



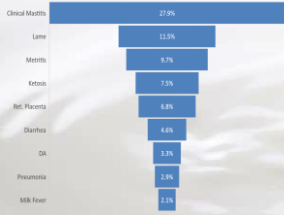
Treatment of Clinical Mastitis The past, present and future

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1

Mastitis is the Most Frequent Disease of Adult Dairy Cows

Incidence (1st cases) of Diseases in 37 WI Dairy Herds



Disease	Incidence (%)
Clinical Mastitis	27.9%
Lameness	15.5%
Mastitis	9.7%
Ketosis	7.5%
Ret. Placenta	6.6%
Diarrhea	4.6%
DA	3.3%
Pneumonia	2.9%
Milk Fever	2.1%

About 15 - 35% of cows have subclinical mastitis everyday

About 20 - 40% of cows develop a clinical case each lactation

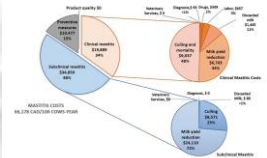
Goncalves, Leite de Campos, Ruegg, et al., 2021 preliminary data

2

Mastitis is the Most Costly Disease of Dairy Cattle

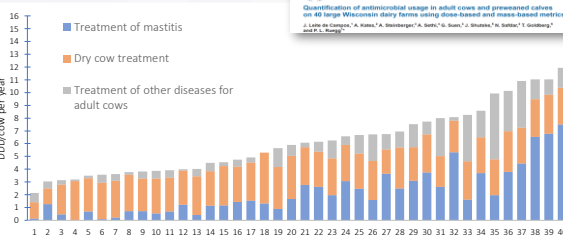
- Mastitis has direct and indirect economic consequences
 - Direct
 - Reduced Milk Yield
 - Reduced Value of Milk
 - Discarded milk
 - Cost of Treatment & Prevention
 - Indirect
 - Reduced Reproductive performance
 - Final product quality
 - Ability to sell milk
- Opportunity costs
 - Value of inputs used to reduce risk of mastitis
 - Udder preparation
 - Teat dips
 - Bedding

- Mastitis was estimated to cost \$662 CDN per cow per year (from Aghamohammadi et al., 2018)
 - 48% Subclinical losses
 - 34% Clinical mastitis losses
 - 15% Use of preventive measures



3

Mastitis Treatment Accounts for the Most Doses per Cow per year of Antibiotic



DDC/cow per year

Treatment of mastitis

Dry cow treatment

Treatment of other diseases for adult cows

Farms

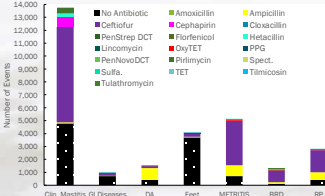
J. Dairy Sci. 105:1-108
https://doi.org/10.3168/jds.2021-19125
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4

3rd Generation Cephalosporins are Most Common Drug Used to Treat Mastitis

- Antibiotics have been classified relative to their value for treating humans
- Highest priority critically important Should only be used if other less important antibiotics will not be effective
 - Fluoroquinolones
 - Baytril™
 - Macrolides
 - Tylan™
 - 4th Generation cephalosporin
 - none in US
 - 3rd Generation cephalosporins
 - SpectramastLC™ & DC™
 - Exceld™, Excenel™, Naxcel™

Use of Antimicrobials to Treat 1st Cases of Disease in Dairy Cattle on 37 WI Dairy Farms



Number of Events

Clin. Mastitis GI Diseases DA Feet METRITIS BRD RP

Goncalves, Leite de Campos and Ruegg, 2021 preliminary data

9

Objective

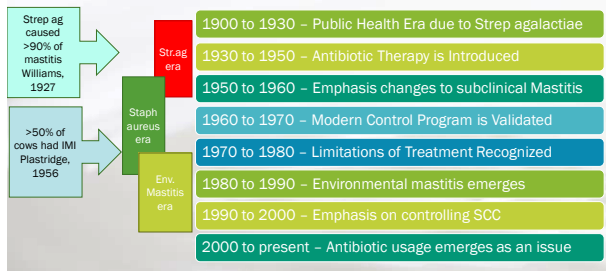
Discuss:

- Historical basis of mastitis therapy
- Options for improving current therapies
- Forecast future trends that will influence treatment of bovine mastitis



10

Treatment of Mastitis – THE PAST



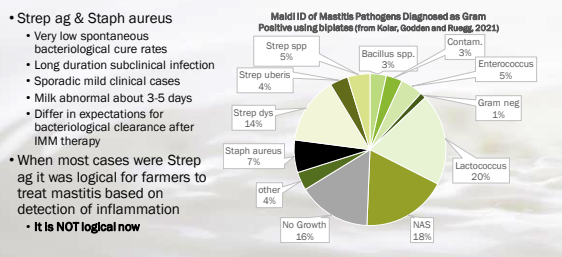
11

6 of 7 IMM products in N.America Were developed to Treat Strep ag & Staph aureus

	Amox-Mast	Polymest	DariClox	Mast-Clear	Pirauve	Spectra-mastLC	Today
Active Ingredient	Amoxicillin	Ampicillin	Cloxacillin	Penicillin	Pirlimycin	Ceftiofur	Cephapirin
Label Claim	Str ag	YES	YES	YES	YES		
	S aureus	YES	YES	YES	YES		YES
	Str dys.				YES	YES	
	Strp ub.				YES	YES	
Other		E. coli				CNS & E coli	
Label Dosing & Duration	3 tubes @ 12 h	3 tubes @ 24 h	3 tubes @ 12 h	3 tubes @ 12 h	2-8 tubes @ 24 h	2-8 tubes @ 24 h	2 tubes @ 12 h
Company	Merck	BI	Merck	Hanford	Zoetis	Zoetis	BI

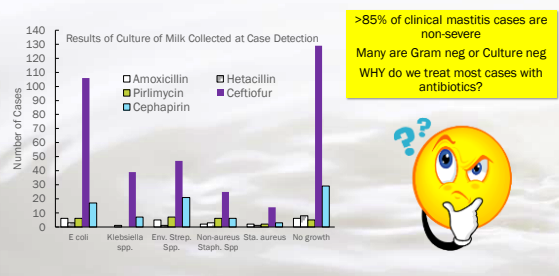
12

Our “normal” treatment strategies were developed to treat non-severe mastitis caused by Strep ag



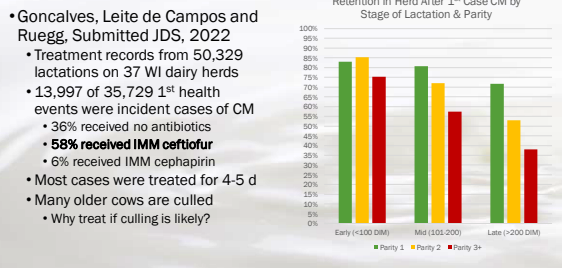
13

Treatments given to 558 cases of CM on 51 WI dairy farms in 2010



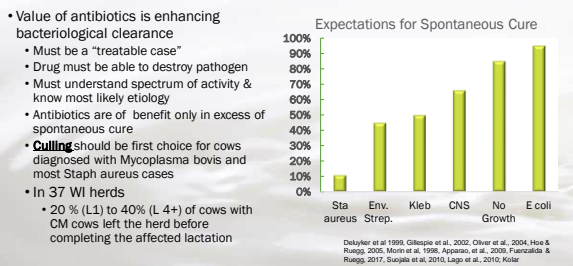
14

Treatment of Mastitis – THE PRESENT



15

When are Antibiotics Helpful?



16

Appropriate Treatment of Non-Severe Primary Cases of Clinical Mastitis

- Most non-severe cases on most farms should not receive antibiotics
- Must have knowledge of types of pathogens present on the farm
- When possible, should be selective therapy based on culture results
 - IMM antibiotics for Gram +
 - Systemic therapy reserved for sick cows
 - Don't treat chronic cows
 - Review SCC and health history of cow before using AB
- Standard protocols should follow label guidelines
 - When no AB are given, the cow must be able to mount effective immune response
- When the pathogen is not known,
 - The duration of IMM therapy should be short



Large Dairy Herd Management <http://ldhm.adsa.org/>

17

What about Non-Antimicrobial Treatments?

- Francoz et al., 2017: Systematic review of alternative mastitis treatments
- Included 41 trials from 39 manuscripts
 - 1990 through 2014
- Biologics: n = 9 studies
- Homeopathy: n = 5 studies
- Probiotics: n = 2 studies
- Vitamin derivatives: n = 2 studies
- Oxytocin +/- frequent milking: n = 5 studies
- Anti-inflammatory drugs: n = 14 studies



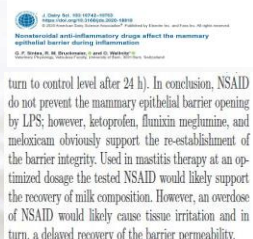
No evidence of efficacy for oxytocin, homeopathic remedies and probiotics

Limited power to identify treatment effects in most studies

18

What about NSAID?

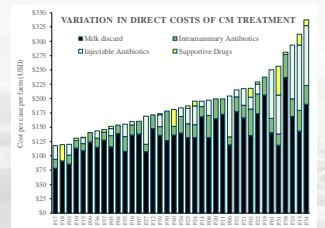
- Corticosteroids & NSAIDs have been evaluated for mastitis therapy based on reduction of inflammation & mediation of endotoxin induced effects
- Steroids impair neutrophil function & have been replaced by NSAID
- Most studies of NSAID efficacy are experimental challenges with LPS or E Coli
- Conflicting results are common
 - No consistent impact on clinical signs
 - Breen 2017, Livestock 22:182-185
- Pain control of moderate or severe cases is best justification of use



19

Present Trends in Mastitis Treatment

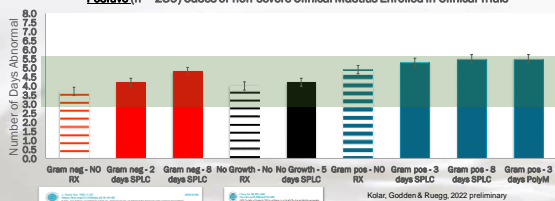
1. Reduced duration of IMM treatments
2. Greater adoption of selective treatment protocols
3. Increased adoption of "no AB treatment" for mastitis



20

Milk is Abnormal for 3 – 5.5 Days With or Without Treatment

Days of Abnormal Milk for **Gram-negative** (n = 168), **Culture-Negative** (N = 124) & **Gram Positive** (n = 239) Cases of non-severe Clinical Mastitis Enrolled in Clinical Trials



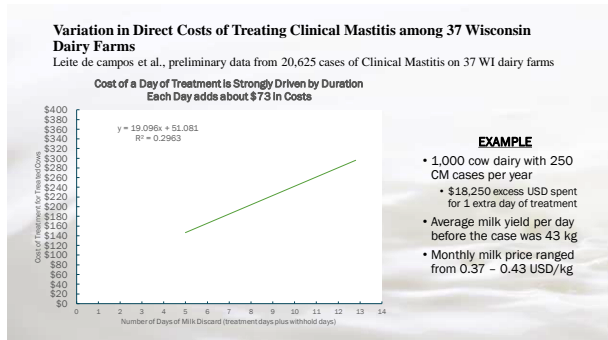
21

Impact of Extralabel treatment on Costs Use of IMM Antibiotics on 40 WI dairy farms

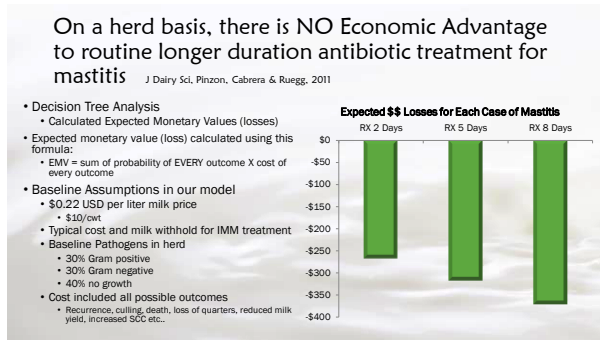
Leite de Campos, et al., 2022 preliminary

Product	Herds (n)	(n)	%	Tube price	Label Directions			Observed Rx ± Withhold	Cost per case (USD)			Excess Cost per Case
					Doses per day	Days	Withhold		Observed Mean	Label Mean	Observed Mean	
Amoxicillin	6	88	1%	\$3.15	2	1.5	2.5	4.0	6.9	\$77.50	\$151.15	\$37.65
Ceftiofur hydroxyl	32	7368	82%	\$3.77	1	2-8	3.0	5-11	8.0	\$93.56	\$156.52	\$62.96
Cephapirin sodium	13	846	0%	\$2.78	2	1	4.0	5.0	8.1	\$87.72	\$151.78	\$64.06
Groscocin sodium	1	1	<1%	\$4.99	1.5	1.5	2.0	3.5	4.0	\$77.61	\$90.13	\$12.52
Hetacillin potassium	9	273	3%	\$2.76	1	3	3.0	6.0	6.6	\$120.25	\$132.87	\$12.62
Pivmecillinam hydroxyl	12	363	4%	\$3.90	1	2-8	1.5	3.5-9.5	6.1	\$66.93	\$118.34	\$51.41

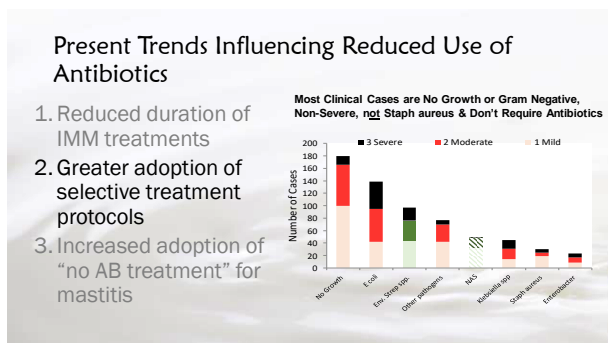
22



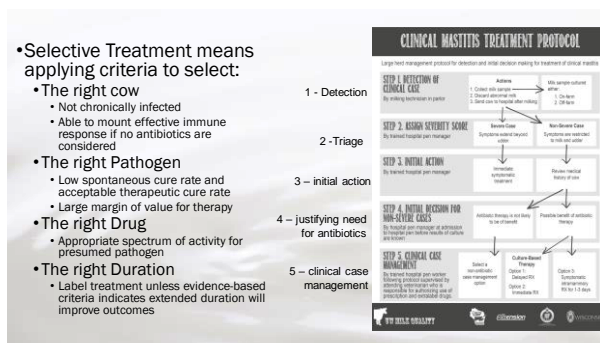
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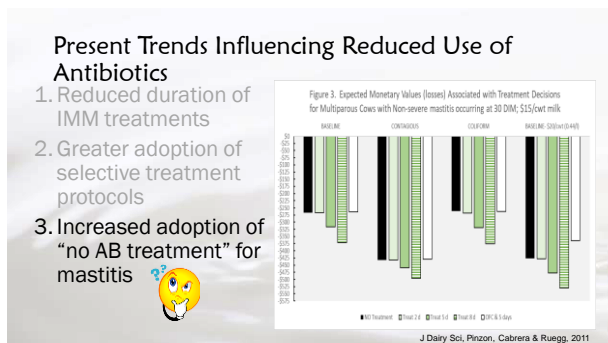
24



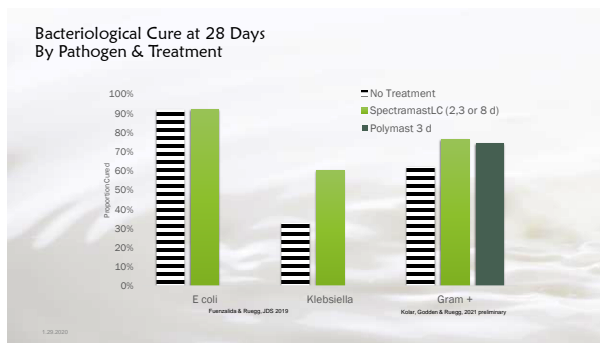
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26



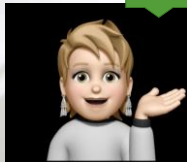
27



28

Treatment of Mastitis: The FUTURE

You can quote me on this...



It is highly unlikely that new treatments for mastitis that contain medically important antimicrobials will be approved in the future

Reducing use of broad spectrum antimicrobials on dairy farms will be an emphasis

29

The Future: New Treatments?

- Lots of substances have been tested
 - Phages
 - Nanoparticles
 - Bacteriocins
 - Lactoferrin
 - Botanicals etc...
- Many are tested against Staph aureus
 - Solution in search of a problem in the field
 - Likely a limited commercial market
 - Many producers have solved this problem
- Approval of new broad spectrum antibiotics for treatment of mastitis is not likely in the US
- Future new therapies will likely be narrow spectrum and directed against Gram positive organisms
 - Dependent on improved point of care tests
- Increased introduction of non-invasive non-antimicrobial therapies
 - that can be marketed without FDA approval if no explicit mastitis efficacy claim
 - Acoustic pulse therapy
 - Immunomodulatory feed additives
 - Others...

Ask for Independent Efficacy Data!



30

Conclusion

- Current mastitis treatment protocols are based on lessons learned during a past era and are gradually evolving
- Antibiotic treatment of non-severe mastitis based on detection of abnormal milk in an otherwise healthy cow is **wrong more frequently than it is right**
- Improved diagnostic tests to guide mastitis therapy are needed
- There are many **cow-level Indicators** that can be used to reduce reliance on antibiotics
- What we can do **today** to improve mastitis treatments
 - Use **shorter duration IMM** treatment
 - Follow label of short duration IMM products
 - Reduce the duration by 1 day of flexible duration products
 - Culture **more clinical mastitis** cases
 - use data to make antibiotic usage decisions
 - Cull (don't treat) cows infected with Staph aureus
 - Use **narrower spectrum** drugs unless you are treating a case that is outside the spectrum of activity of the product

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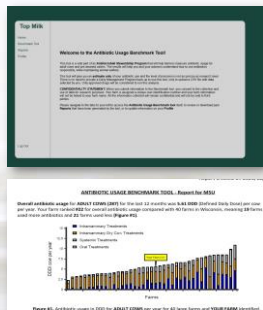
31

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32

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33

Many Thanks to My MSU Team

- Juliana Leite de Campos & Quinn Kolar
 - PhD candidates in Animal Science
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 - MS student in CMIB
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 - Postdoctoral Researchers
- Carolina Pinzon-Sanchez
 - Outreach specialist
- Cara Robison
 - Lab Manager



34