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ICPD Review

-

Reproduktionsmedizin

Karen Wagener, Heiner Bollwein

Barry Bradford (USA)



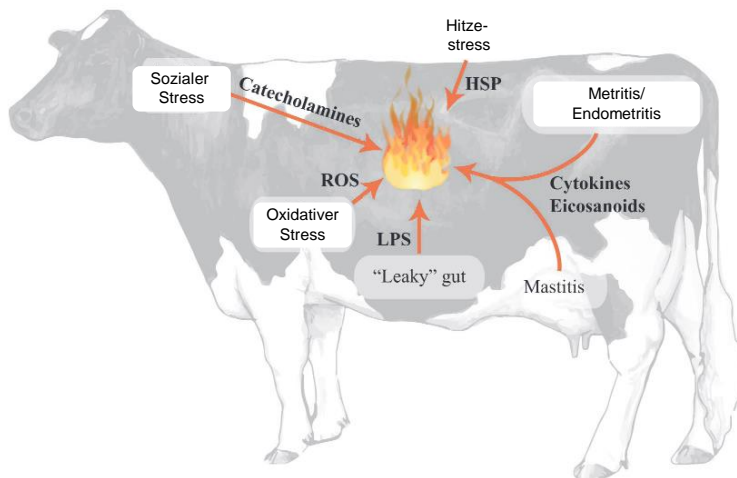
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**Toward a homeostatic view of inflammation:
The transition dairy cow example**



Department of Animal Sciences and Industry
Kansas State University, USA



(Bradford, 2015) 3



J. Dairy Sci. 100:582–587
<https://doi.org/10.3168/jds.2016-11747>
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The effects of periparturient administration of flunixin meglumine on the health and production of dairy cattle

N. C. Newby,* K. E. Leslie,* H. D. Putnam Dingwell,* D. F. Kelton,* D. M. Weary,† L. Neuder,‡ S. T. Millman,§ and T. F. Duffield*¹

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• Zu Studienbeginn:

- Behandlungsgruppe (n=38) Flunixin Behandlung 24h vor der Abkalbung
- Kontrollgruppe (n=34) Placebo
 - → Totgeburtenrate ↑↑↑↑ (PGF_{2α} Reduktion)
 - 27% Behandlungsgruppe vs 5% Kontrollgruppe

• Protokolländerung:

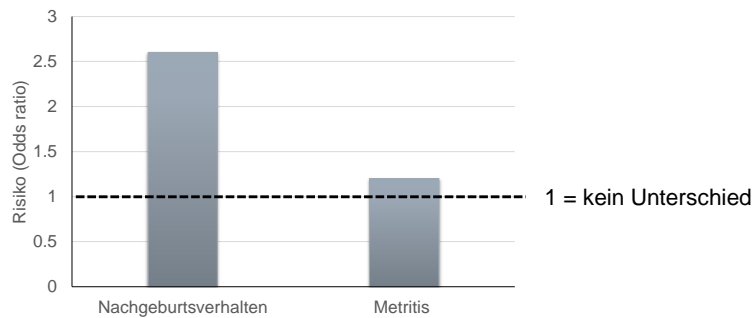
- Behandlungsgruppe (n=660) Flunixin Behandlung 1h und 24h post partum
- Kontrollgruppe (n=661) Placebo

(Newby, 2017)

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Die Behandlung mit NSAID wirkt sich negativ auf das Erkrankungsrisiko aus

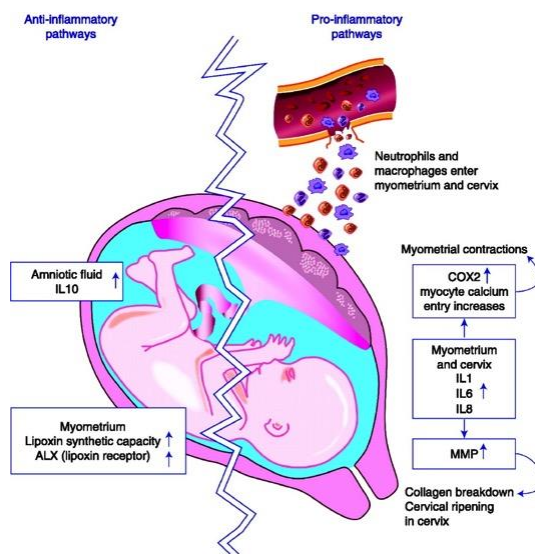
Risiko für das Auftreten von Nachgeburtsverhalten und Metrits in der Behandlungsgruppe war gegenüber der Kontrollgruppe erhöht



(Newby, 2017)

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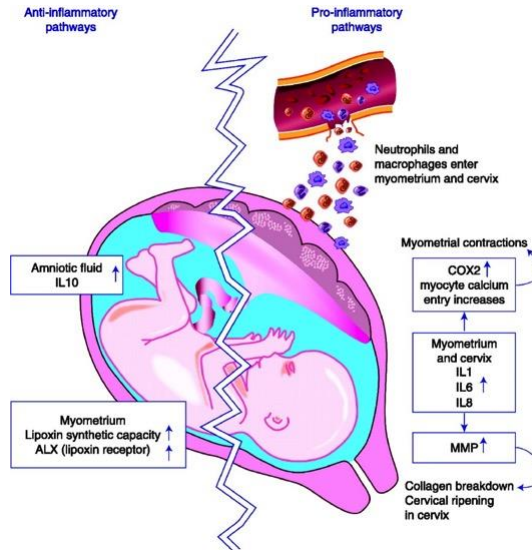
Entzündung ist wichtig für die Geburt



(Jabour, 2009)

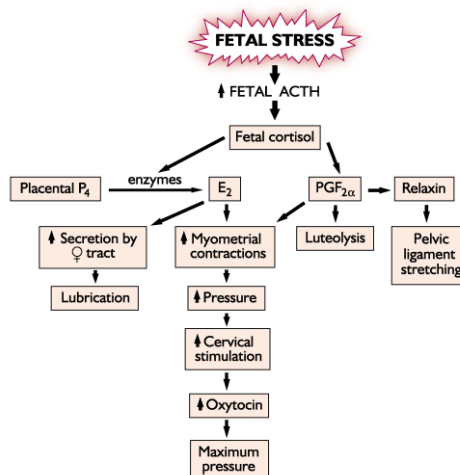
6

Entzündung ist wichtig für die Geburt



(Jabbour, 2009)

Einleitung der Geburt



Metabolism and host-pathogen interactions shape the development of uterine disease in dairy cows



Institute of Life Science, College of Medicine,
Swansea University, Swansea, GB

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Entstehung von Gebärmutterentzündungen

Einleitung

Bakterien, die Gebärmutterentzündung verursachen

- Pathogene/bedingt-pathogene Keime
 - *E. coli*, *T. pyogenes* (Westermann et al. 2010)
 - *F. necrophorum*, *Bacteroides*

(Drillich et al. 2001; Werner et al. 2012)



E. coli



T. pyogenes



Endometritis

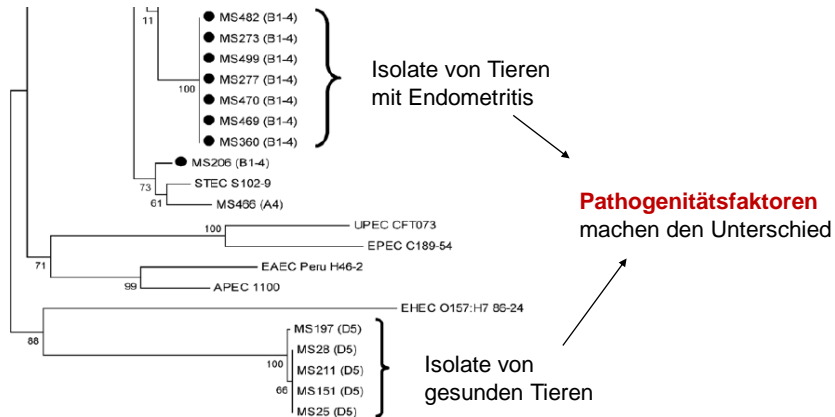
Wovon hängt die Pathogenität der Bakterien ab?



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E. coli ist nicht *E. coli*



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Wovon hängt die Pathogenität der Bakterien ab?

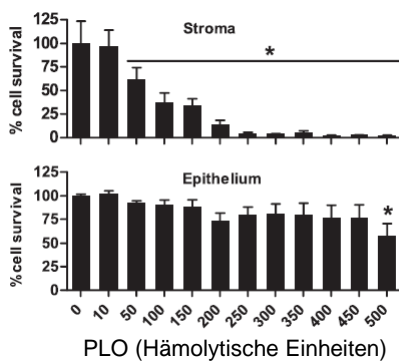


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T. pyogenes

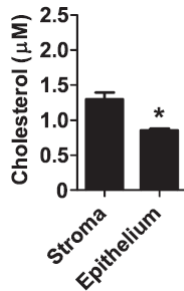
- Pathogenitätsfaktor ist das PLO = Poren-formendes Toxin
- **ABER:** alle *T. pyogenes* Stämme besitzen das PLO



Die Integrität des Endometriums
macht den Unterschied

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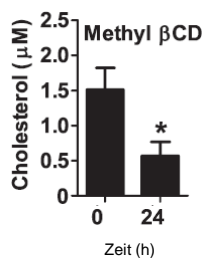
PLO von *T. pyogenes* ist Cholesterin abhängig



- Stromazellen beinhalten mehr Cholesterin
- Cyclodextrin als Behandlungsmethode?
 - Humanforschung: Atherosklerose Therapie (bisher nicht zugelassen)
 - Wirkung: Reduzieren Cholesterin in Plasmamembranen

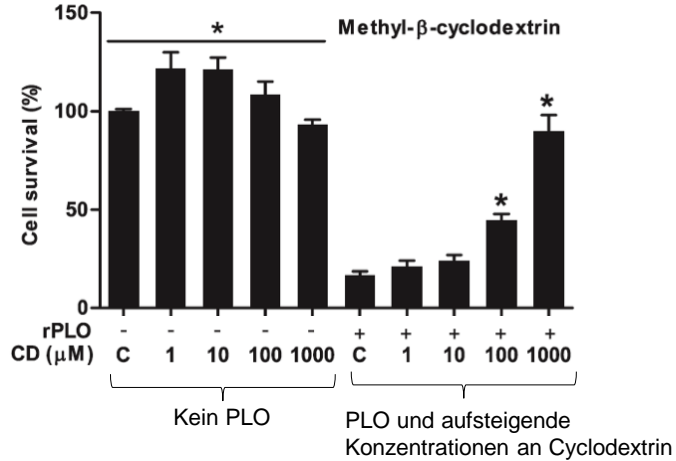
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Cyclodextrin reduziert Cholesterin in Stroma Zellen des Endometriums



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Cyclodextrin verhindert Zelltod von Stromazellen nach PLO Stimulation



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Geert Opsomer (BE)

Innovative insights in the interaction between metabolic stress and reproduction in high yielding dairy cows



Department of Obstetrics, Reproduction and Herd Health, Ghent University, Belgium

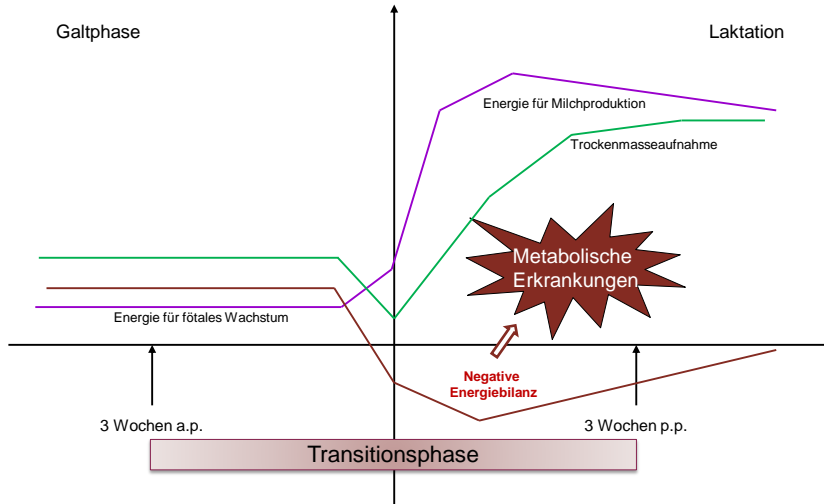
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Transitionsphase



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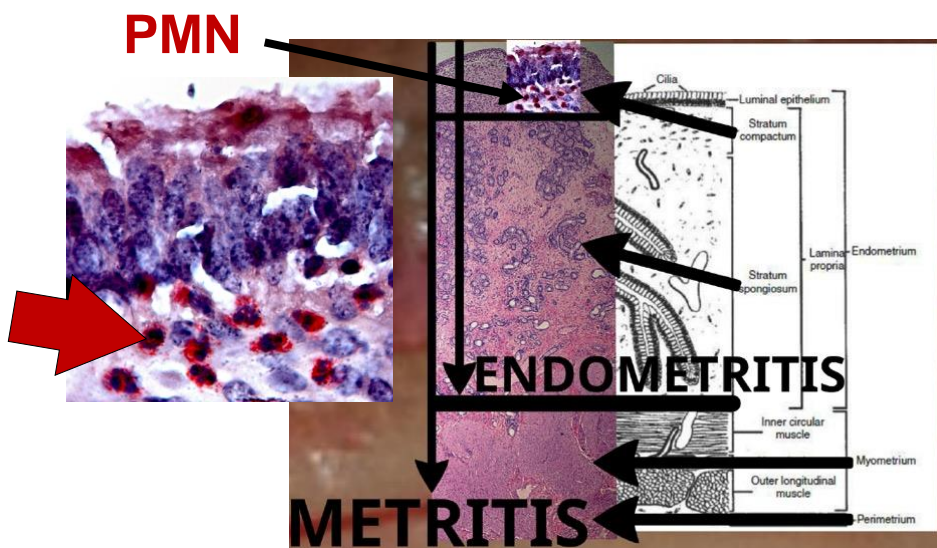
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Subklinische Endometritis

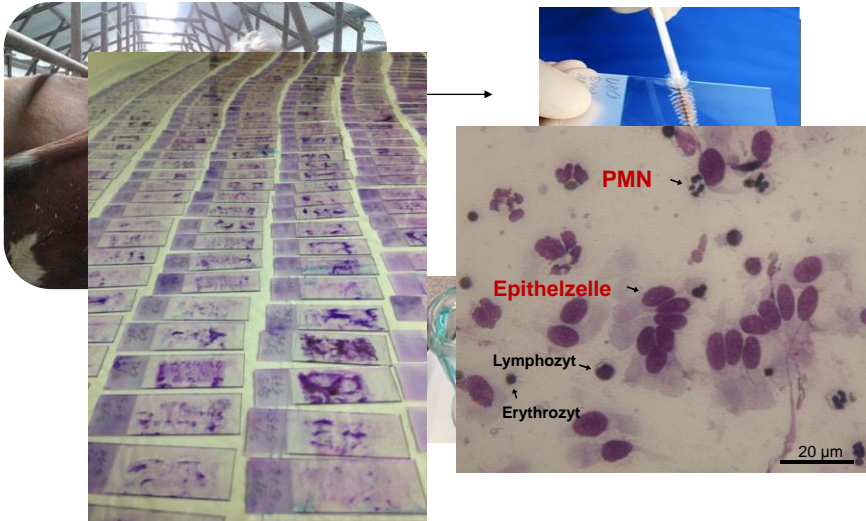


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Offene Fragen

- Wie viele Zellen zählen?
- PMN Schwellenwert in Abhängigkeit der Tage in Milch?
- Wiederholbarkeit und Reproduzierbarkeit?
- Zyklusstand bei der Probenentnahme?
- Wo die Probe nehmen (Uteruskörper, -horn)?

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PMN Schwellenwerte



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Thresholds for the diagnosis of subclinical endometritis and referring prevalence in dairy cows (selected references).

Reference	PMN threshold	Days postpartum	Prevalence
Barlund et al. [15]	8%	28–41	11.1%
Baranski et al. [18]	18%	21–28	18.9–75.4%
Cheong et al. [11]	10%	40–60	4.8–52.6% ^a
Galvão et al. [38]	6.5%	35	37.9–38.4% ^a
Gilbert et al. [12]	5%	40–60	37–74% ^a
Kasimanickam et al. [1]	18%	20–33	35.1%
	10%	34–47	34.0%
Kaufmann et al. [49]	18%	28–35	12.4%
Madoz et al. [9]	5%	21–62	17%
Plöntzke et al. [10]	5%	18–38	38%
Ribeiro et al. [46]	5%	46–52	13.4%
Sens and Heuwieser [17]	18%	21–27	13.4%

^a Authors did not exclude cows with clinical endometritis.

(Wagener, 2017)

Seite 21

PMN Probenentnahme während der KB



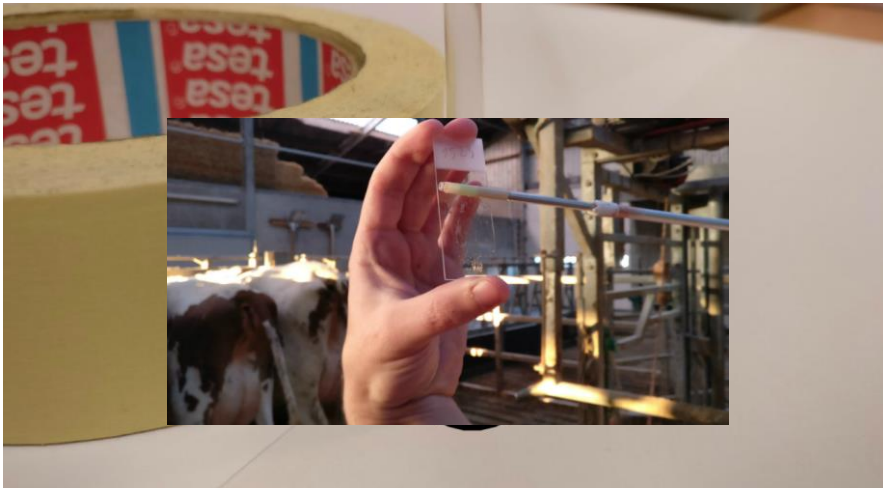
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(Pascottini, 2015)

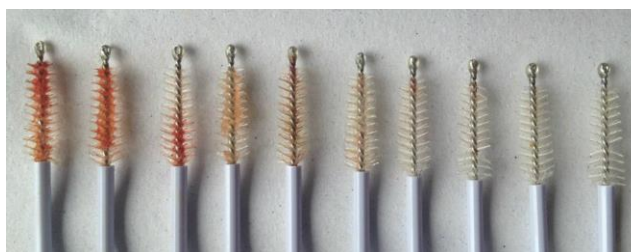
Seite 22



(Pascottini, 2015) Seite 23

Cytotape vs. Cytobrush

- PMN% ähnlich
- Keine Unterschiede in der Zellularität
- Cytobrush ist blutiger
- Cytotape zeigt Proben besserer Qualität



(Pascottini, 2015)

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- 1625 KBs bei 873 Kühen (Parität ≥ 1)
- Während KB Cytotape Beprobung
- ROC Analyse: PMN% \rightarrow 1%
- SE Prävalenz: 27.9%
- Konzeptionsraten: SE positiv: 32.7%; SE negativ: 47.1%
- Wahrscheinlichkeit einer Trächtigkeit war 1.79 mal höher bei SE negativen Tieren

(Pascottini, 2015) 25



- Risiko an SE zu erkranken
- Erhöht
 - bei Parität ≥ 2
 - Warme Jahreszeit (Juli, August, September)
- Erniedrigt
 - Spätere KB (≥ 124 DIM)

(Pascottini, 2015) 26

- 496 KBs bei 359 Rindern
- Während KB Cytotape Beprobung
- ROC Analyse: PMN% → 1%
- SE Prävalenz: 7.9%
- Konzeptionsraten: SE positiv: 38.5%; SE negativ: 62.8%

- Risikofaktoren für SE: vorhergehende erfolglose KB

(Pascottini, 2015) 27

- Biomarker (Cytokine)
(Gabler, 2009; Fischer, 2010)

- Biopsie, Ultraschall
(Lenz, 2007; Rodenbusch, 2007; Chapwanya, 2010)

- Urinteststreifen
(Cheong, 2012; Couto, 2013; Pascottini, 2018)

- Optische Dichte nach Lavage
(Machado, 2012)

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Einheitliche Aussagen in der Endometritisforschung...



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- Genereller Schwellenwert von 5% PMN zwischen Tag 21 und 62 pp
- Genauigkeit und Wiederholbarkeit bei der mikroskopischen Untersuchung ist hoch (300 Zellen zählen)
- Hohe Prävalenz (20-40%)
- Negativer Effekt auf Fruchtbarkeit (niedrigere Konzeptionsrate, verlängerte Rast- und Service Periode)
- Wahrscheinlich keine pathogenen Keime beteiligt

(Wagener, 2017) 29

José Santos (USA)



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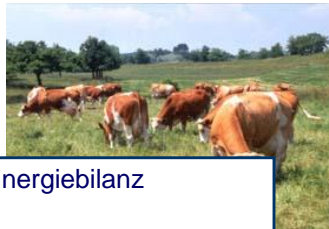
Mechanisms and impact of inflammatory diseases on reproduction in dairy cows



Department of Animal Sciences, University of Florida, Gainesville, Florida, USA



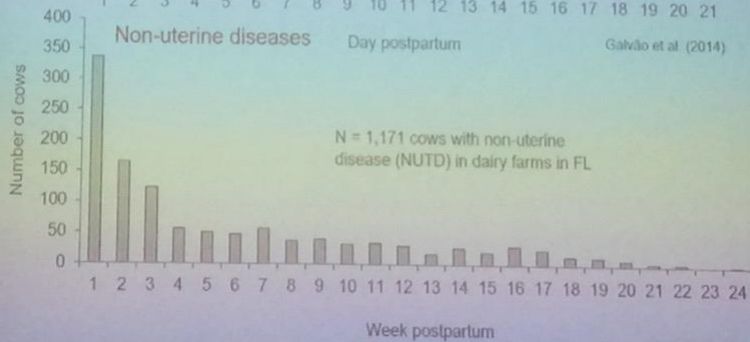
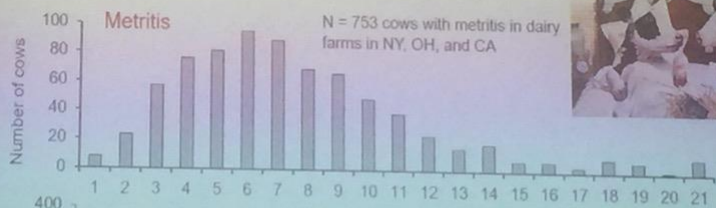
30



- ausgeprägte negative Energiebilanz
- gestörte Immunfunktion
- hohe Inzidenz von Produktionskrankheiten

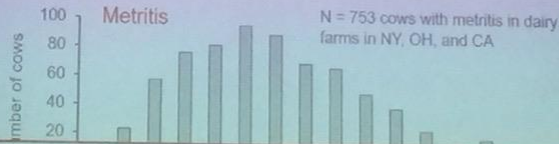


Morbidity is a Problem of Early Lactation Cows



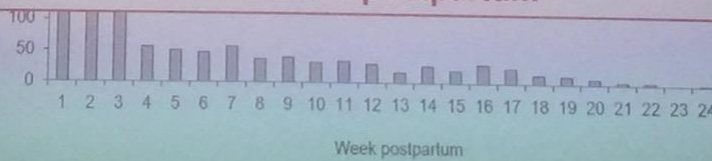
Ribeiro et al. (2016) J. Dairy Sci. 99: 2201-2220

Morbidity is a Problem of Early Lactation Cows



30 to 35% of cows are affected by disease in the first 3 weeks of lactation

78% the first disease diagnosis occurs within the first 3 weeks postpartum



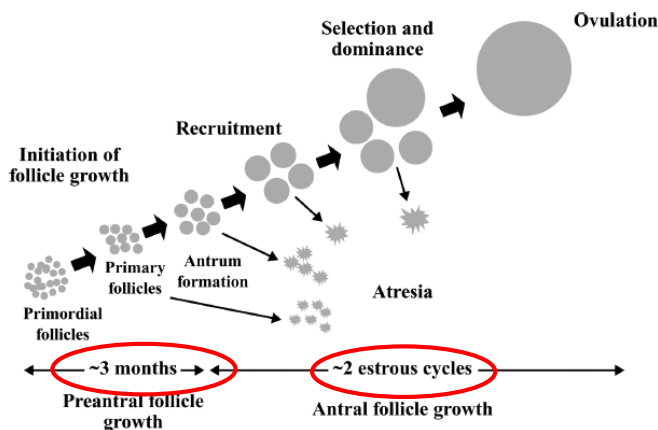
Ribeiro et al. (2016) J. Dairy Sci. 99: 2201-2220

Langzeiteffekte auf die Follikel



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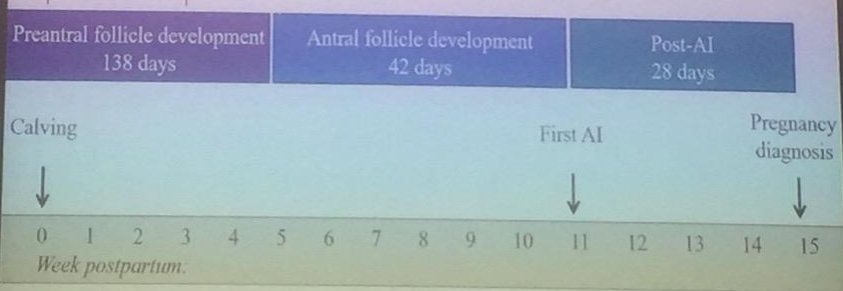
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(Webb et al., 2003)

Timing of Diagnosis of Diseases and Fertiity

78% of the cows distressed by diseases had the first diagnosis in the first 3 wks postpartum.
100% of UTD
53% of NUTD



Ribeiro et al. (2016) J. Dairy Sci. 99:2201-2220

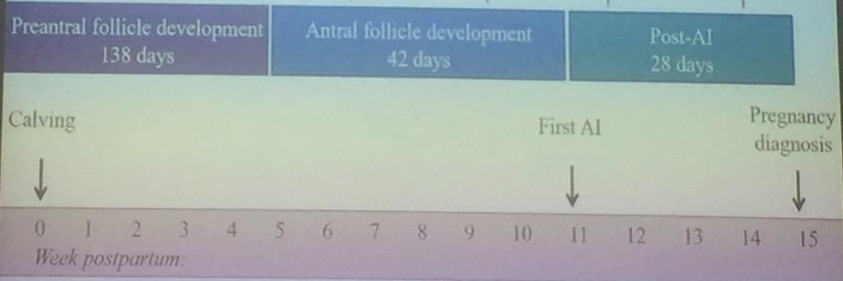
Timing of Diagnosis of Diseases and Fertiity

Incidence of NUTD

11.8%
n = 497

5.1%
n = 213

5.6%
n = 236



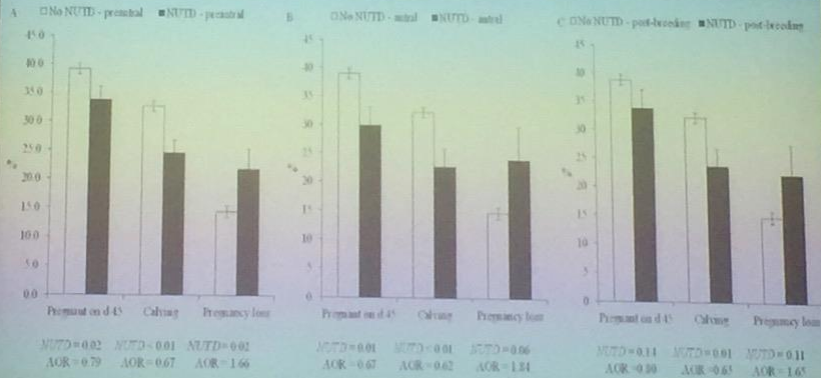
Ribeiro et al. (2016) J. Dairy Sci. 99:2201-2220

Timing of Diagnosis of Diseases and Fertility

Preantral follicle development
138 days

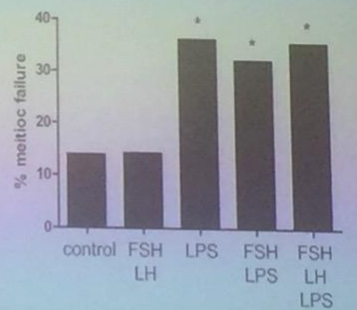
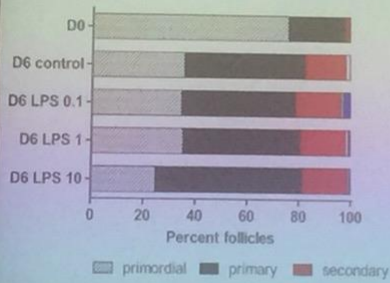
Antral follicle development
42 days

Post-AI
28 days



Ribeiro et al. (2016) J. Dairy Sci. 99:2201-2220

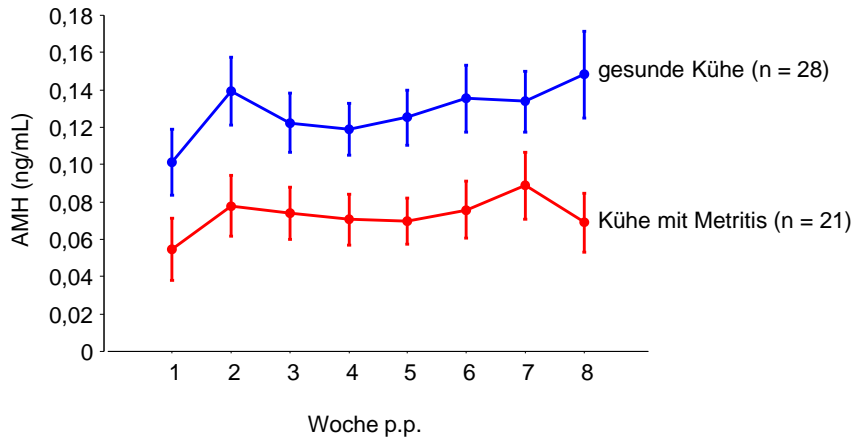
LPS increases primordial follicle activation and failure of meiotic division in oocytes



* $P < 0.05$

Bromfield and Sheldon (2013) Biol Reprod 88: 98

Bromfield e Sheldon (2011) Endocrinology 152: 5029



(Bollwein et al. unveröff.)

Post-insemination intrauterine treatment with cephapirin in dairy cows with mild endometritis

**K. Wagener¹, P. Panagiotis², U. Reinländer¹, R. Schlegl¹,
M. Ehling-Schulz², M. Drillich¹**

¹Clinical Unit for Herd Health Management in Ruminants

²Functional Microbiology, Institute for Microbiology

Vetmeduni Vienna, Austria

Introduction

- CE persisting beyond the end of the puerperal period (50 DIM)
 - Cows with an impaired immune function
 - No treatment during the puerperal period
 - Therapy resistant animals
- Mild CE at the time of artificial insemination
 - Prevalence up to 59% (Dubuc et al. 2010; Lambertz et al. 2014)



Introduction

- Possible strategies to manage cows with mild CE at AI
 - Postpone AI to next estrus with or without treatment
 - Days open ↑↑
 - Inseminate cow despite of mild CE
 - Pregnancy rate: ~17-30% (Pascottini et al. 2016)
 - Inseminate cow and perform Åström treatment
 - Original: intrauterine infusion of iodine-potassium solution 2 to 4 days after AI (Åström, 1935)
 - Detrimental effect of disinfectants on fertility (Heuwieser et al. 2000)



Introduction

- Modified Åström treatment: intrauterine treatment with cephalosporin
 - Poor scientific evidence of the benefit of this treatment strategy

➤ Objective of the study:

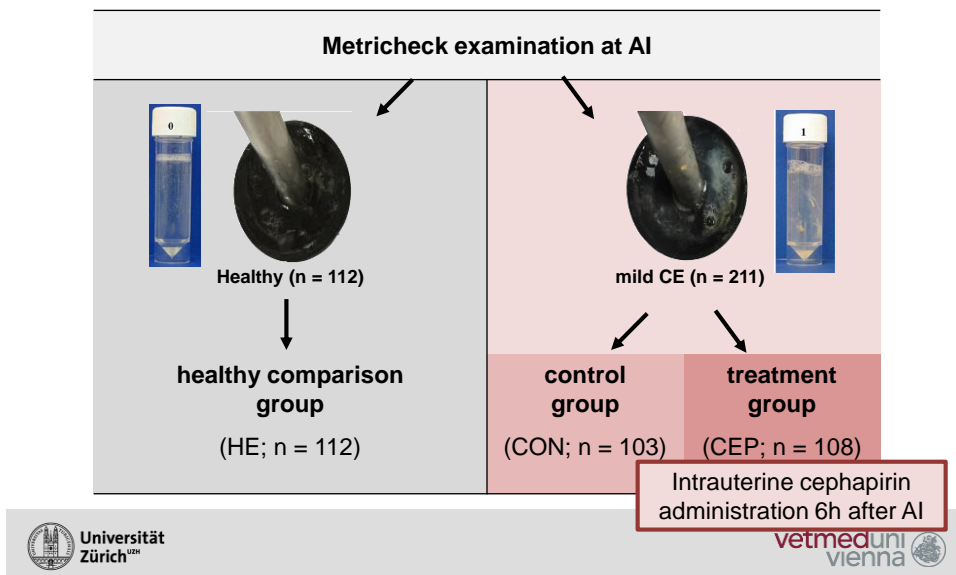
- To evaluate the effect of this modified Åström treatment in cows with mild CE at AI on pregnancy rates

Materials & Methods

- Study animals
 - 341 dairy cows previously enrolled in an Ovsynch program
- Metricek examination at AI
 - Assessment of uterine discharge



Materials & Methods



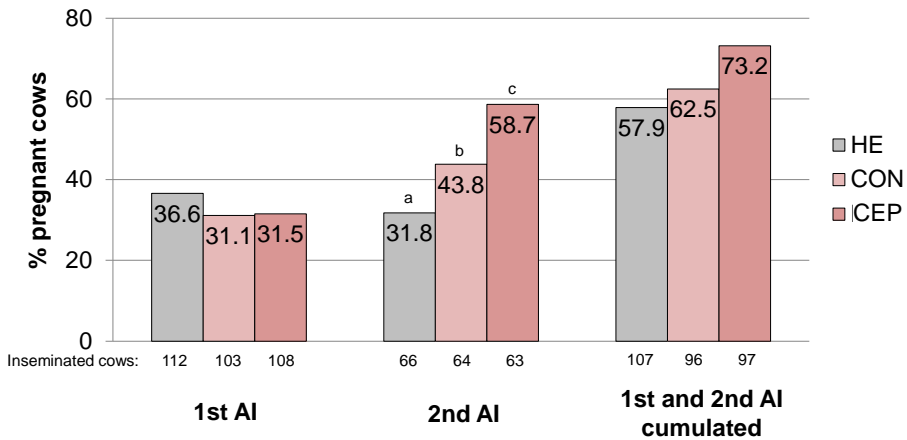
Materials & Methods

- Bacteriological examination
 - Uterine sampling with the Cytobrush technique (n = 62)

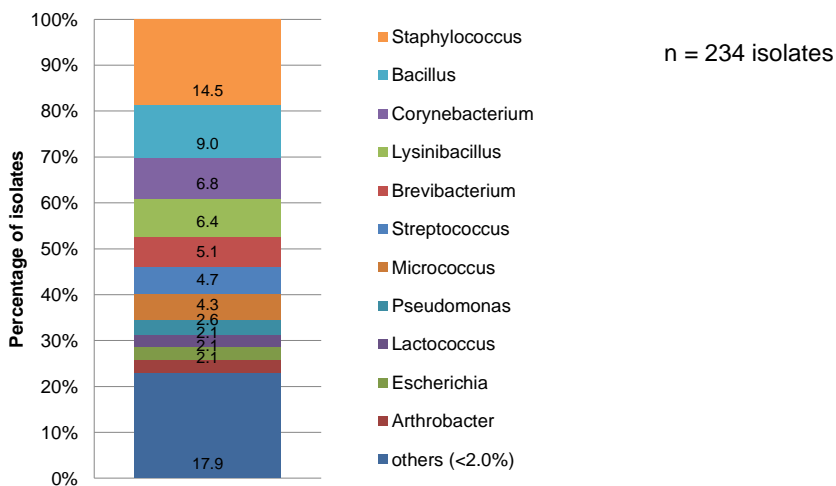


- Cultivation of bacteria
 - Identification by Matrix-Assisted Laser Desorption/Ionization-Time of Flight (MALDI-TOF)

Results - pregnancy diagnosis



Results – Bacteriological examination



Discussion

- No beneficial effects of cephalosporin treatment on fertility after first AI, but after the second AI after treatment
 - Hypothesis: Time between treatment and arrival of the fertilized oocyte was not sufficient to regenerate inflamed endometrium
- Pathogenic bacteria are not responsible for mild CE at AI
 - Future studies: Comparison of uterine bacterial flora between healthy cows and cows with mild CE at AI

Timing of artificial insemination using fresh or frozen semen after automated activity monitoring of estrus in lactating dairy cows

S Borchardt, C Tippenhauer, A Madureira, R Cerri, JL Plenio, W Heuwieser

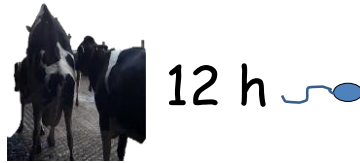
Clinic of Animal Reproduction
Freie Universität Berlin



Foundation of the AM/PM rule

Conception Rate in Dairy Cattle by Artificial Insemination at Various Stages of Estrus

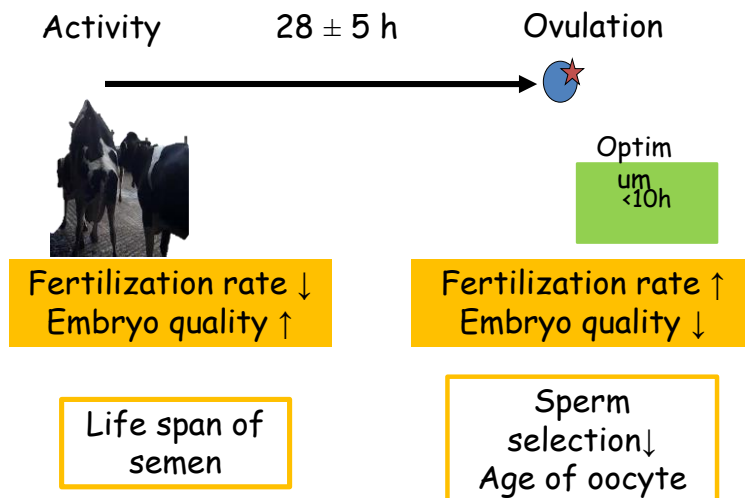
George W. Trimberger and H. P. Davis



Trimberger and Davis (1943)

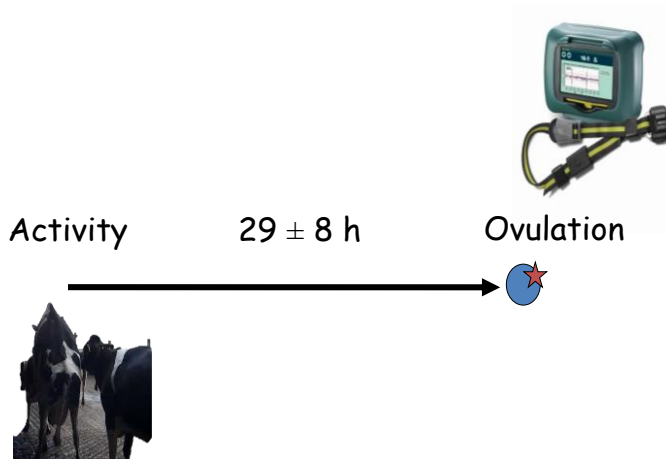
LINCOLN, NEBRASKA
APRIL, 1943

Timing of AI is a compromise



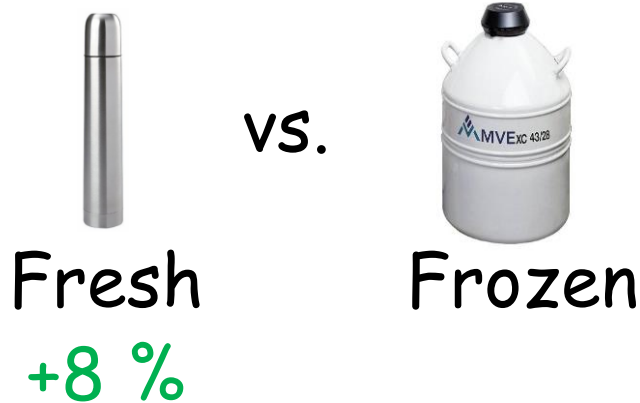
Dalton et al. (2001)

Optimum timing of AI?



Valenza et al.
(2012)

Difference between fresh and frozen semen using
timed AI



Borchardt et al.
(2017)

Objective of this study



What is the optimum timing of AI using activity monitoring?

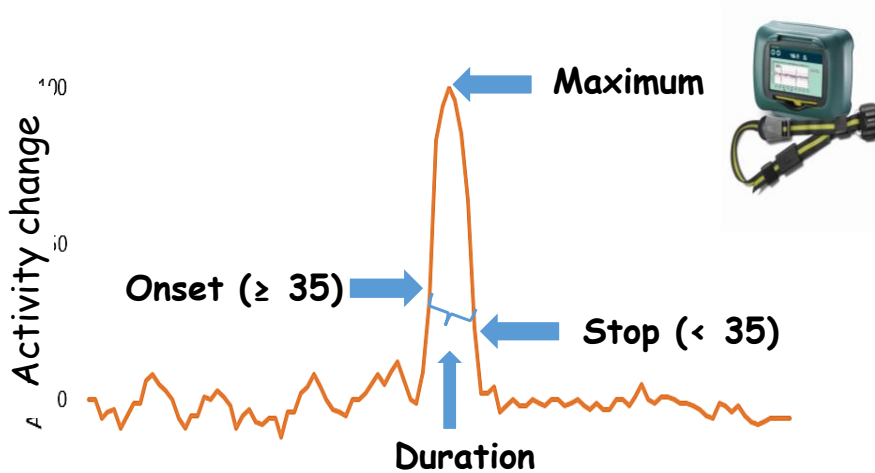


vs.

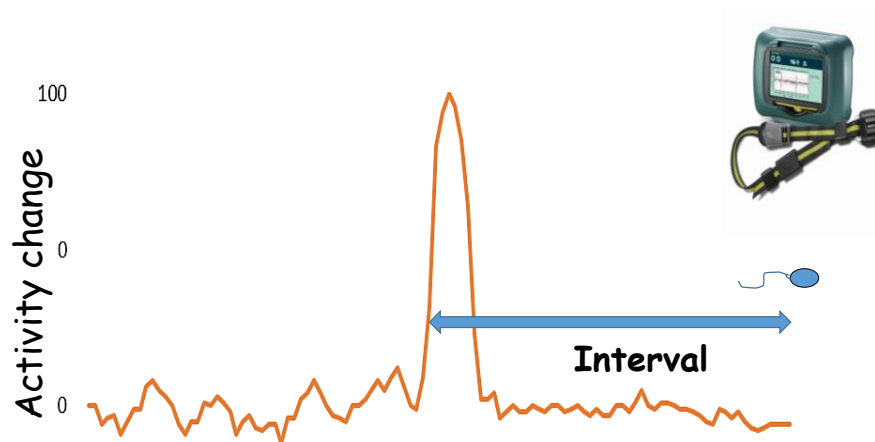


7 Farms
avg. 700 cows (400 - 1,200)

We focused on activity change...



We focused on activity change...



Statistical Analysis

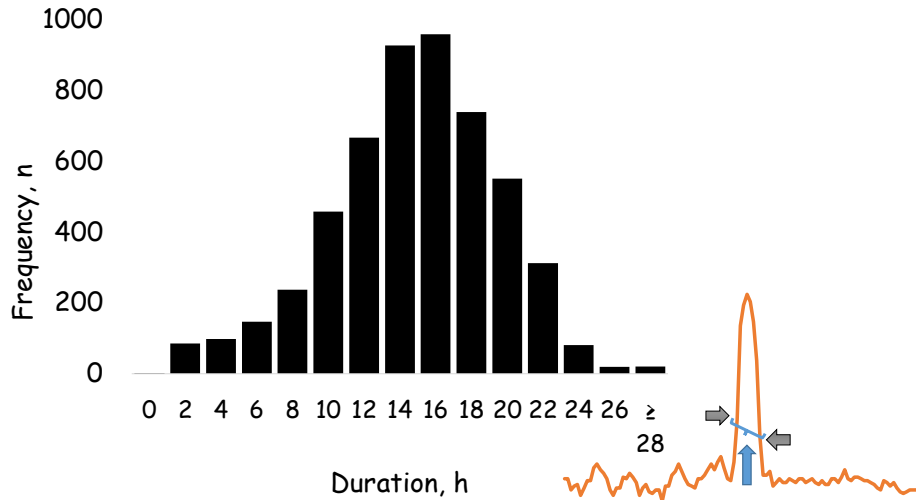
7 farms
4,600 cows



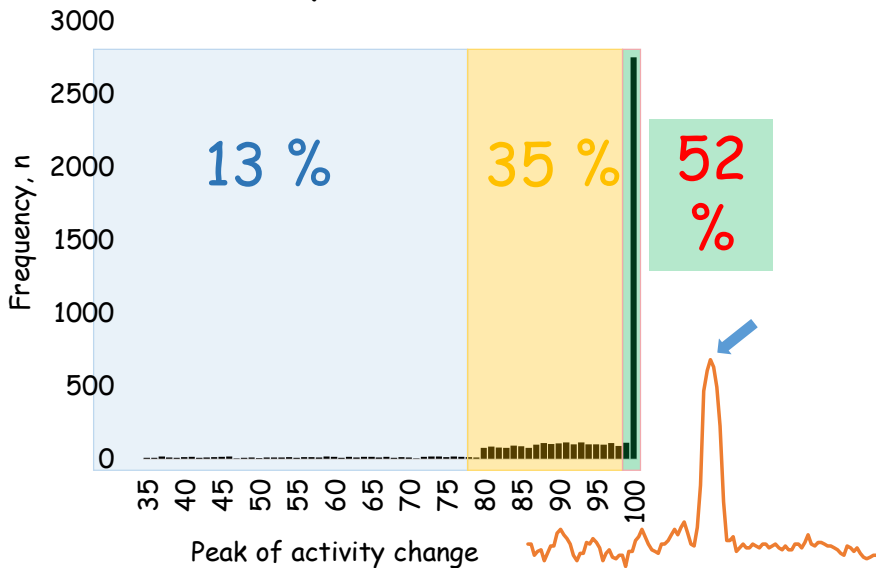
GENLINMIXED
Primary outcome
P/AI



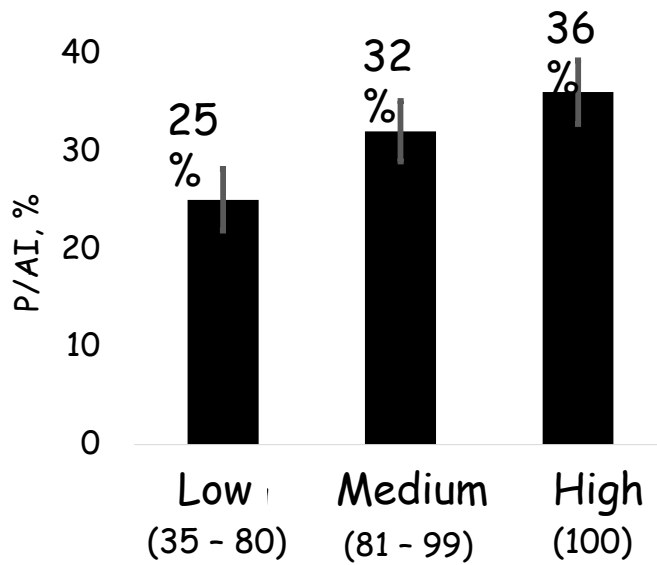
Average duration of high Activity...15 h



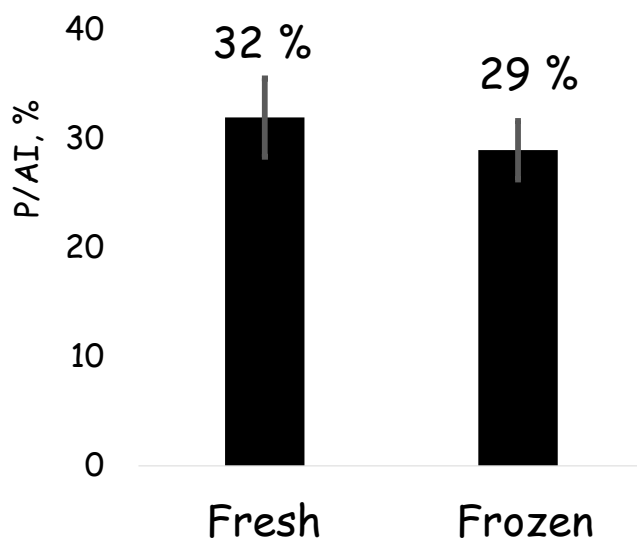
Only Half of cows showed maximum estrus intensity



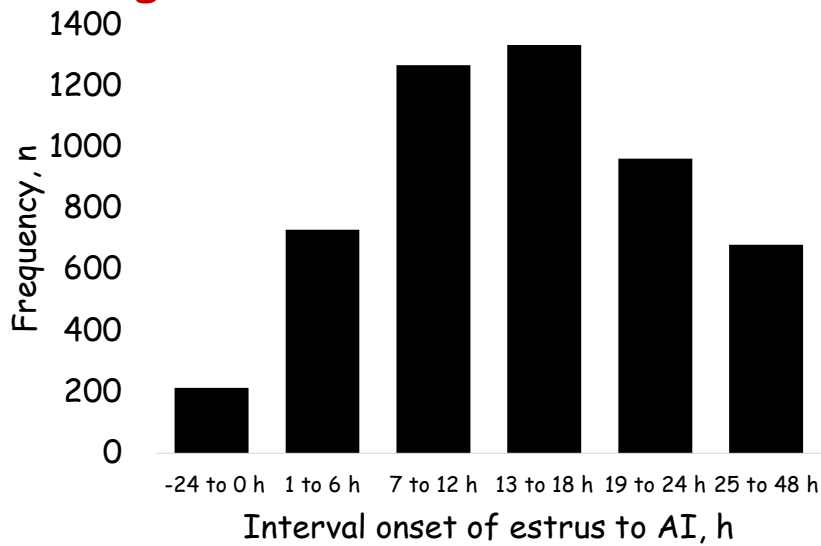
Estrus intensity ~ Fertility



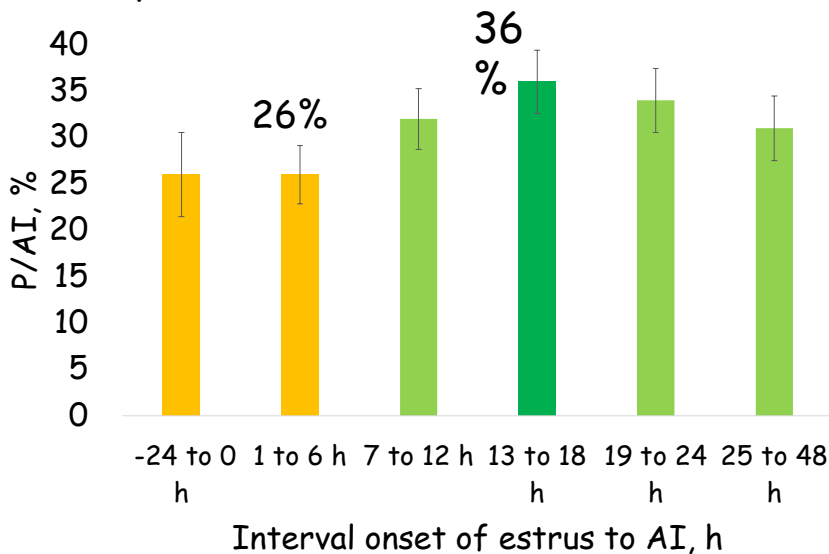
Fresh semen = Frozen semen



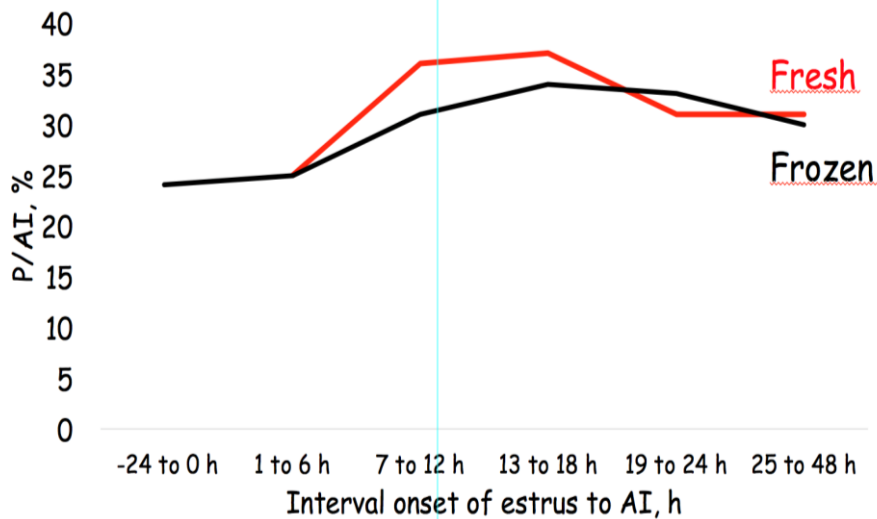
Time between onset of estrus and AI...avg. 14h



Optimum timing of AI...13 to 24 h after onset of estrus



No interaction of timing of AI and Type of semen



Conclusions

- No difference between fresh and frozen semen
- Optimum timing of AI...13 to 24 hours after passing the AT
- High intensity estrus was favorable for P/AI

Danke für's Zuhören!

