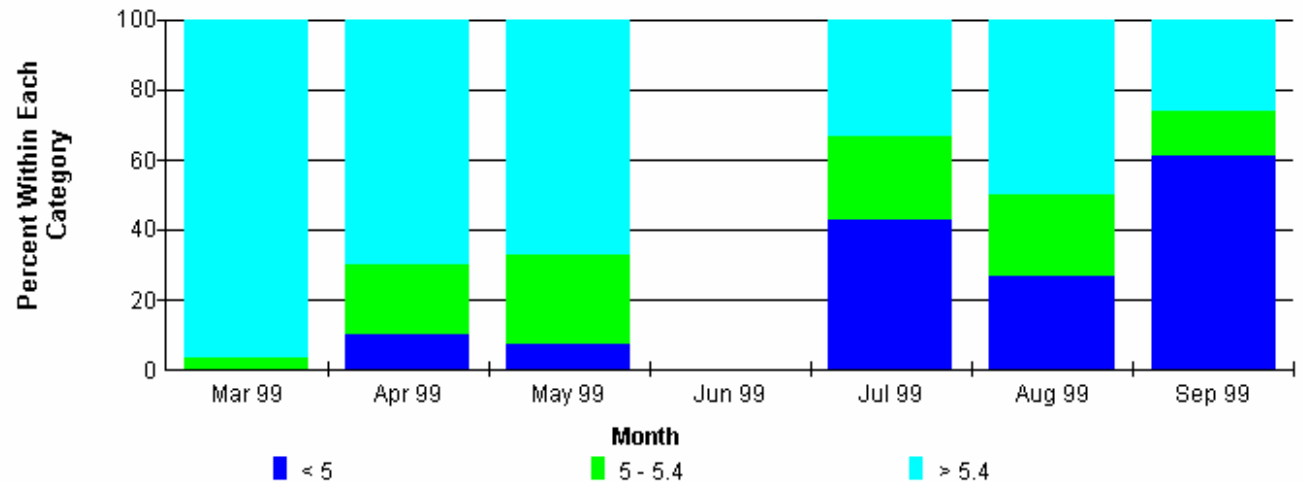
Control Point Surveillance



Monthly Colostrum Microbial Quality Monitoring



Monthly Distribution of Calf Serum Proteins



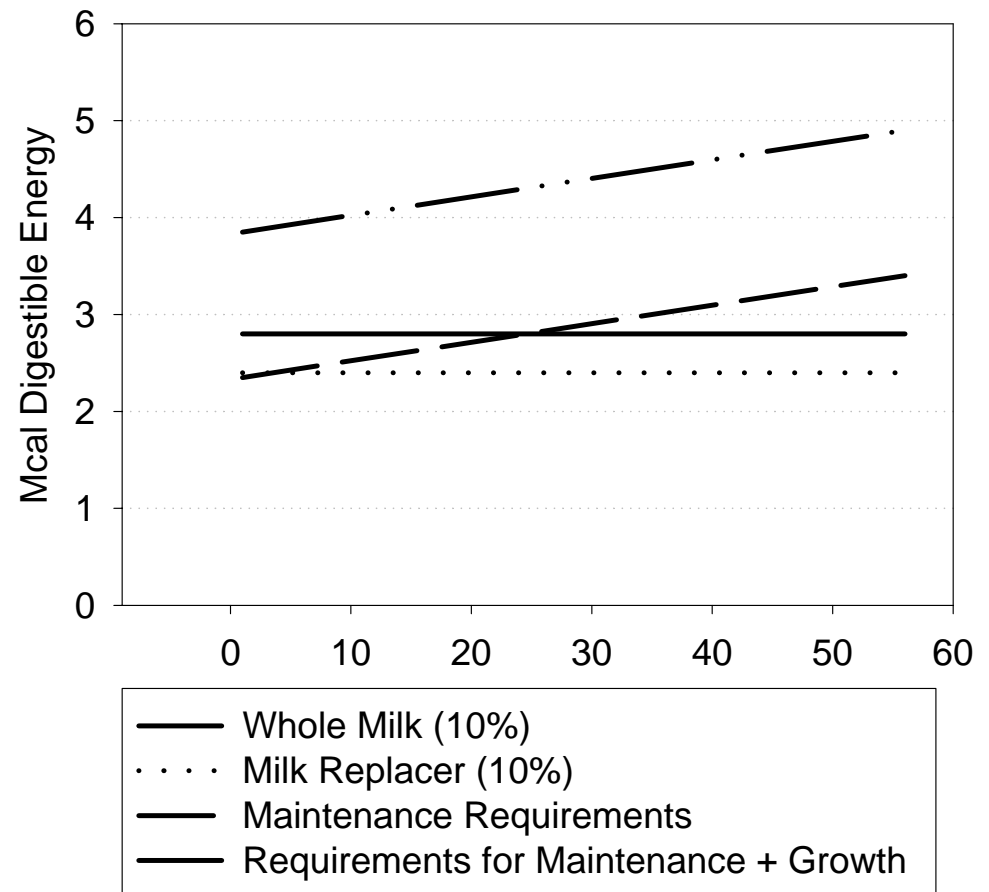
- Salmonella
- *Mycobacterium paratuberculosis*
- *Mycoplasma spp*
- Bovine Leukosis

Maintaining Host Immunity

- Nutrition
- Environmental stress
- Vaccination



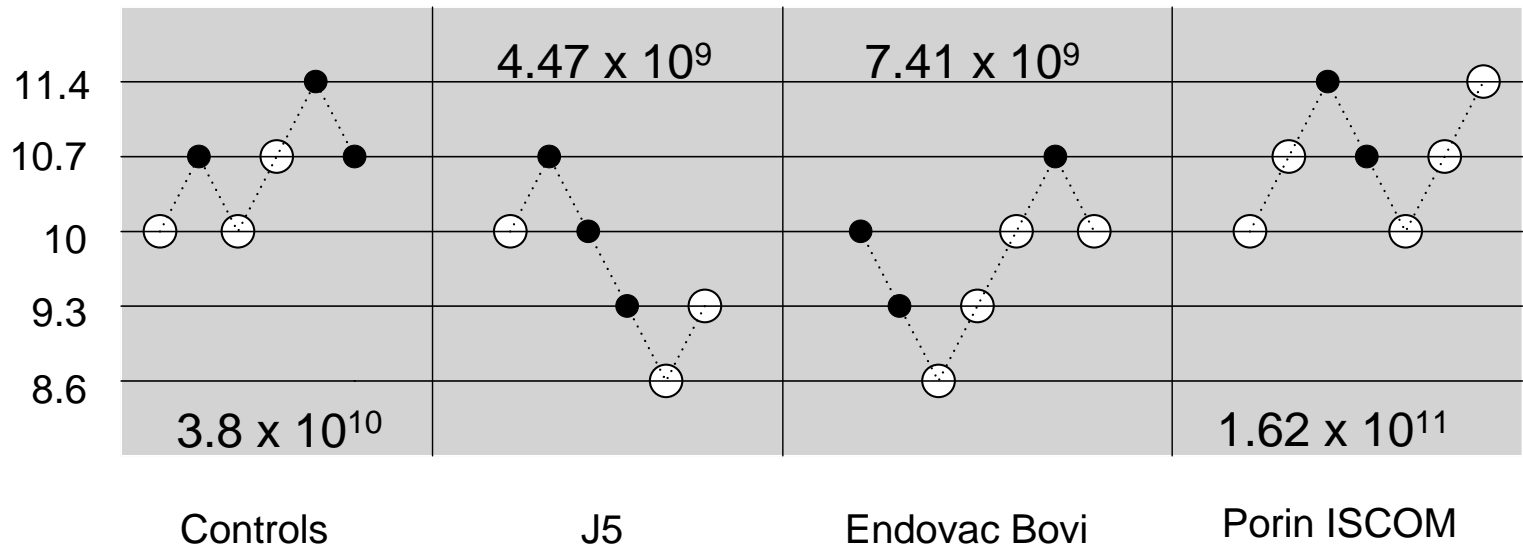
Digestible Energy Supplied by Milk and Milk Replacer When Fed at 10% Body Weight in Relationship to Maintenance and Growth Requirements



Enhancing Host Immunity

- Environmental management
- Nutrition
- **Vaccination**

Log 10 Dose



Vaccine

X_f = last dose administered

k = tabular value

d = dose interval

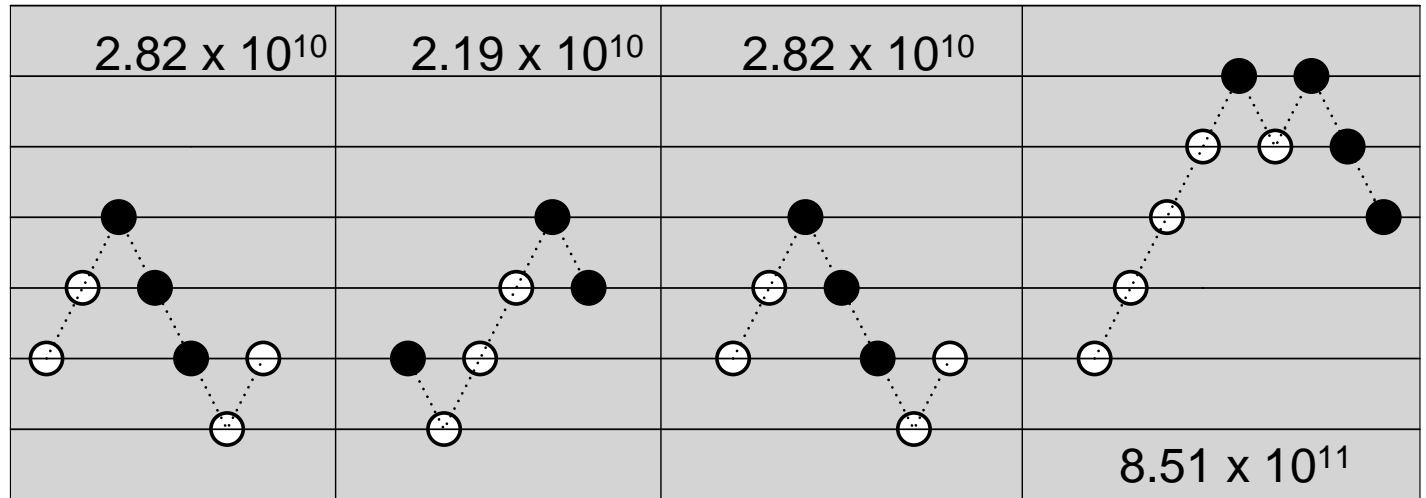
$$LD_{50} = X_f + kd$$



Enhancing Host Immunity



Log Dose



Porin
Montenide 206

Porin
ISCOM Vitamin E

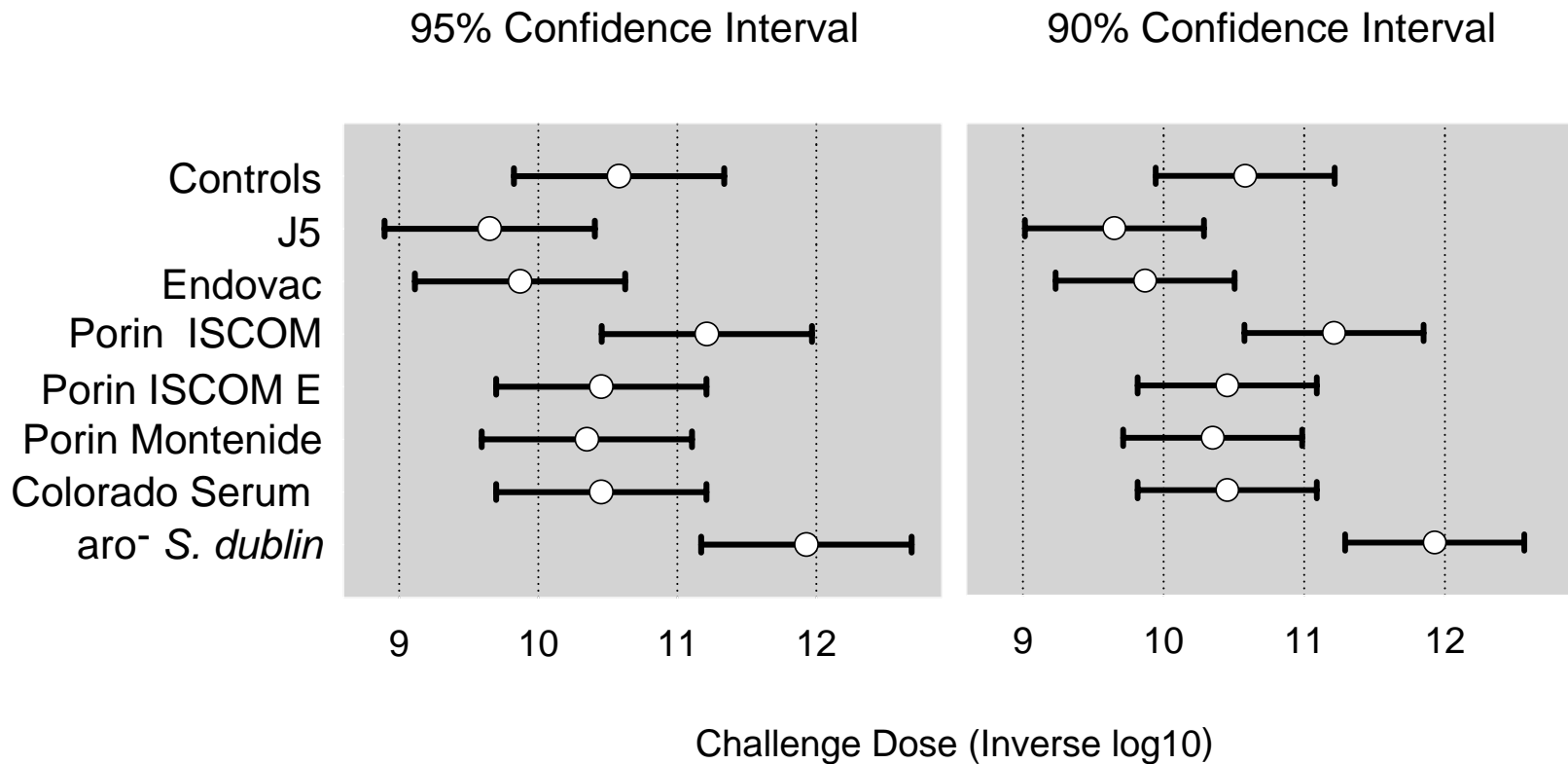
Colorado Serum
Company Bacterin

Modified Live
aro⁻ S. dublin

Vaccine

Enhancing Host Immunity

Estimated LD50 and Confidence Intervals

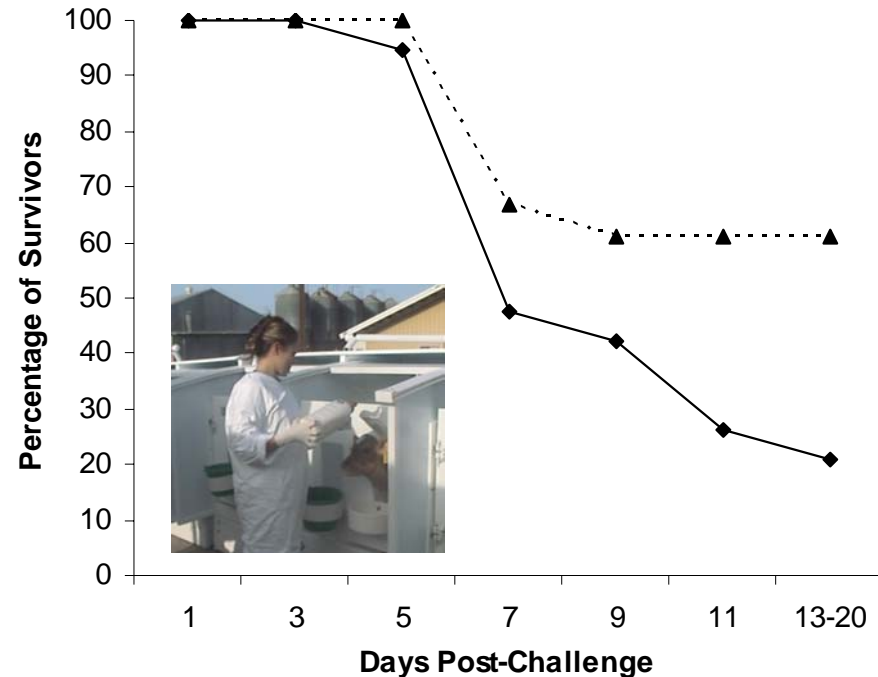
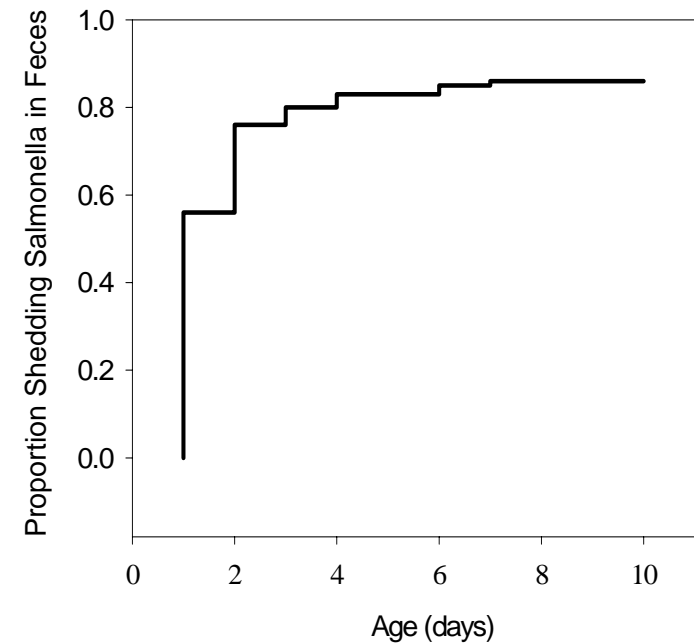


Timing of Vaccination

- Precede virulent exposure
- Modified live vaccines provide protection within 24 hours of administration

Calves vaccinated at 1 – 7 days of age with DAM attenuated *S. Typhimurium*. Challenged 24 hours following vaccination

DAM attenuated vaccines also provide protection against heterologous challenge.



Maternal Vaccination



Outcome Assessment	Group		
	SC 54	Bacterin	Controls
Salmonella Culture Results			
Cows (n = 450)			
Percentage of cows that shed <i>Salmonella</i>	98.1	99	100
Frequency of Salmonella shedding (Isolation from fecal swabs % recovery)			
All <i>Salmonella</i> serogroups	63 ^{ab}	71 ^a	73 ^b
Serogroup C1 <i>Salmonella</i>	41 ^c	48	50 ^c
Non serogroup C1 <i>Salmonella</i>	22	23	23
Calves (n = 80)			
Percentage of calves that shed <i>Salmonella</i>	86.2	85.2	88.8
Frequency of Salmonella shedding (Isolation from fecal swabs % recovery)			
All <i>Salmonella</i> serogroups	37 ^d	54 ^d	44
Serogroup C1 <i>Salmonella</i>	25 ^e	44 ^e	37
Non serogroup C1 <i>Salmonella</i>	12	10	7

Managing Disease Outbreaks

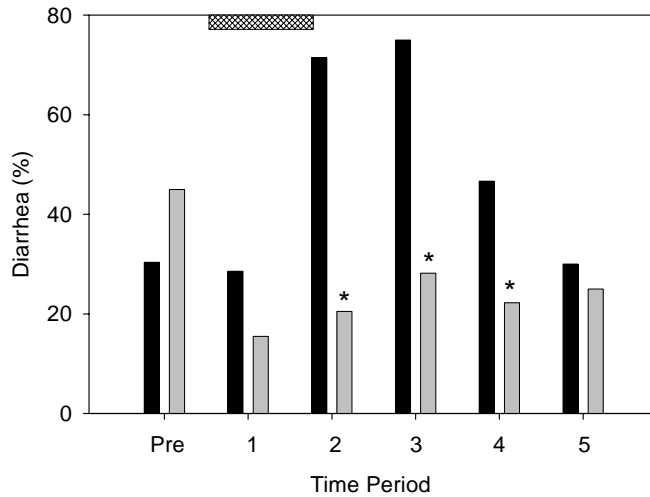
- Emphasize management strategies to enhance immunity and reduce challenge dose.
- Treatment of sick animals
 - Calves
 - Electrolytes
 - Antimicrobials
 - Non steroidal anti-inflammatories
 - Cows
 - Fluids
 - Non steroidal anti-inflammatories
 - +/- Antimicrobials ??



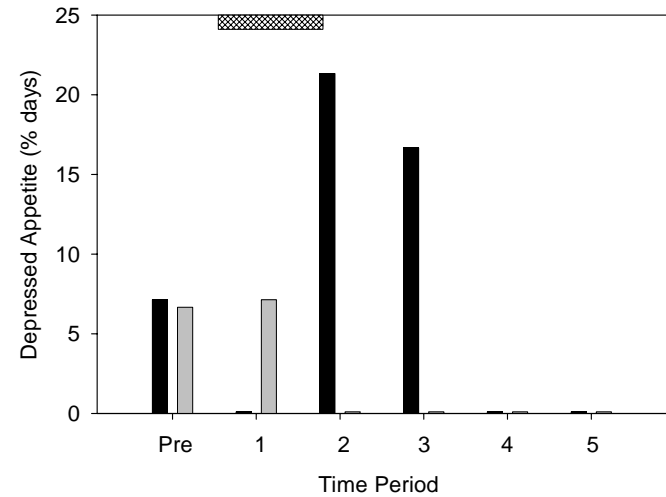
Antimicrobial Therapy



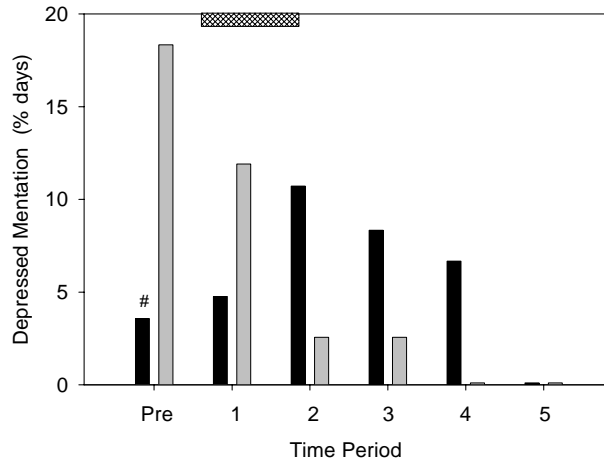
Diarrhea



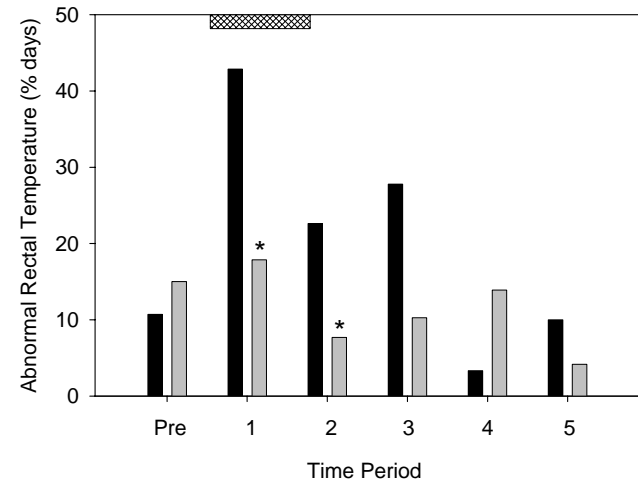
Depressed Appetite



Depressed Mentation



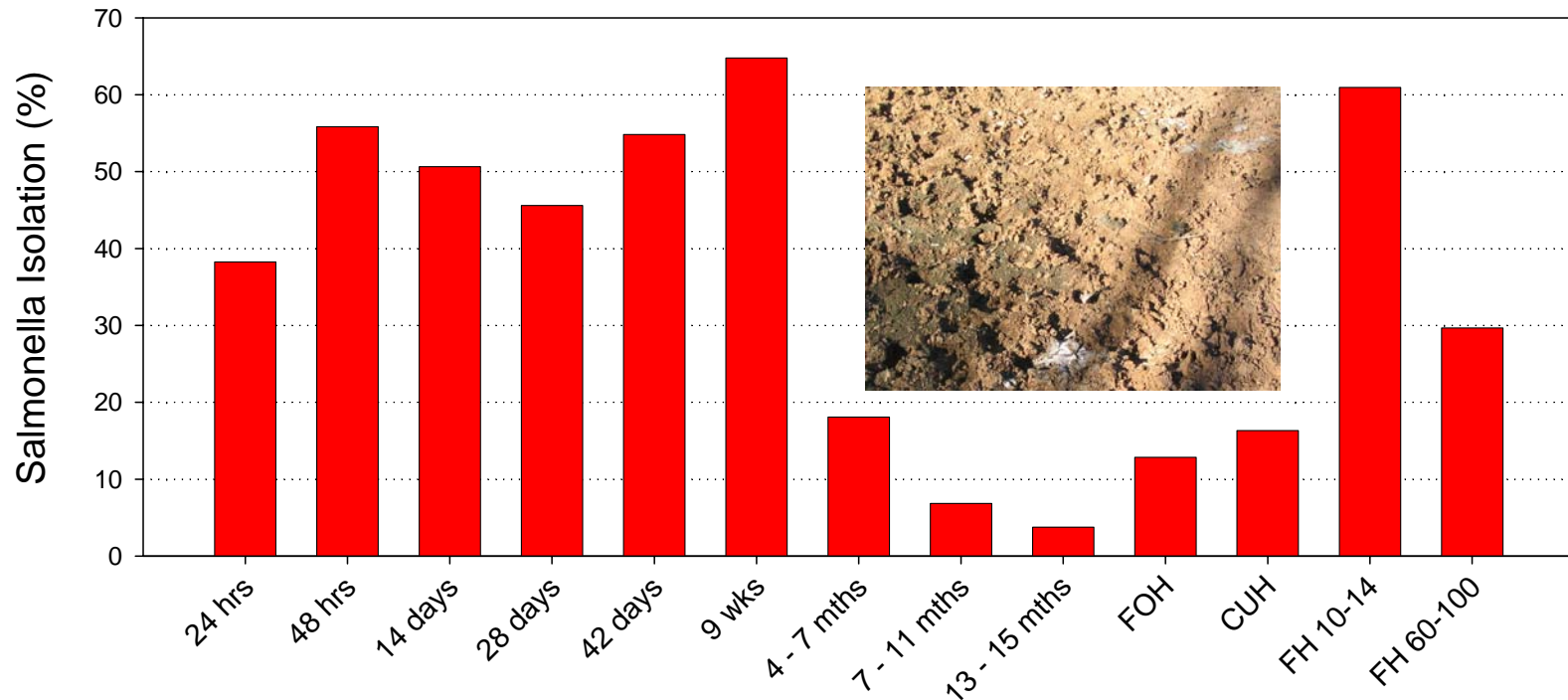
Abnormal Rectal Temperature



Non-medicated Controls
 Ceftiofur Medicated Calves (5mg/kg)

Heifer Replacement Management

Salmonella Fecal Shedding by Young Stock





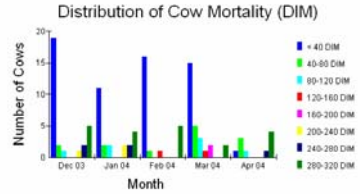
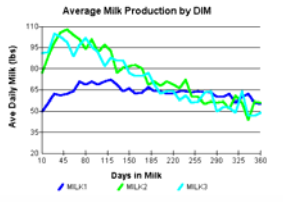
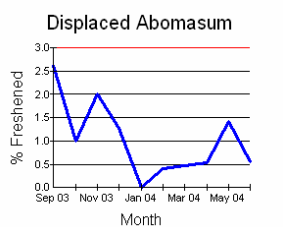
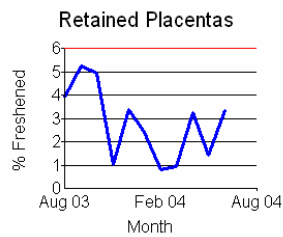
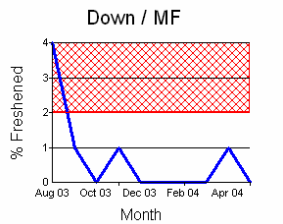
Parturition, Cow Risks

- Host Immunity
 - Pregnancy induced Immune modulation
 - Dietary Δ
 - Metabolic disease
 - Environmental stress
- Pathogen Exposure
 - Environmental contamination
 - Feed
 - Infected cattle
 - Personnel
 - Equipment
 - Water



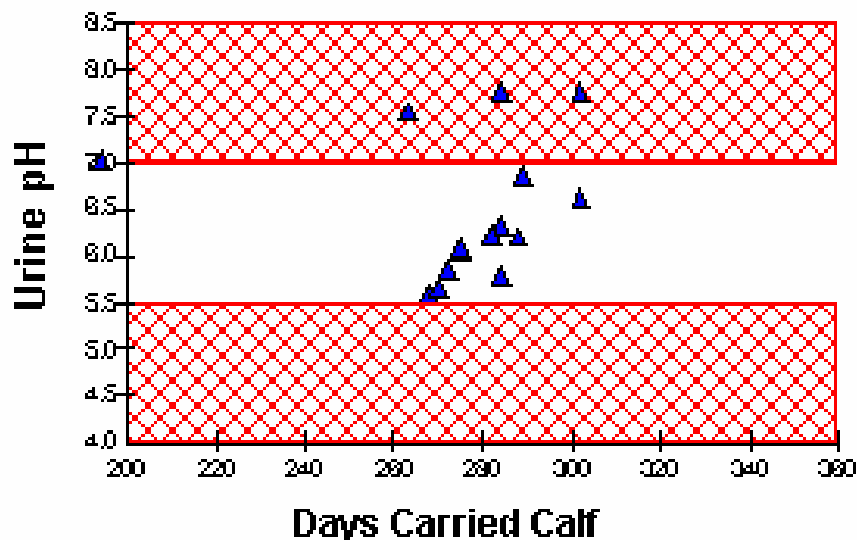
Control Point Surveillance

- Calcium homeostasis
 - Close up cow urine pH
 - Incidence of milkfever
- Energy balance
 - Dry matter intake
 - Milk production
 - Body condition score
 - Milk fat test (first 30days)
- Ruminal acidosis
 - Manure consistency
 - Dry matter intake
 - Rumen pH (when necessary)
- Incidence of post partum disease and mortality

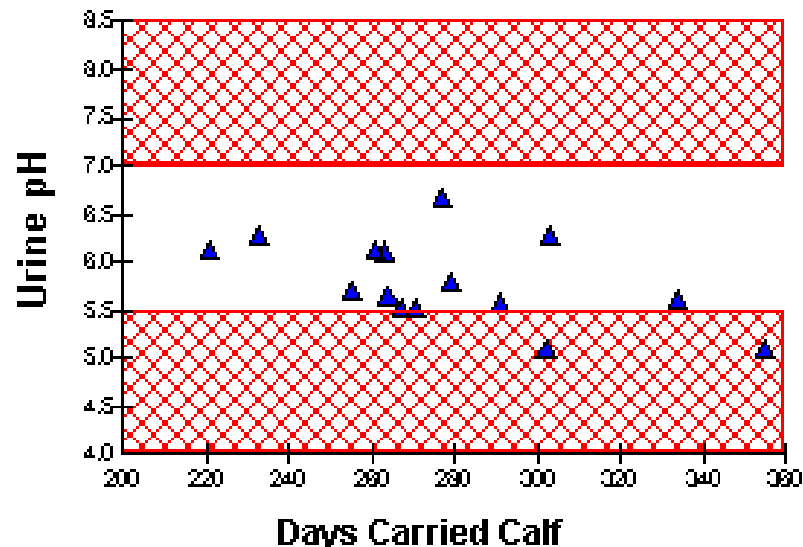


Transition Cow Management

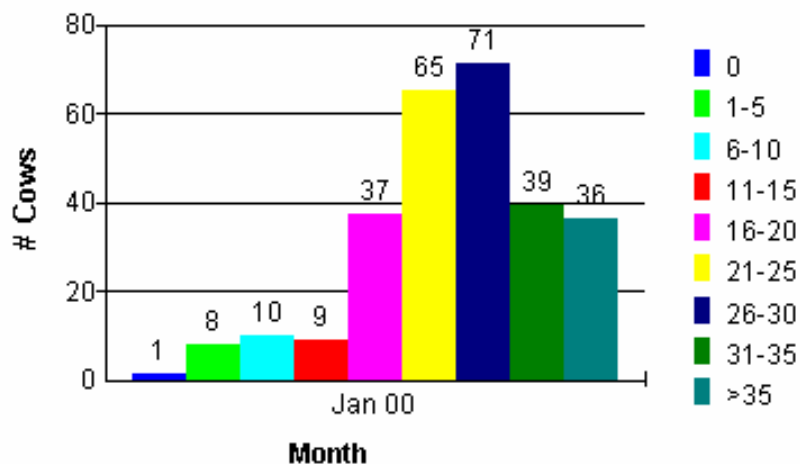
Urine pH vs Days Pregnant for Closeup Cows



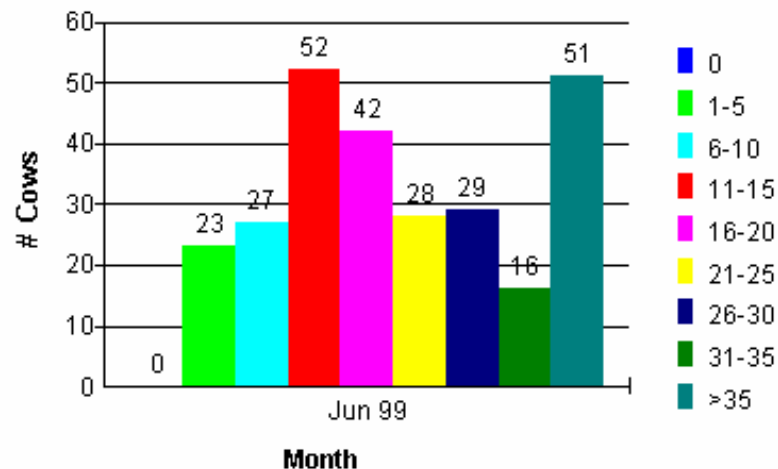
Urine pH vs Days Pregnant for Closeup Heifers



Days on DCAD Live Cows



Days on DCAD Live Heifers



Days on Closeup 14 day increments * DOA Category * Parity Crosstabulation

Parity				DOA Category		Total
				No	Yes	
Cow	Days on Closeup 14 day increments	0 - 14 days	Count % DOA	721 92.6%	58 7.4%	779 100.0%
		15 - 28 days	Count % DOA	3889 94.1%	243 5.9%	4132 100.0%
		29 - 42 days	Count % DOA	1840 93.0%	139 7.0%	1979 100.0%
		43 - 150 days	Count % DOA	454 89.9%	51 10.1%	505 100.0%
		Total	Count % DOA	6904 93.4%	491 6.6%	7395 100.0%
Heifer	Days on Closeup 14 day increments	0 - 14 days	Count % DOA	914 83.1%	186 16.9%	1100 100.0%
		15 - 28 days	Count % DOA	1010 85.4%	173 14.6%	1183 100.0%
		29 - 42 days	Count % DOA	532 89.1%	65 10.9%	597 100.0%
		43 - 150 days	Count % DOA	738 84.3%	137 15.7%	875 100.0%
		Total	Count % DOA	3194 85.1%	561 14.9%	3755 100.0%





Heifer ME 305 by Days on Closeup

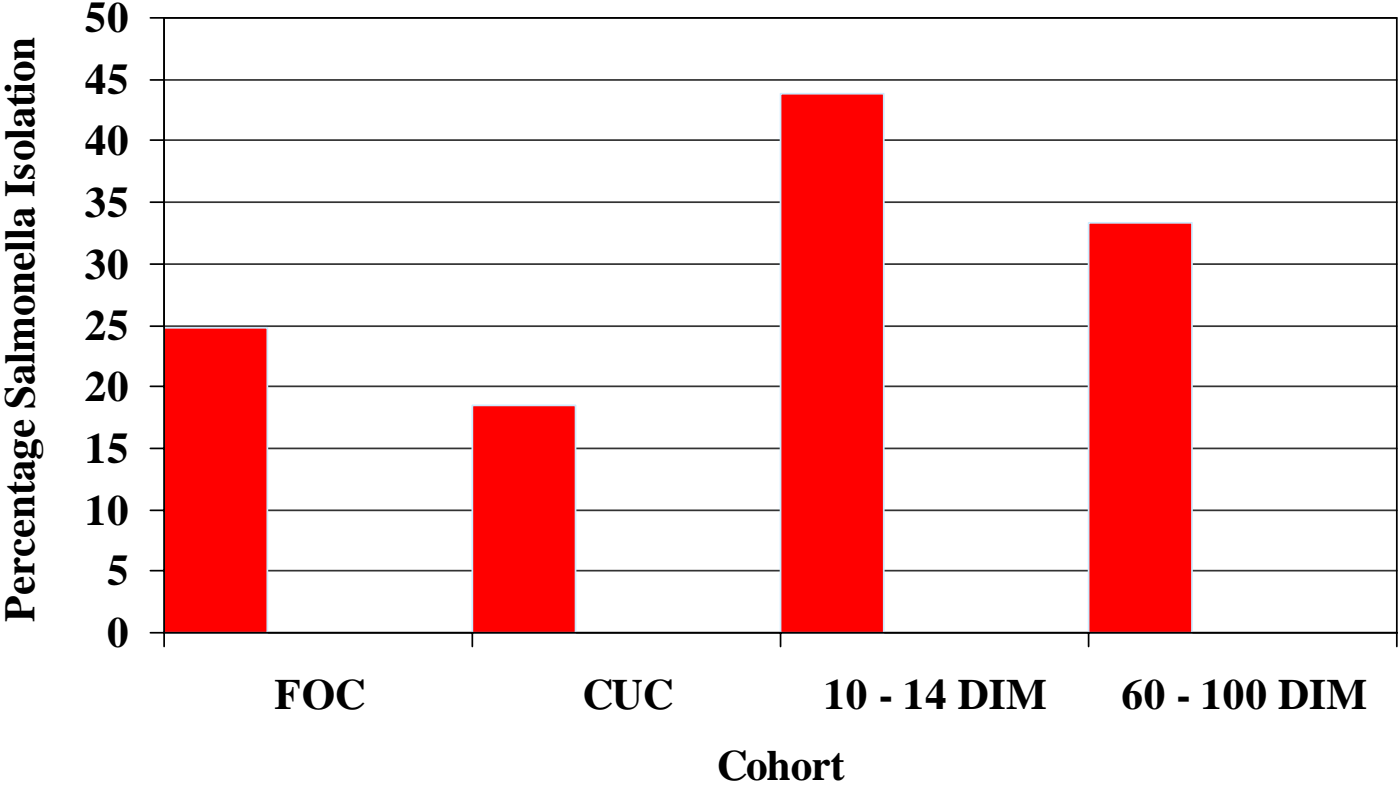
		N	Mean
Days on Closeup	0 - 14 days	1028	23402.51
	15 - 28 days	1098	24571.31
	29 - 42 days	548	25009.49
	43 - 150 days	792	25166.28
	Total	3466	24429.88

Cows ME305 by Days on Closeup

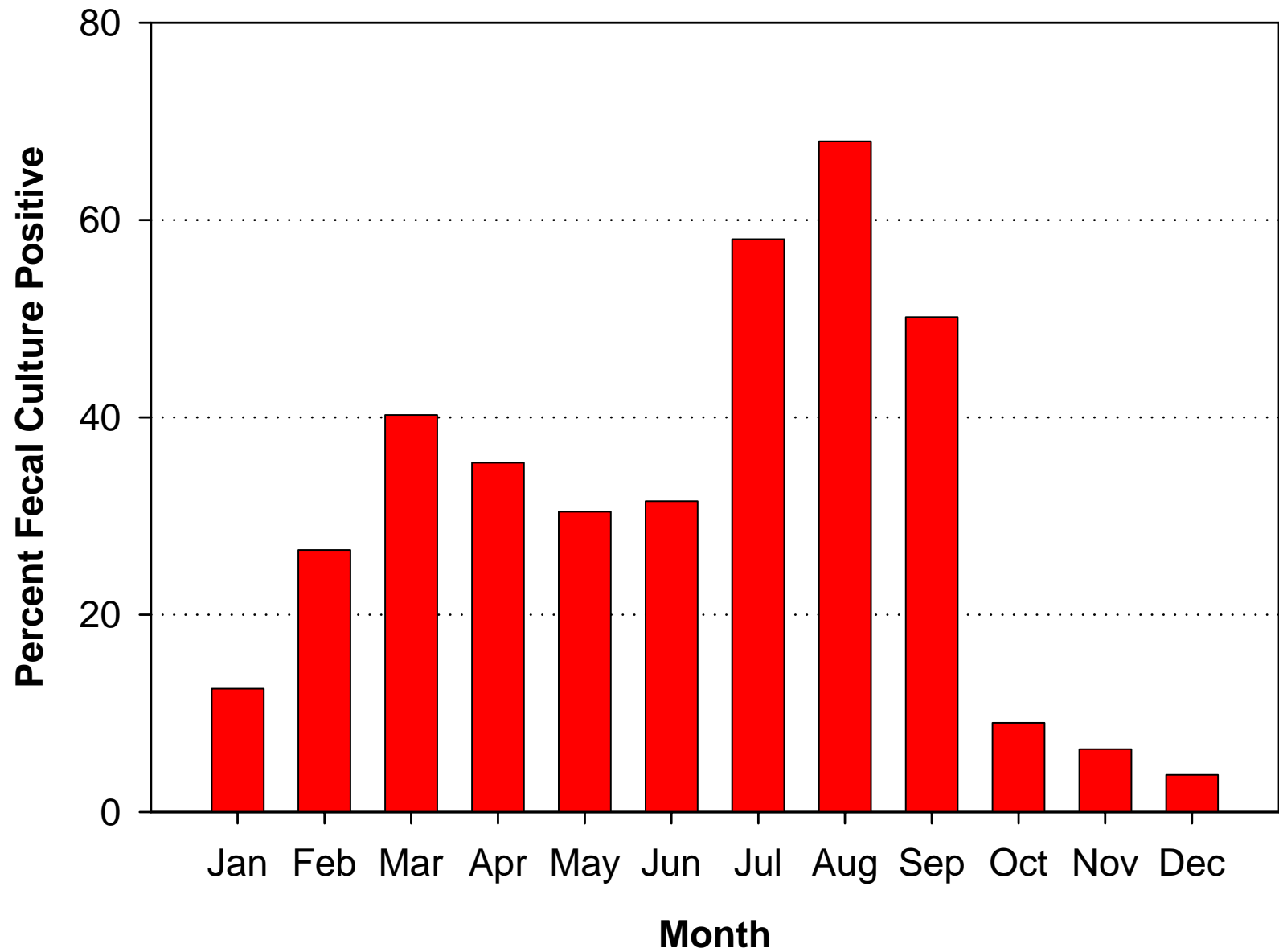
		N	Mean
Days on Closeup	0 - 14 days	702	23126.78
	15 - 28 days	3764	23752.53
	29 - 42 days	1784	24343.35
	43 - 150 days	432	24344.98
	Total	6682	23882.83



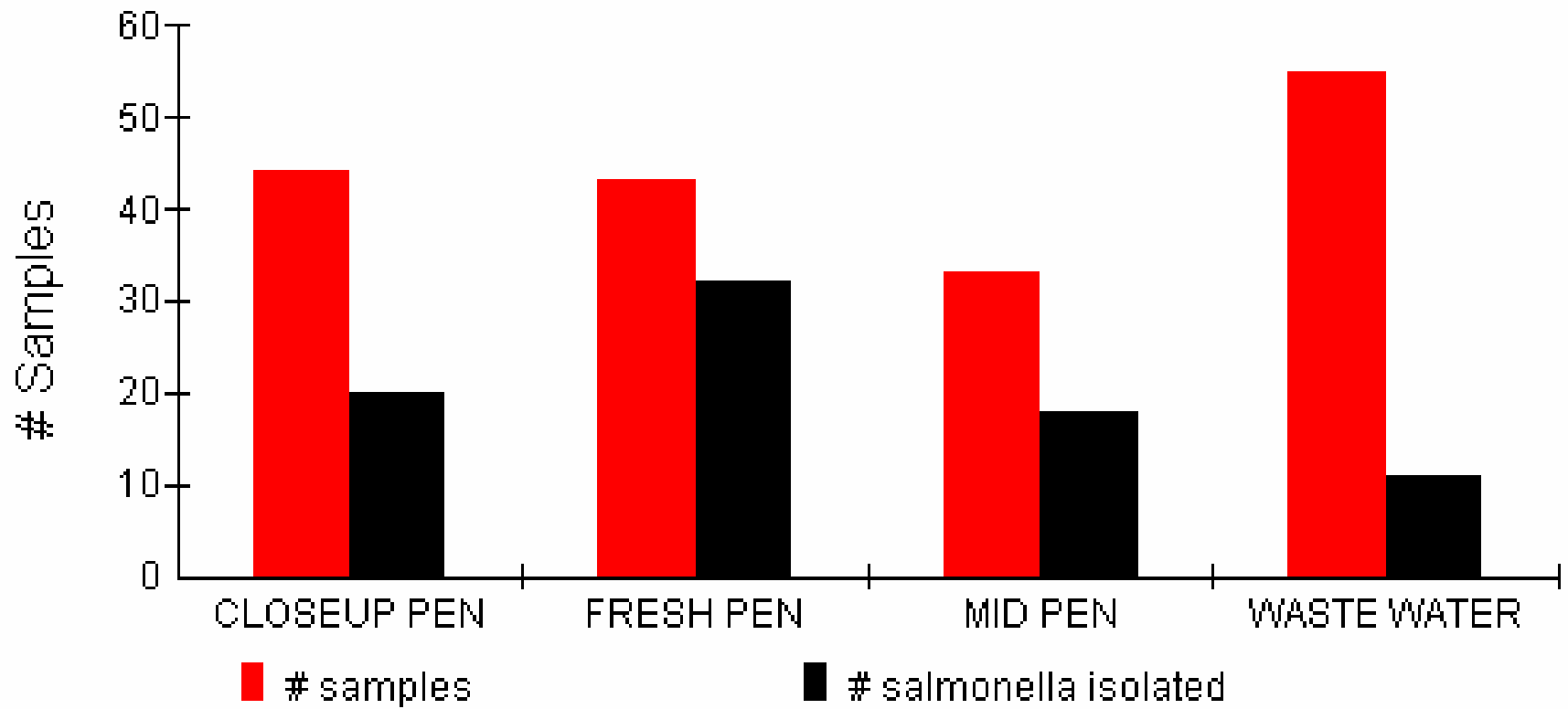
Adult Cows



Monthly Fecal Salmonella Shedding Cows



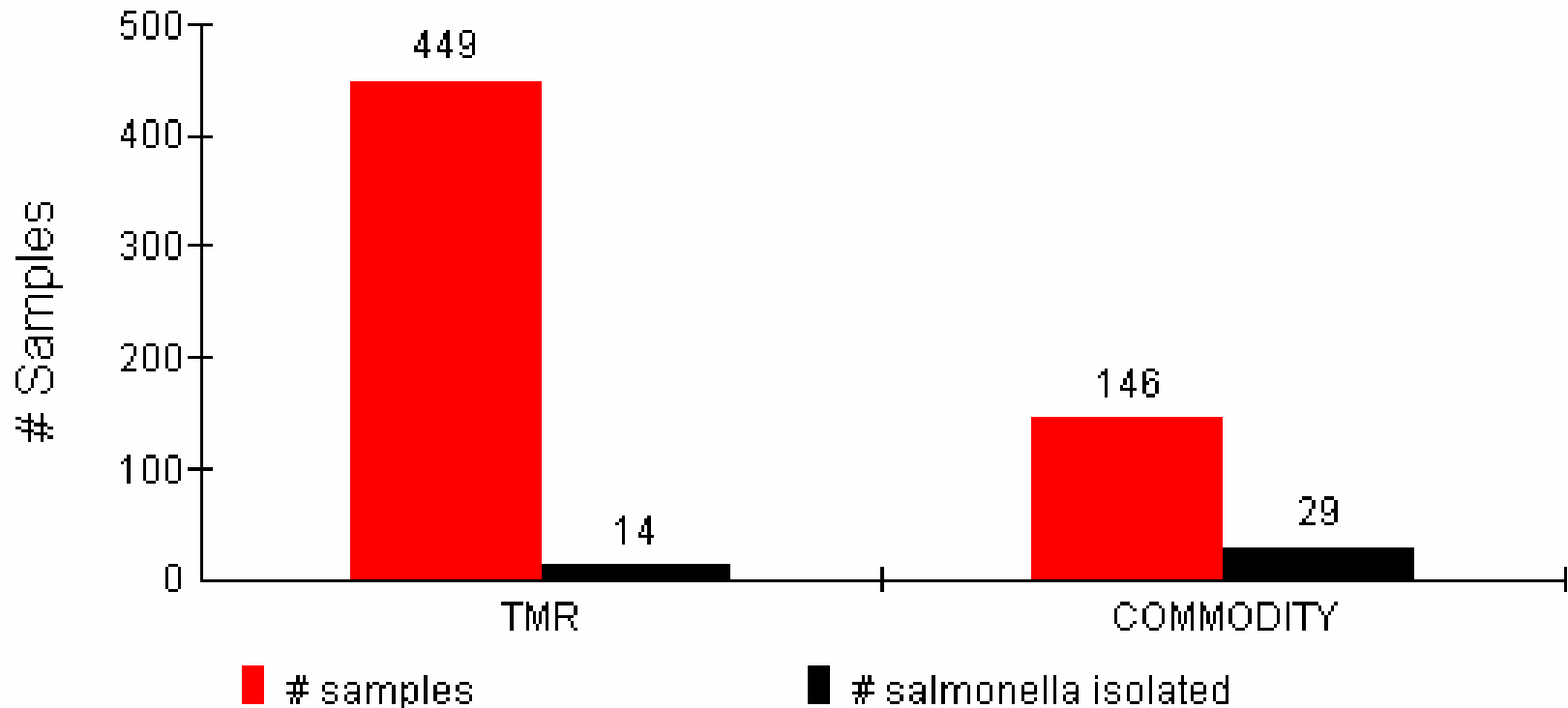
Salmonella Isolates from Environmental Samples

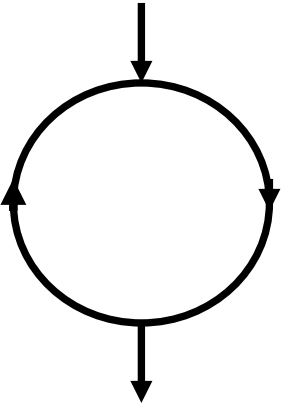




- Oat Silage 5/29
- Alfalfa Hay 10/29
- Blood Meal 8/29
- Other 6/29

Salmonella Isolates from Feed Samples

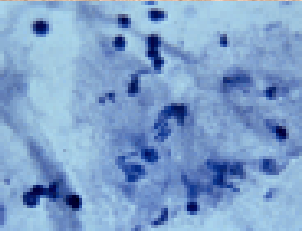
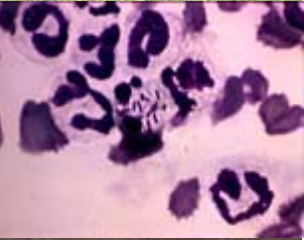
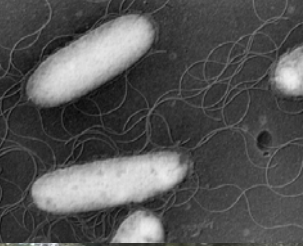




Conclusions

- Strategies to prevent salmonellosis are directed at:
 - Enhancing host immunity
 - Reducing pathogen exposure
- Herd benefits include
 - Improved calf health
 - Reduced transmission of other infectious pathogens
 - Improved milk production
 - Reduced mortality (neonatal and adult)
 - Reduced incidence of
 - Metabolic disease
 - Mastitis
 - Lameness





Salmonella

Antimicrobial Resistance on the Farm

John House

The University of Sydney

Signalment

- Dry lot dairy farm in New Mexico
- Milking 10,000 cows
- Expanding herd
- 25,000 head on site
- 7 Milking parlours
- Laboratory set up on site
 - Herd production monitors
 - Milk cultures
 - Salmonella cultures



Salmonella serotypes

~ 3,000 isolates banked, 490 from 1999 - 2000 typed

Feed Isolates 1995

S Agona

S Alachua

S Anatum

S Cerro

S Cubana

S Livingstone

S Mbandaka

S Newport

S Oranienburg

S Rubislaw

S Senftenberg

S Taksony

Fecal Isolates 1995

S Typhimurium

S Saintpaul

S Albert

S Kentucky

S Rubislaw

S Give

S Anatum

S Mbandaka

S Hadar

S Orion

S Senftenberg

Untypable

Mixed source Isolates 1999/2000

S Montevideo (C1, 233/490)

S Kentucky (C3, 101/490)

S Anatum (E1, 46/490)

S San Diego (B, 31/490)

S Cerro (K, 21/490)

S Meleagridis (E1, 19/490)

S Cubana (G2, 6/490)

Untypable (5/490)

S Agona (B, 4/490)

S Havana (G2, 3/490)

S Taksony (E4, 3/490)

S Brandenburg (B, 2/490)

S Bredeney (B, 2/490)

S Java (B, 2/490)

S Mbandaka (C1, 2/490)

21 Serotypes identified in the 490
isolates from 1999-2000

Sources of Salmonella Isolates

Sample distribution	Feed (n = 16)	Milk (n = 88)	Feces (n = 298)	Environment (n = 88)	Total (n = 490)
Isolates from antimicrobial use location	0	58	189	36	283
Isolates from calves < 6 months of age	0	0	149	18	167
Isolates from 1999	9	30	183	39	261
Isolates from 2000	7	58	114	49	228

Source and Serotypes of Salmonella Isolates

Serotype Distribution	Feed (n = 16)	Milk (n = 88)	Feces (n = 298)	Environment (n = 88)	Total (n = 490)
<i>S Montevideo</i>	10	57	115	51	233
<i>S Kentucky</i>	0	11	68	22	101
<i>S Anatum</i>	1	7	33	5	46
Other	5	13	82	10	110

Assessment of Antimicrobial Resistance (n = 490)

Amikacin

Ceftiofur

Ceftriaxone

Ciprofloxacin

Gentamicin

Naladixic acid

Trimethoprim

All Isolates Susceptible

Amoxicillin/clavulanic acid

Ampicillin

Apramycin

Cefoxitin

Cephalothin

Chloramphenicol

Kanamycin

Sulphamethoxazole

Less than 1.5% of isolates resistant

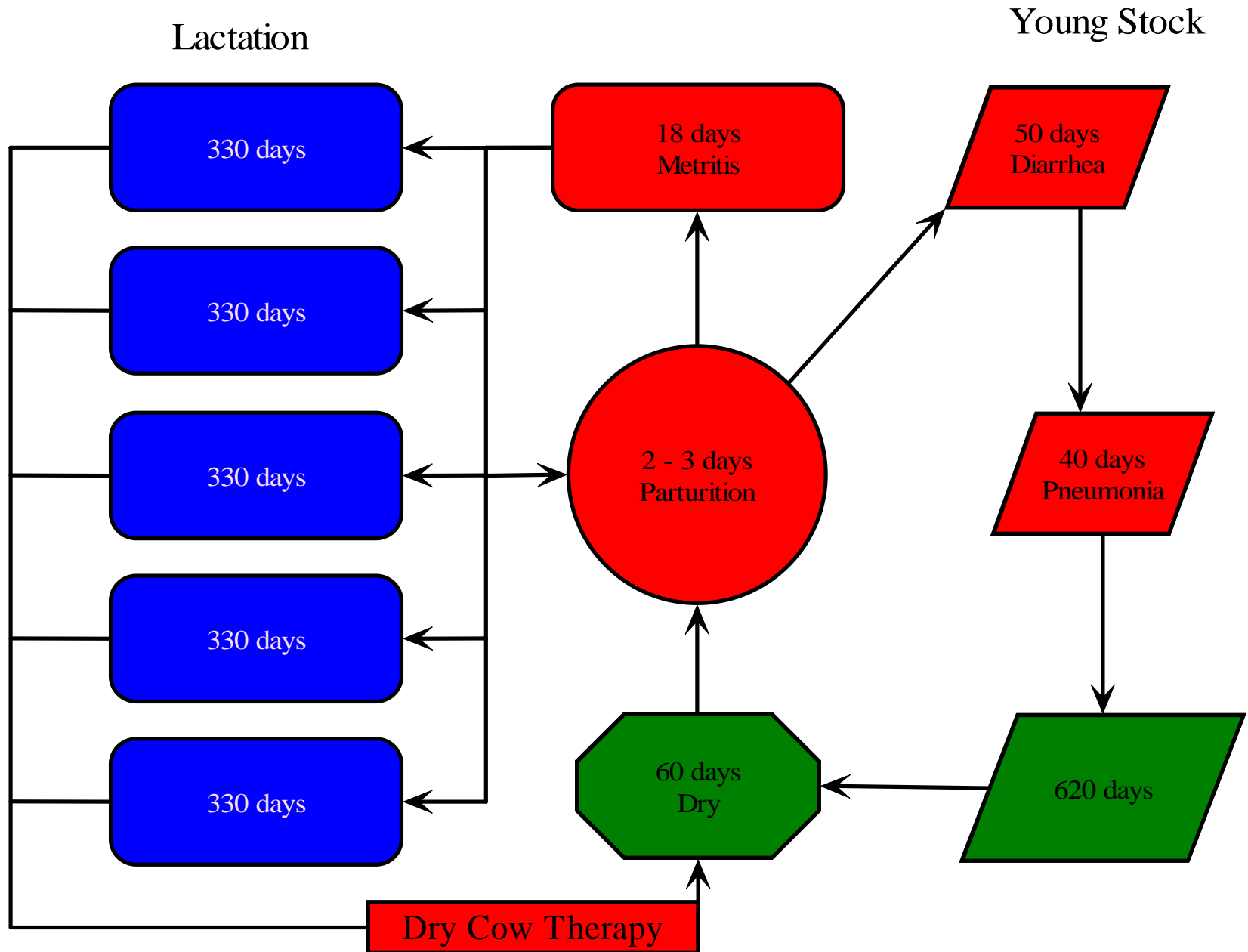
Tetracycline

Streptomycin

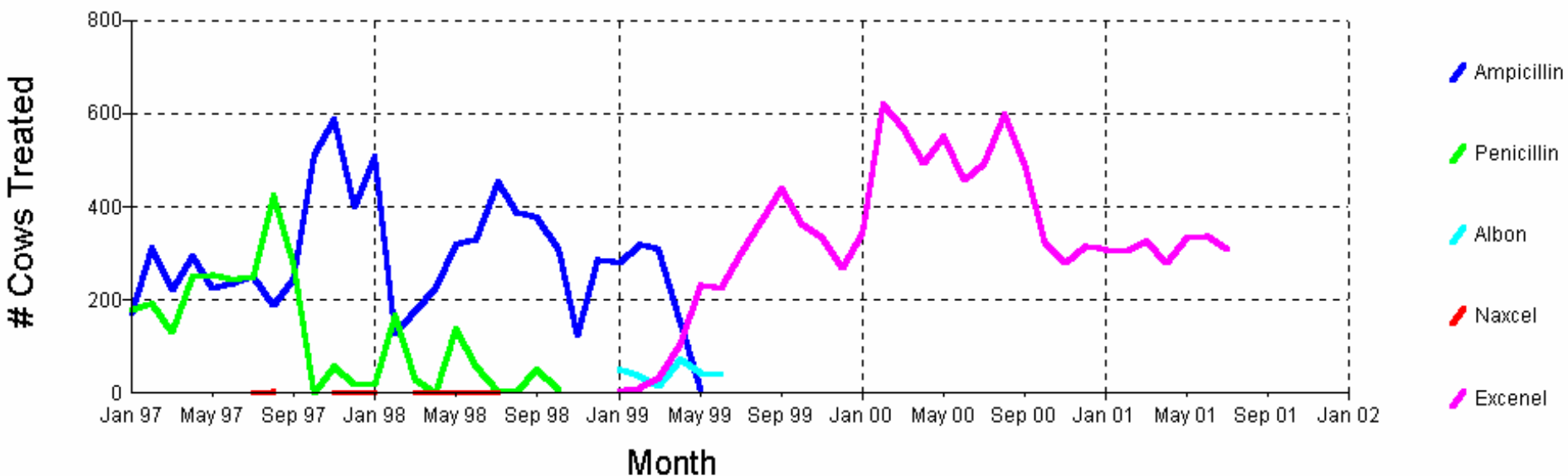
5.5 % of Isolates Resistant

21.2% of Isolates Resistant

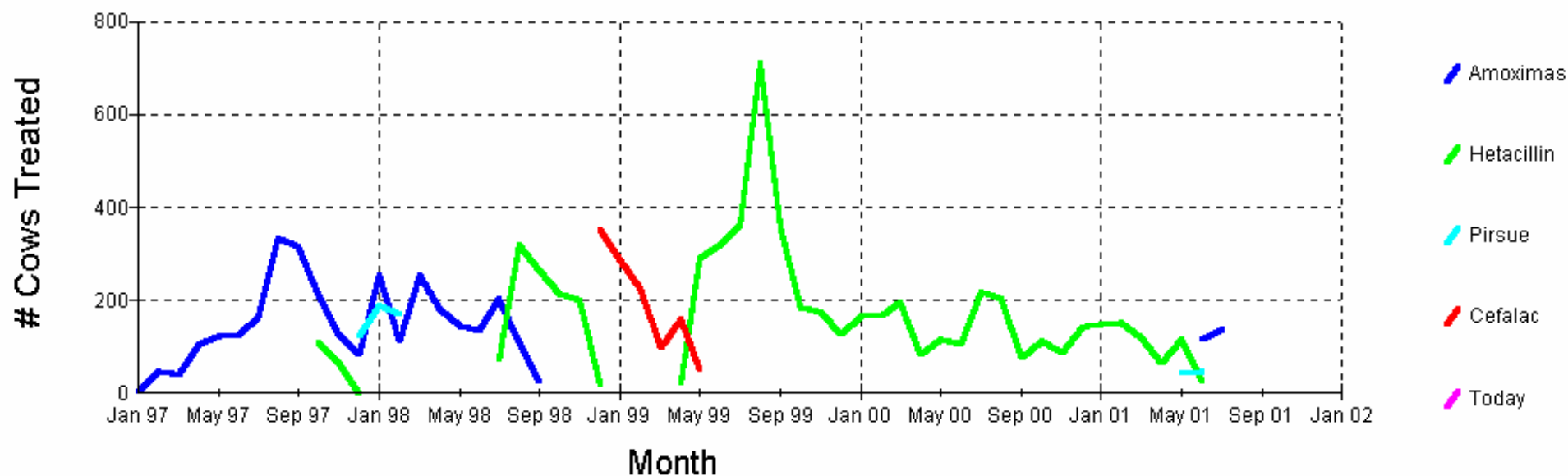
Schematic of Dairy Layout and Antimicrobial Use



Antimicrobial Drug for Fresh Cows vs Time



Antimicrobial Drug Use For Mastitis vs Time



Percentage of Isolates Resistant to Antimicrobials

Antimicrobial	Year		Serotype				Age	
	1999	2000	A	B	C	D	Adult	Calf
Streptomycin	22.5	19.7	9.0 ^{ab}	77.2 ^{acd}	0 ^{bc}	4.5 ^d	19.2	26.9
Tetracycline	2.7 ^f	8.8 ^f	8.2	4.0	0	3.6	3.3 ^g	10.2 ^g
Other antimicrobials	1.9	2.6	2.6	4.0	0	0.9	2.0	3.0
Resistant to one or more	23.3	20.6	10.7 ^{kl}	77.2 ^{kmn}	0 ^{lm}	4.5 ⁿ	20.2	27.5
Resistant to multiple	4.2 ^p	9.6 ^p	9.9	5.0	0	4.5	4.6 ^q	11.4 ^q

A = S Montevideo

B = S Kentucky

C = S Anatum

D = Other

Percentage of Isolates Resistant to Antimicrobials

Antimicrobial	Source				Use	
	Feed	Milk	Environment	Fecal	Yes	No
Streptomycin	0 ^e	18.2	27.3 ^e	21.5	23.0	18.8
Tetracycline	0	9.1 ^h	10.2 ⁱ	3.4 ^{hi}	8.5 ^j	1.4 ^j
Other antimicrobials	0	3.4	5.7	1.0	2.8	1.4
Resistant to one or more	0 ^o	19.3	28.4 ^o	22.1	23.7	19.8
Resistant to multiple	0	10.2	12.5 ^r	4.4 ^r	9.5 ^s	2.9 ^s

Logistic Regression Analysis

- Forward stepwise regression
 - entry at $p < 0.05$
 - removal at $p > 0.1$
- Outcomes
 - Resistance to Streptomycin
 - Resistance to Tetracycline
 - Resistance to Multiple Antibiotics
- Covariates
 - Age
 - Year
 - Serotype (S Montevideo, S Kentucky, S Anatum, other)
 - Antimicrobial use in location
 - Sample type (Feed, Milk, Environment, Fecal)

Logistic Regression

Resistance to Tetracycline

- Sample type (compared to fecal)
 - Milk OR = 41.5 (P < 0.001)
 - Environment OR = 10.0 (P < 0.001)
- Age
 - Young stock OR = 28.7 (P < 0.001)

Logistic Regression

Resistance to Streptomycin

- Serotype (compared to S Montevideo)
 - S Kentucky OR = 32.6 (P < 0.001)

Logistic Regression

Resistance to Multiple Antimicrobials

- Sample type (compared to fecal)
 - Milk OR = 14.8 (P < 0.001)
 - Environment OR = 7.6 (P < 0.001)
- Age
 - Young stock OR = 11.2 (P < 0.001)

Conclusions

- The prevalence of Salmonella on the Dairy is high.
- Salmonella prevalence varies seasonally.
- Fecal Salmonella shedding varies during the production cycle.
- The environment acts as a dynamic reservoir of Salmonella.
- Waste water perpetuates cycling of Salmonella.
- Salmonella contamination of milk occurs frequently.

Conclusions

- On this farm antimicrobial resistance to therapeutic drug use is minimal.
- Antimicrobial resistance to prophylactic antimicrobials was observed.
- Isolates from young stock were more likely to be resistant to antimicrobials.
- Isolates from the environment were more likely to be resistant to antimicrobials than fecal isolates.
- Isolates from milk were more likely to be resistant to antimicrobials than fecal isolates.

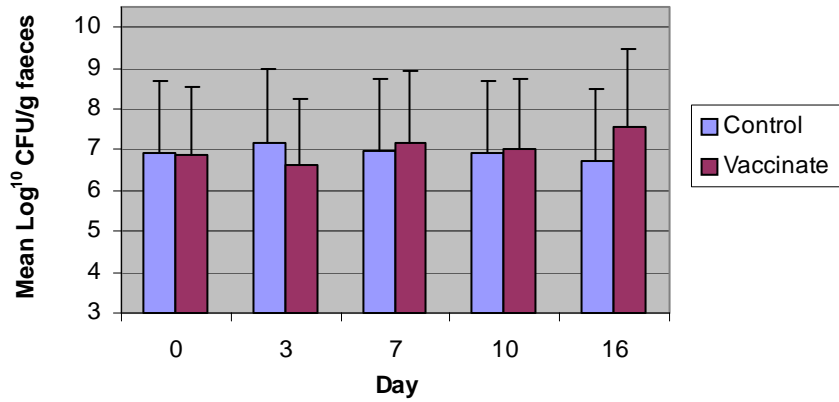
Interpreting Antimicrobial Resistance on the Farm

- When do we request a culture and sensitivity?
- Milk
- Faeces
- Blood
- Nasal swabs
- Urine
- Tracheal wash
- Tissues

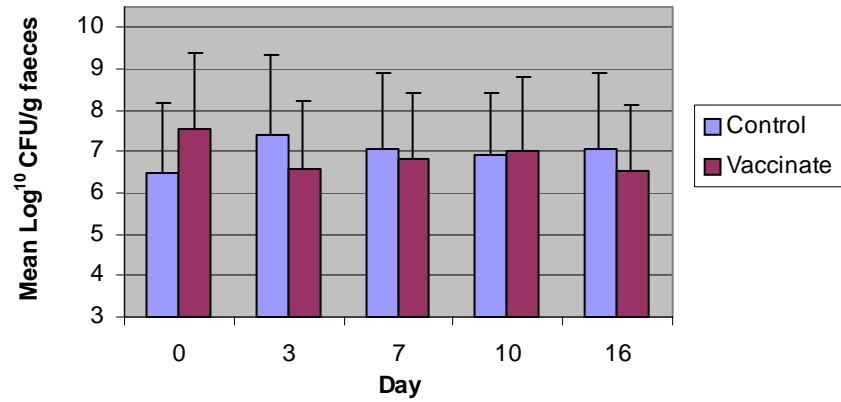


What does it mean

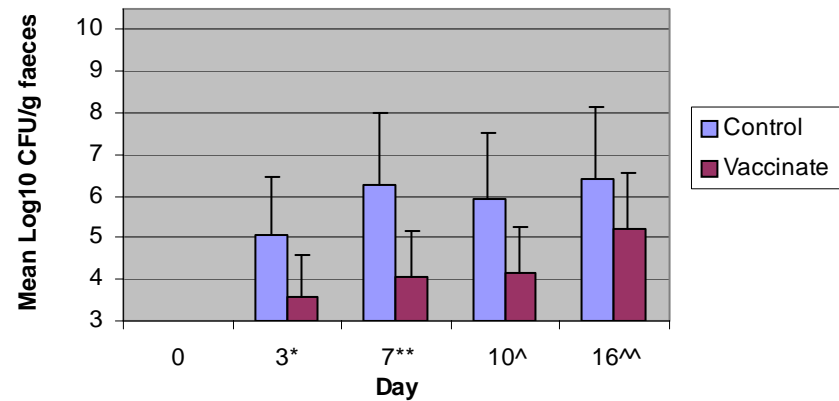
Faecal Coliforms Resistant to Ampicillin



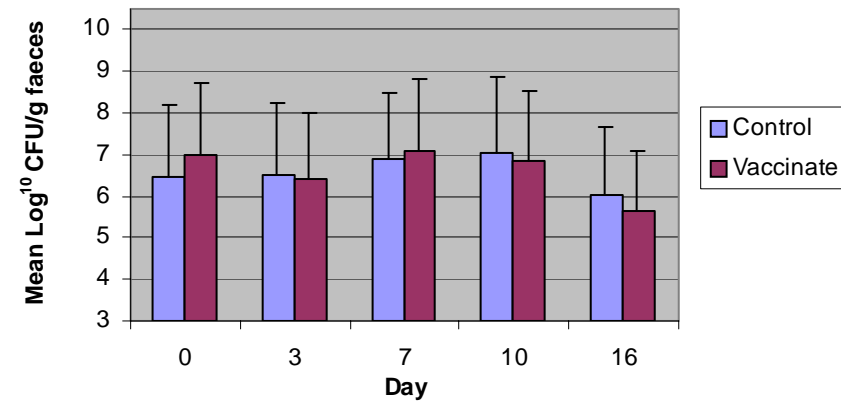
Faecal Coliforms Resistant to Oxytetracycline



Faecal Coliforms Resistant to Ceftiofur



Faecal Coliforms Resistant to Neomycin



Questions ?