Session 10

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The interface between bioenergetic status and the reproductive axis in lactating dairy cows

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EAAP, Vilnius, August 2008.

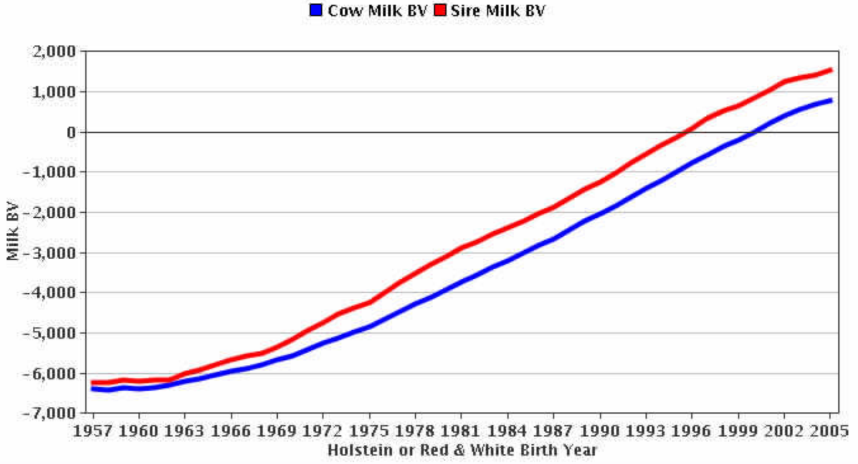
Overview

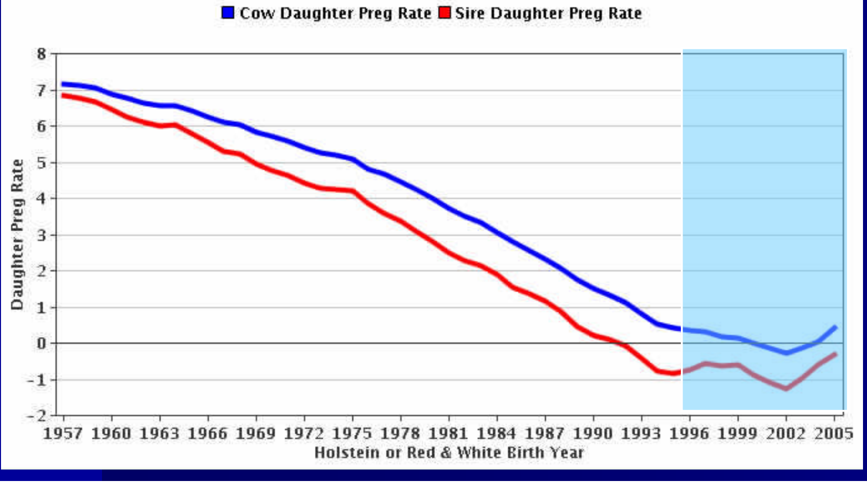
- Reasons for declining fertility
- Physiology of subfertility
- Strain of cow effects on fertility
- Strategies for improvement
- Conclusions

Why is cow fertility declining?

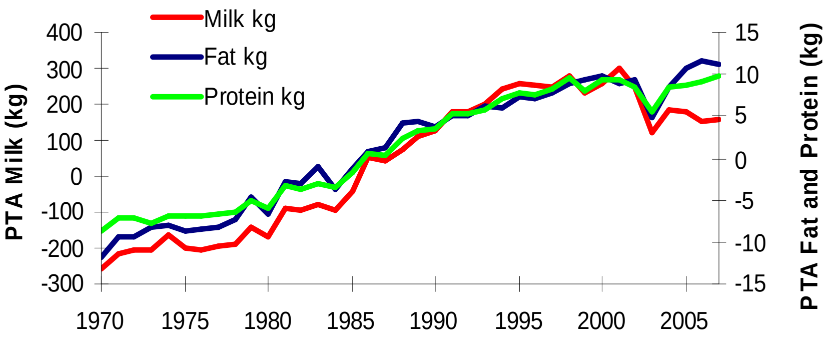
Selection for increased milk yield

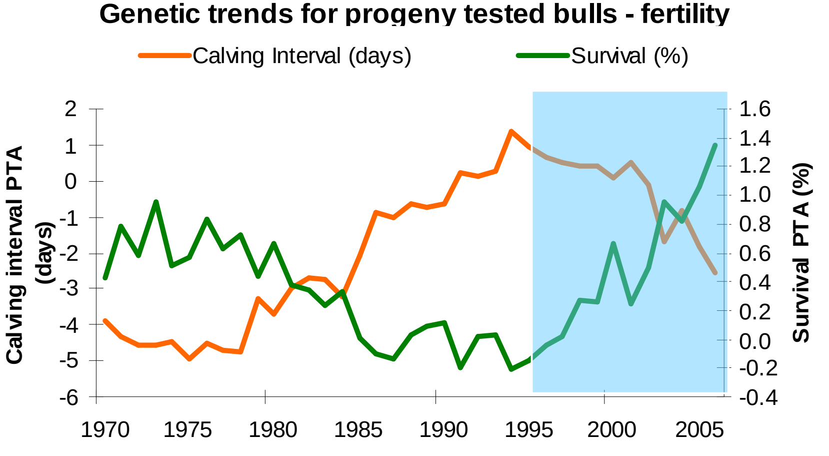
USA





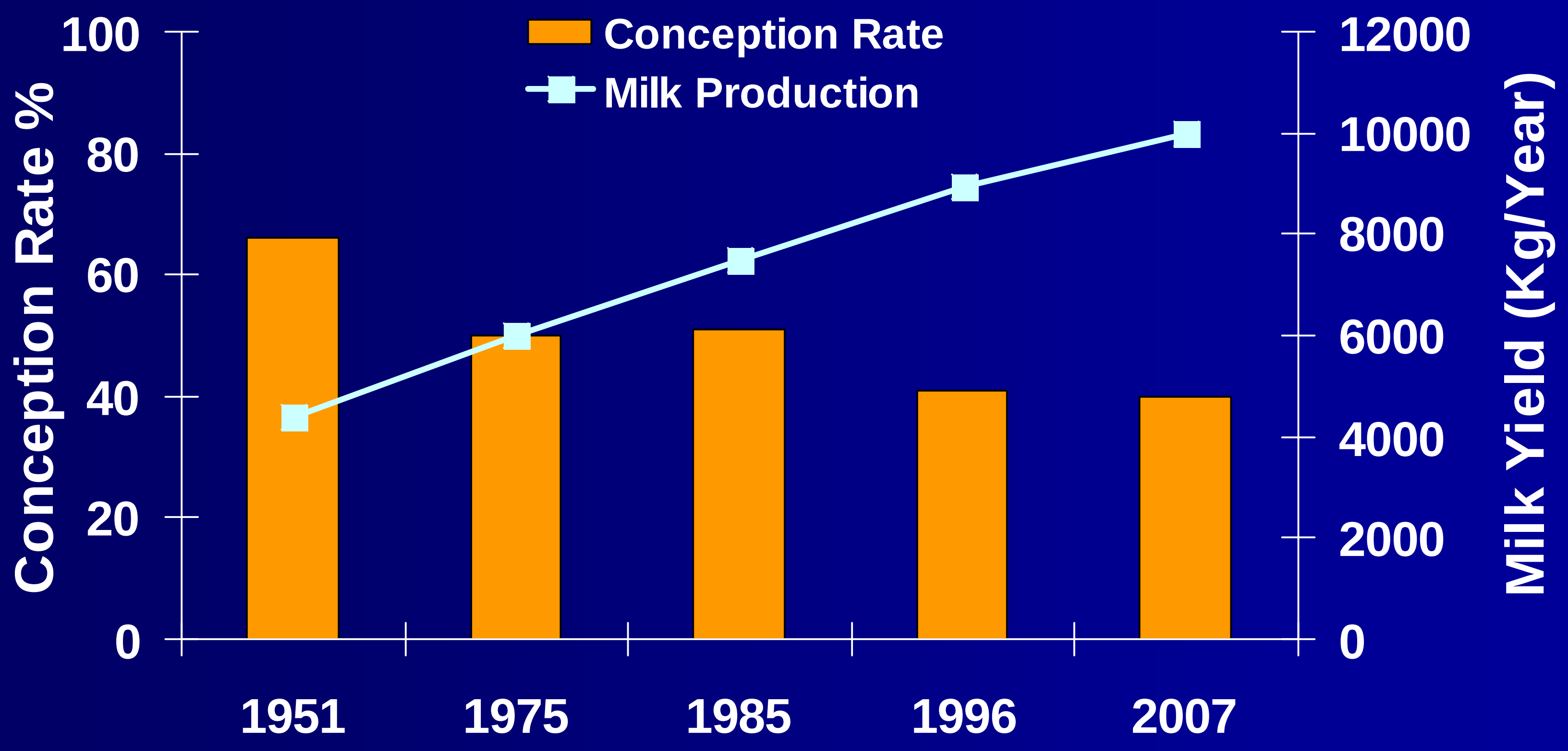
Ireland





Why is cow fertility declining?

Phenotypic milk and fertility performance NY



Updated from Butler, 2003

Why is cow fertility declining?

Phenotypic fertility performance IRL

No Cows	Calv rate 1st service	Infertile rate %	Source
3706	60	<10	Crowley et al. (1967)
5660	64	5	White and O'Farrell (1972)
6318	66	<5	Roche et al. (1972)
2355	69	<4	Cunningham et al. (1978)
4542	60	<2	Cunningham and O'Byrne (1980)
13000	44	14	Buckley, Berry, Dillon et al (1999, 2000)

Milk production and conception rate % in New York Holstein herds*- July 2007

Milk Range, kg/cow	Number of Herds	Avg Milk/cow, kg.	CR %, 1st service	CR %, 2nd service,	CR %, 3rd+ services
8,000 - 8,999	341	8,636	45	45	46
9,000 - 9,999	368	9,541	41	42	41
10,000 - 10,999	350	10,416	37	39	39
11,000 - 11,999	180	11,257	35	36	36
12,000 - 12,999	66	12,166	34	34	32
> 13,000	28	13,355	33	31	31
			Mean = 39	41	41

* DHI herds (N=1333) data processed at Raleigh,NC (DairyMetrics report)

Why is cow fertility declining?

Changing management structures

- Confinement systems
  - TMR
  - ↑ energy density
  - ↑ herd size
  - Year round calving
  - Heat detection vs. synchronisation
  - bST (NA)
- Pasture based systems
  - ↑ herd size
  - Holsteinization
  - Supplement feeding
  - Split calving (spr & aut)
  - Heat detection vs. synchronisation

Physiology of subfertility

Gestation-lactation cycle

- Reduced conception rates
- Greater # of services
- Longer calving intervals
- Increased days open
- Less compact calving pattern

Parturition Breeding Dry-off Parturition

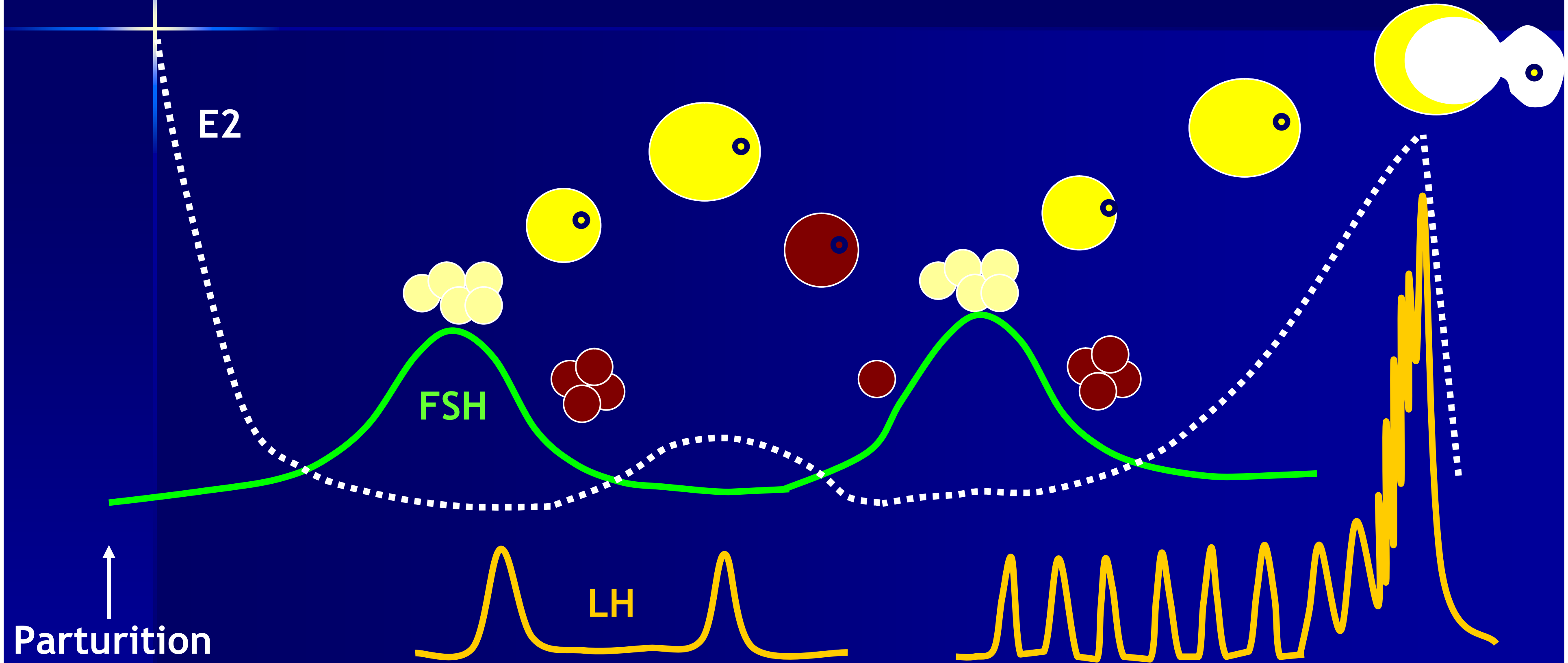
60 Day dry period	305 Day lactation			60 Day dry period
Mammary involution Foetal growth Mammogenesis BCS repletion	Uterine involution Uterine infection Return to cyclicity Increasing milk yield NEB/BCS loss	Peak yield Increasing DMI -ve/neutral EB	Declining milk yield Stable DMI Neutral EB/+ve EB Stable BCS/BCS gain	Mammary involution Foetal growth Mammogenesis BCS repletion

280 Day gestation

280 Day gestation

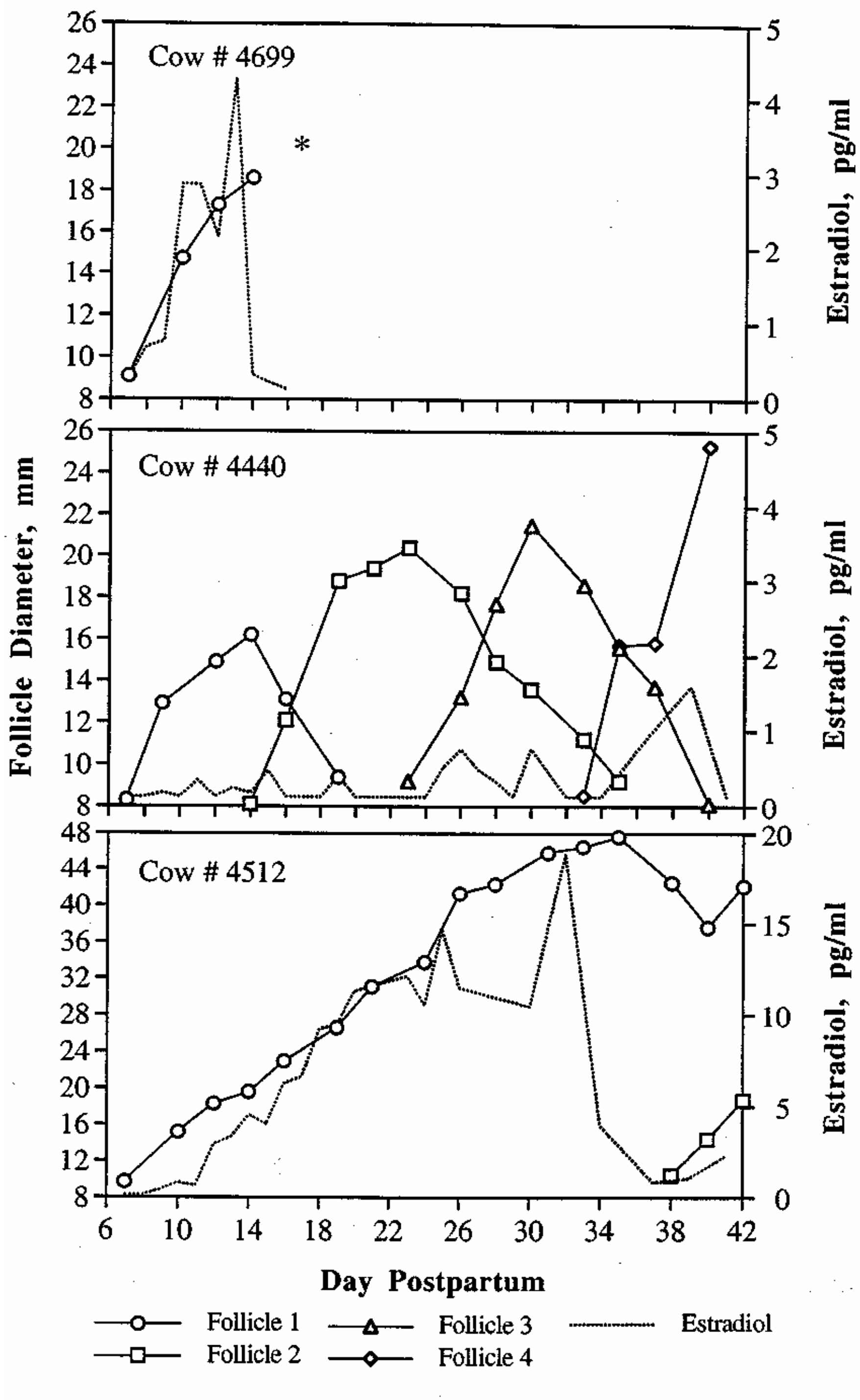
Physiology of subfertility

Postpartum resumption of cyclicity

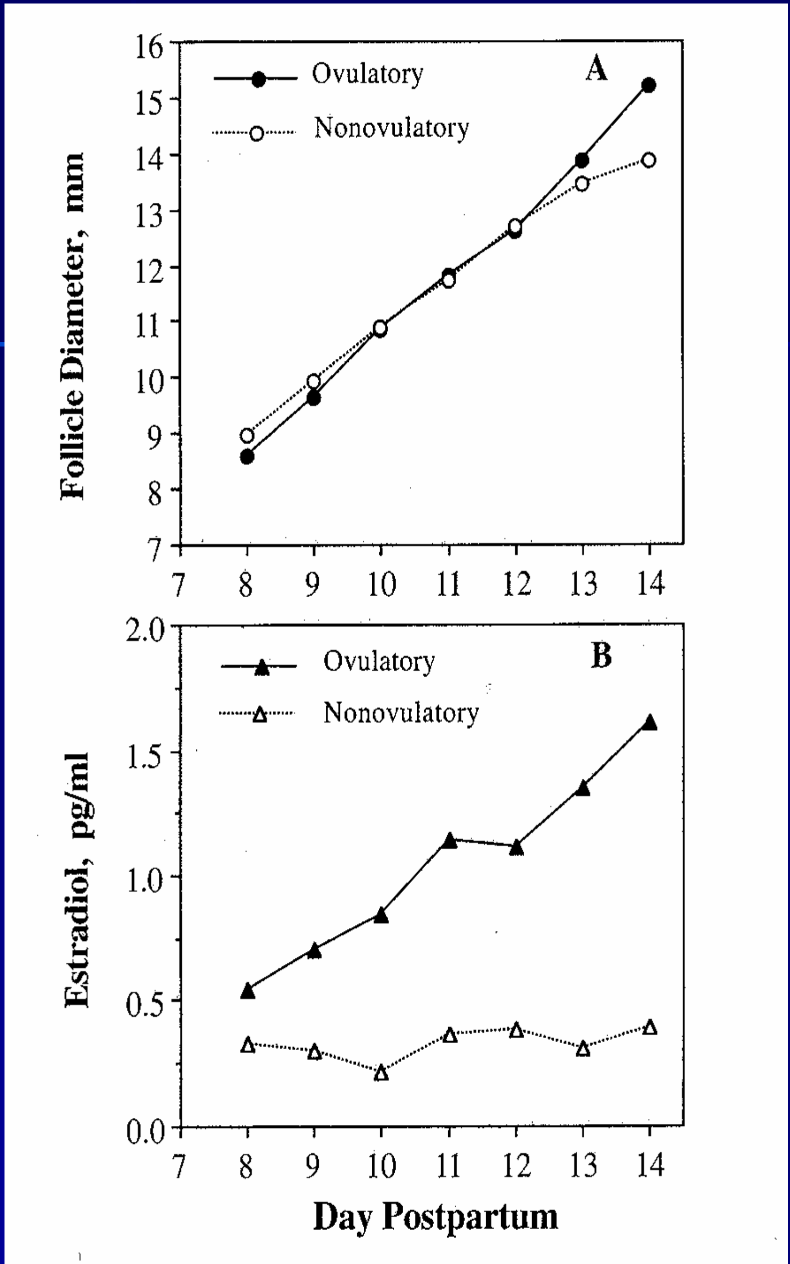


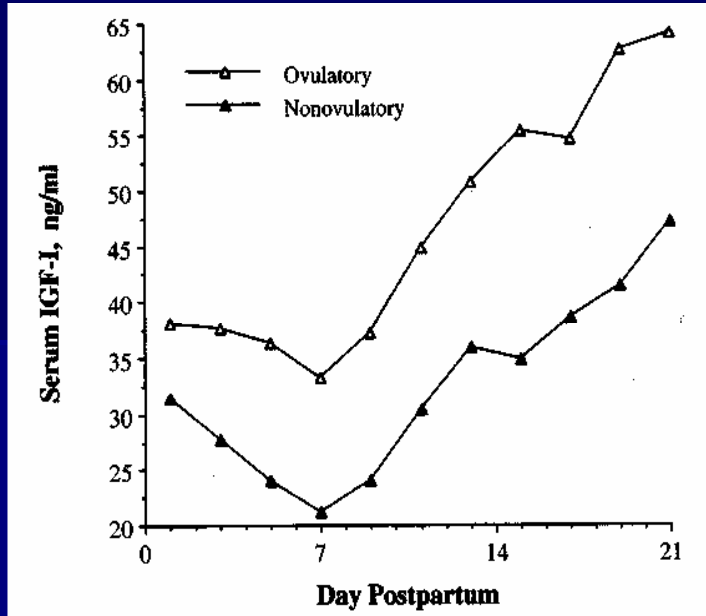
EB Insulin IGF-I LH responsiveness DF E2 synthesis	NEFA BHBA E2 -ve feedback

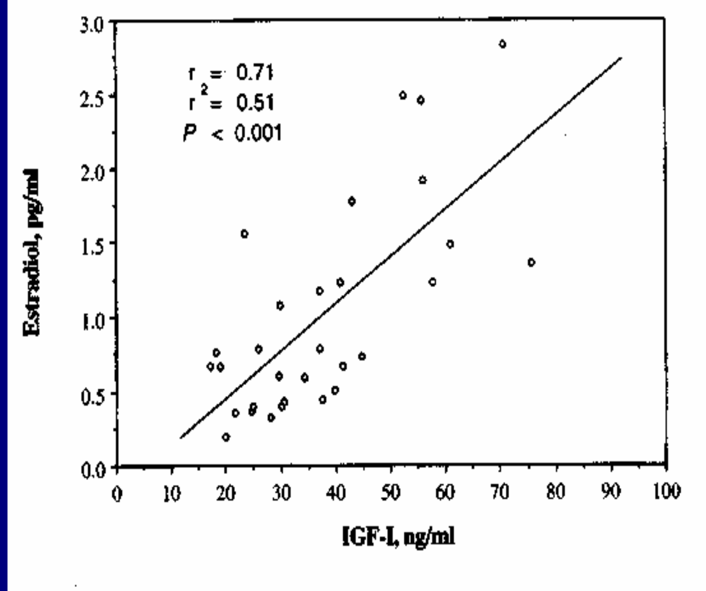
EB Insulin IGF-I LH responsiveness DF E2 synthesis	NEFA BHBA E2 -ve feedback



Outcome	Incidence	Days to Ovulation
Ovulation	40%	20
Regression	40%	50
Cystic	20%	48
Average		30

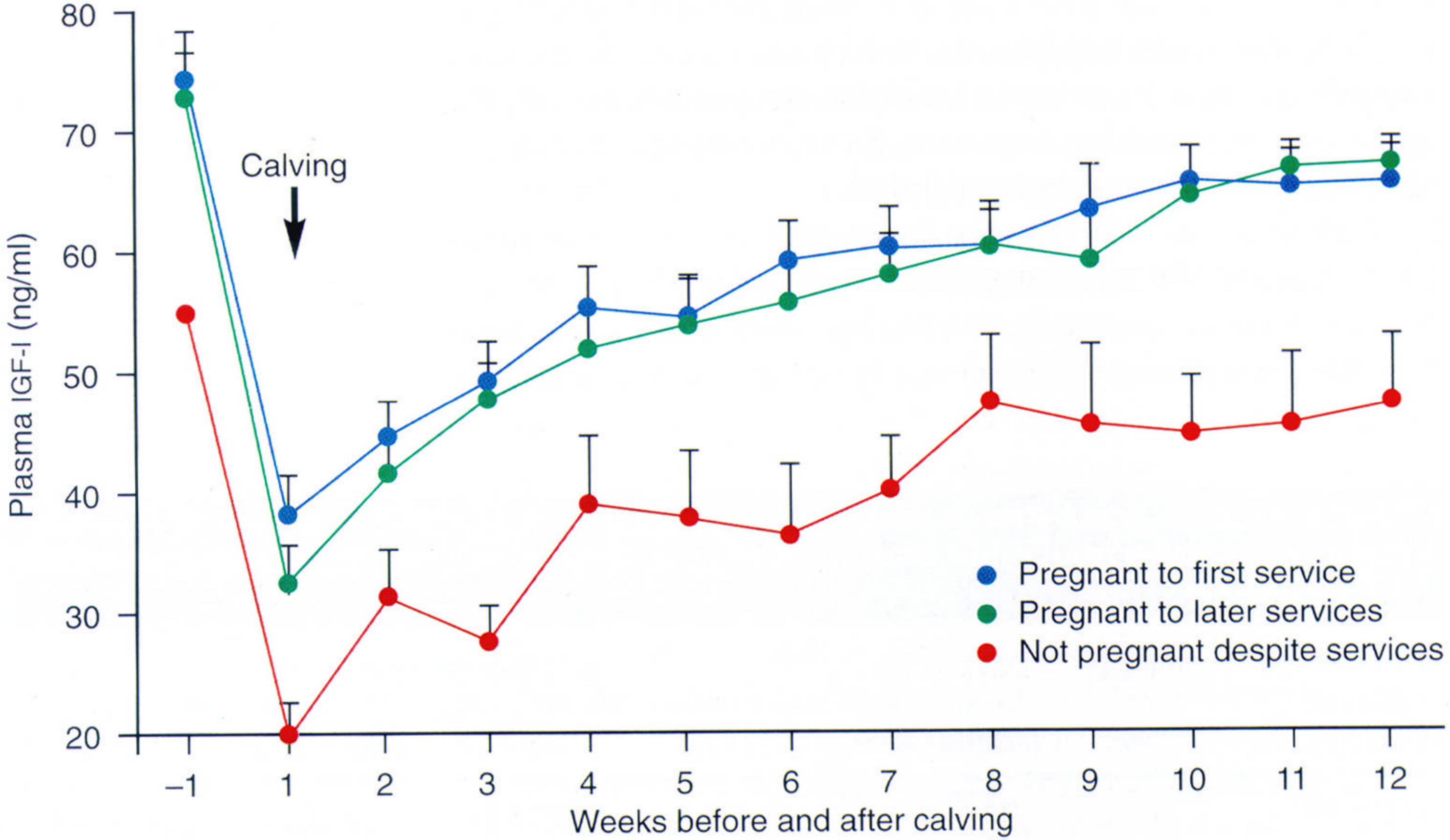






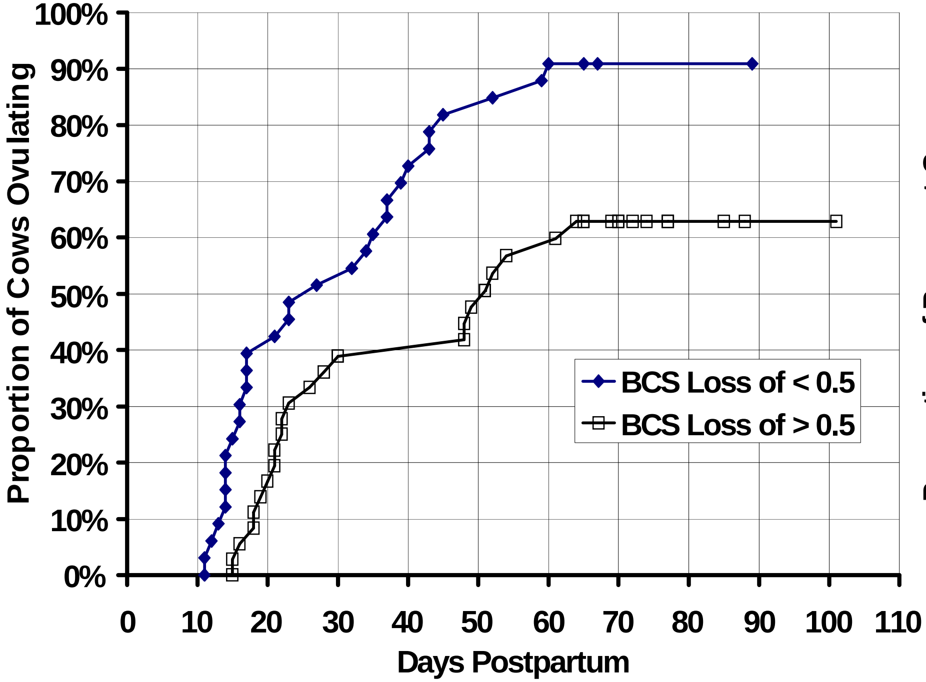
Beam and Butler, 1997; 1998

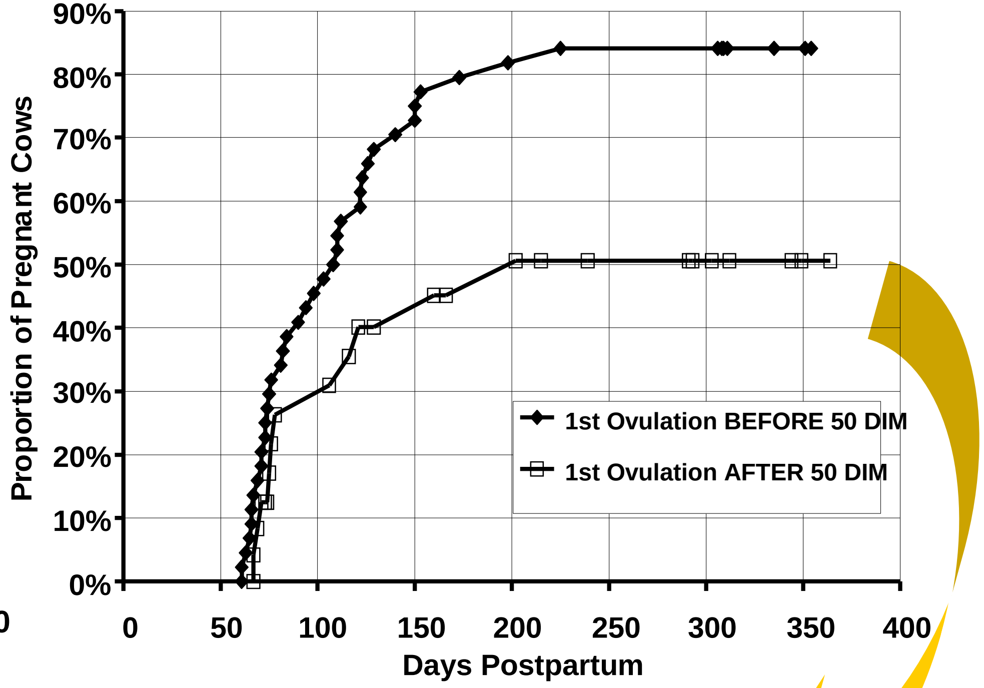
177 mature cows,142 primiparous;
IGF-I >50 ng/ml @AI = 5x
likelihood for conception



Taylor et al., The Veterinary Record 155:583-588. 2004.

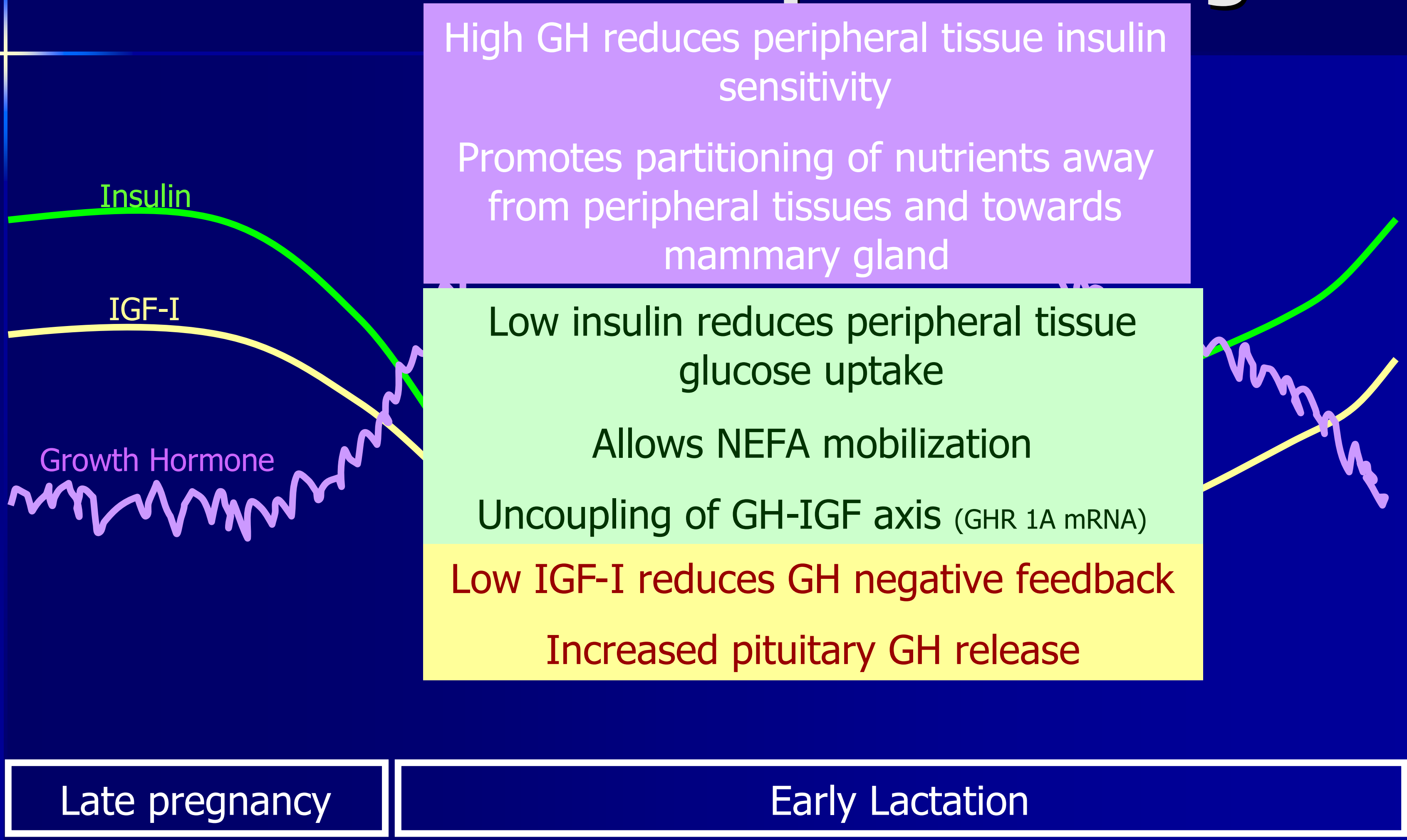
Early NEBAL & BCS loss delays first ovulation and relates to poor fertility/increased risk of culling





Culling

Hormonal control of early lactation nutrient partitioning



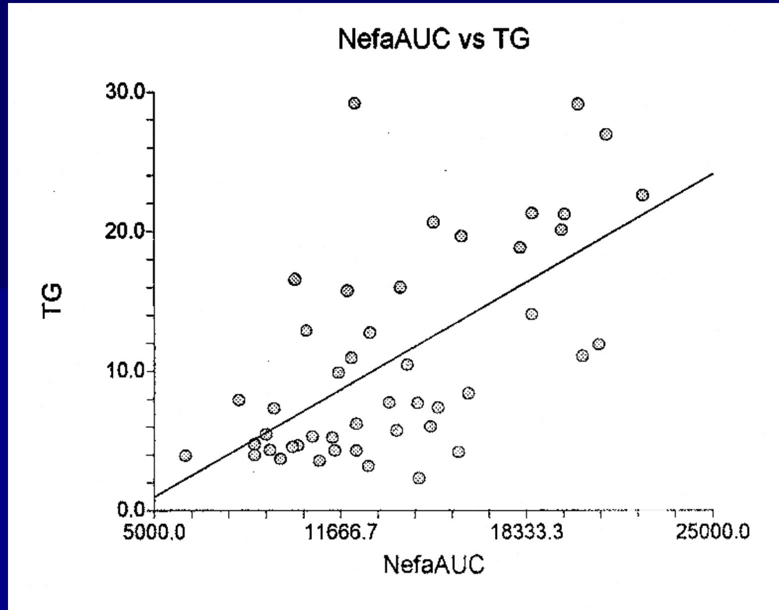
Insulin resistance (IR) in periparturient dairy cows

IR exists when normal insulin concentrations produce a less than normal biologic response (Kahn, 1978).

- **Causative factors:**
  - **Overfeeding (obesity) – elevated NEFA**
  - **Growth hormone – increases prepartum**
  - **Stress – infections, endotoxins, cytokines**
  - **Estradiol – increases prepartum**

Liver triglycerides (TRIG)

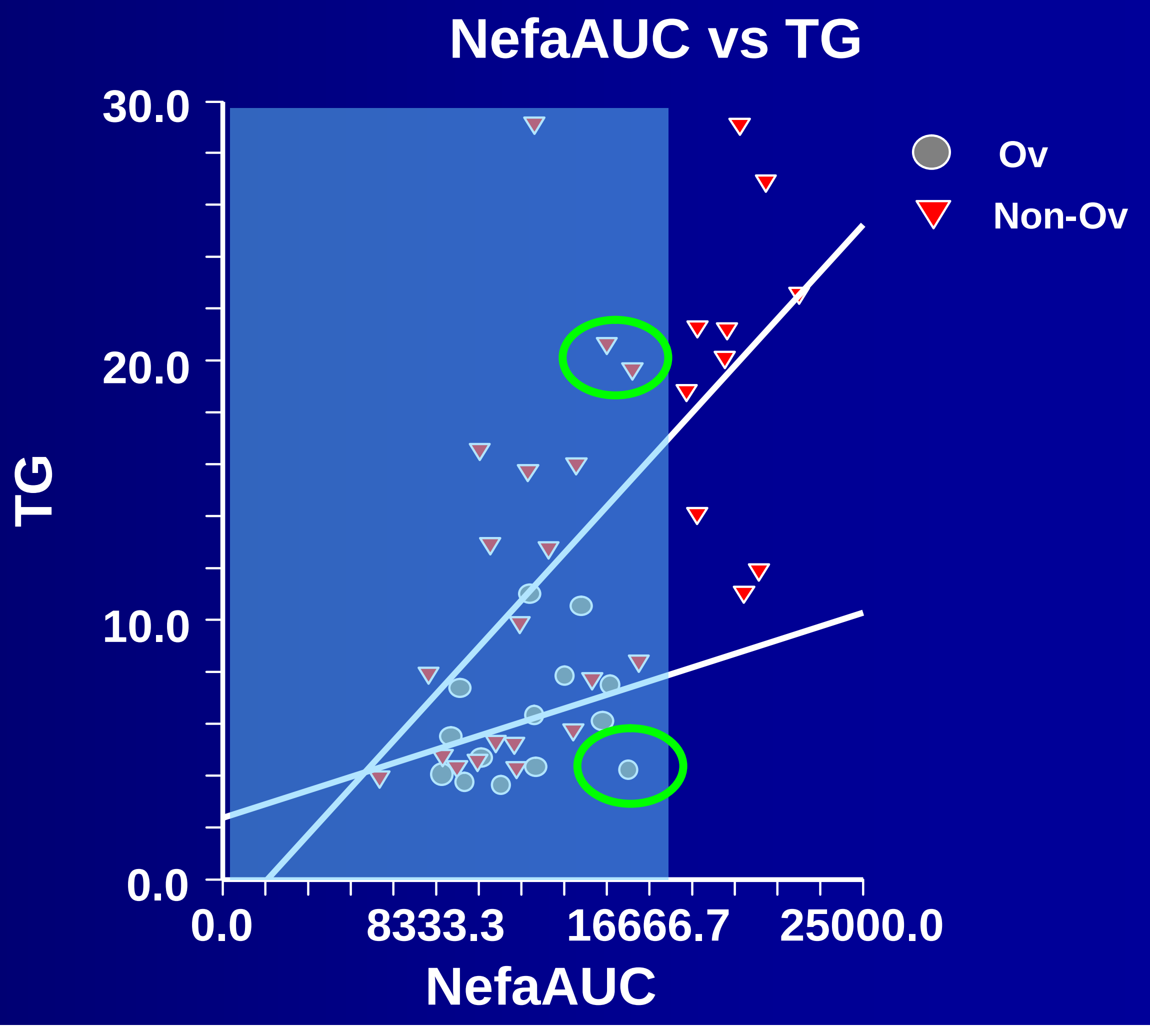
- **Liver TRIG accumulation during the transition period is directly related to plasma NEFA concentrations.**



- **TRIG accumulation impairs gluconeogenesis, ureagenesis, oxidation of fatty acids and liver capacity to clear bacterial endotoxin (Overton, 2001; Murondoti et al., JDS 87:672 & J Dairy Res 71:129, 2004)**

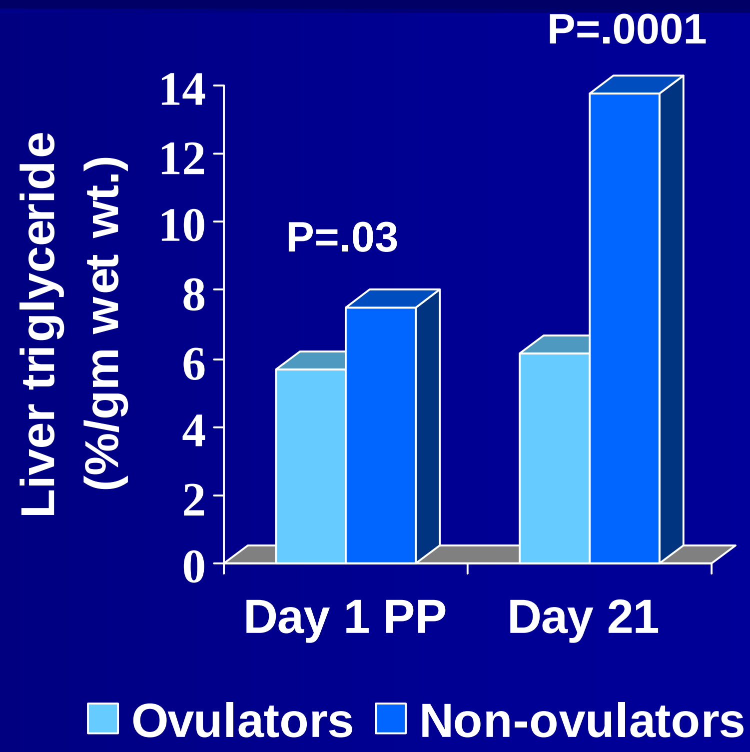
NEFA AUC is related to liver triglyceride accumulation at day 21 and ovulation

Cows with ovulatory 1st dominant follicle have better utilization or disposal of NEFA so less accumulation of triglycerides in liver.

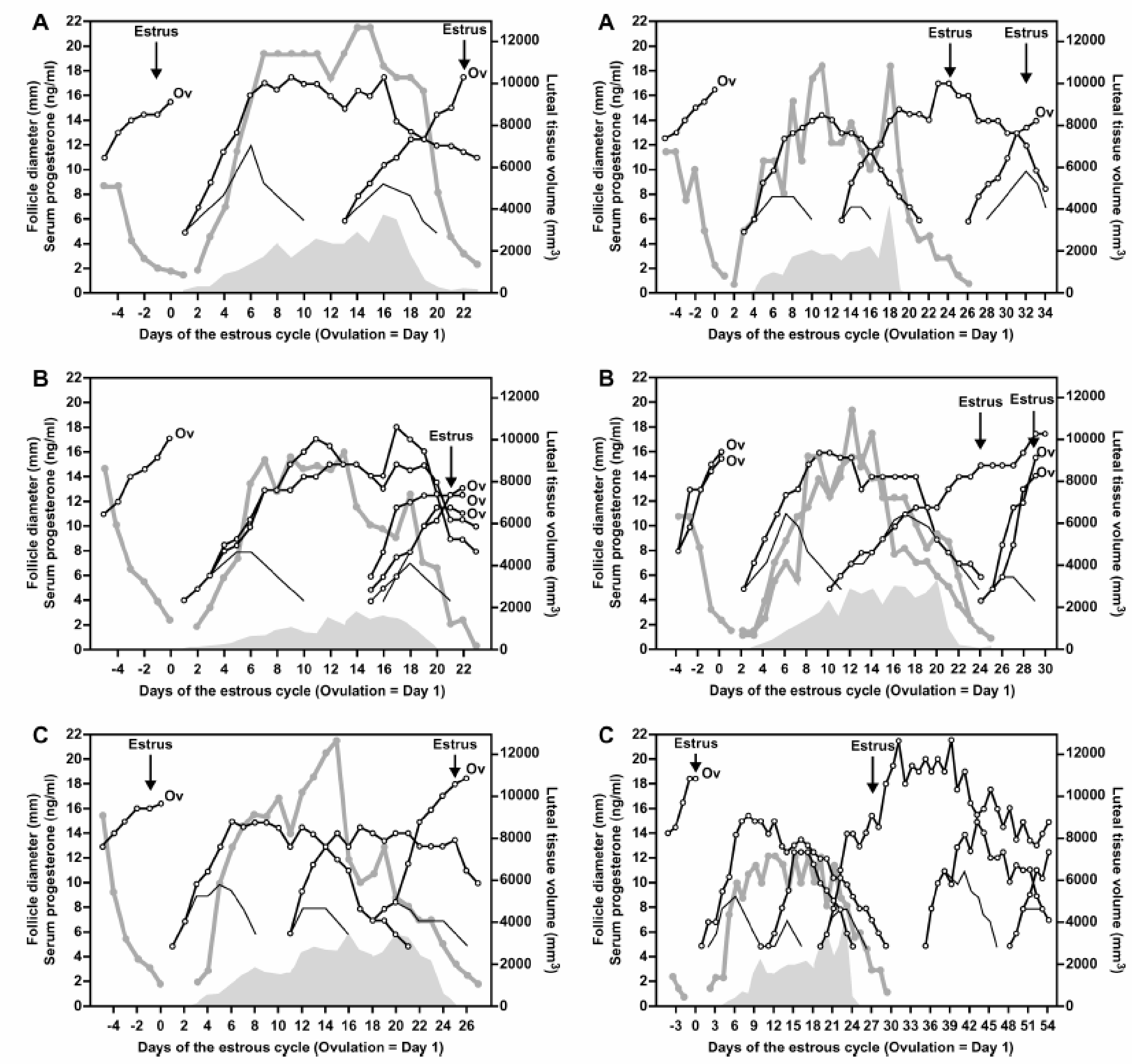


Triglyceride accumulation in liver PP

- **Liver TG was higher at day 1 in cows with non-ovulatory follicles.**
- **Liver TG doubles by day 21 in non-OV cows, but was unchanged in ovulatory cows.**



Oestrous cycles in lactating dairy cows



Typical oestrous cycles **Atypical oestrous cycles**

Atypical vs typical cycles

↑ Ov failure after luteolysis

No ↑ E2 after luteolysis

Ov in wave after luteolysis

↑ incidence of multiple ov

↓ E2 during ovular waves

Normal cows vs heifers

Larger ovarian structures

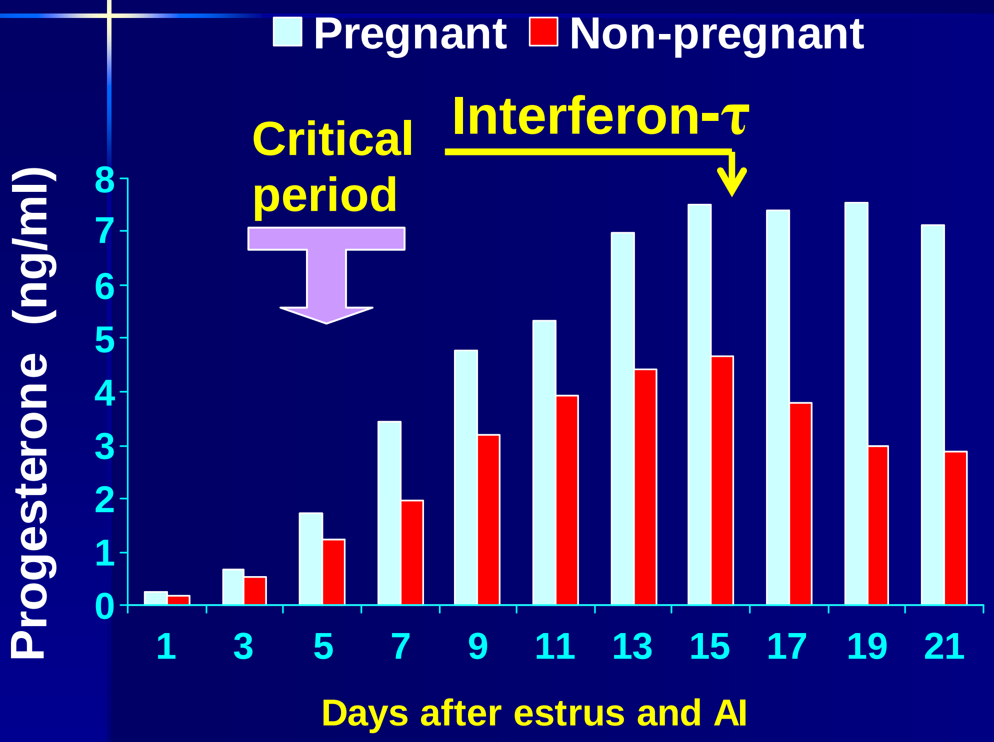
Lower circulating steroids

Ov later after luteolysis

↑ incidence of multiple ov

Sartori et al. (2004) JDS 87:905-920

Post-ovulatory progesterone



Butler et al. (1996) J Anim Sci 74:858 & 1943, 1996

- Pregnancy failure associated with low serum P4
- P4 supplementation from d3 increases embryonic size on d13 & 16 in beef heifers (Carter et al. 2008)
- Cows with larger follicles & greater E2 at AI had greater post-ovulatory P4 & pregnancy rates (Lopes et al., 2007)

Regulation of steroid concentrations

- Cause of low P4 in lactating dairy cows
  - Inadequate luteal production?
  - Greater liver metabolism?
  - Combination of both?

- Ovarian structures larger in lactating cows compared to heifers, but steroid hormones lower (Sartori et al., 2004)

- In vitro studies suggest no difference in CL steroidogenic capacity in cows with early or late P4 rise (Robinson et al., 2005)

- Baseline liver bloodflow 2x higher in lactating vs non-lactating cows (Sangsritavong et al., 2002)
  - Greater DMI increased MCR in both groups

- **BUT isn't higher DMI desirable??**

P4 synthesis or metabolism?

Cows with High or Low P4 on day 28 to 34 post-AI

↓

Luteal tissue removed, assayed for P4, and mRNA abundance of ET and PG

↓

No difference in CL size, luteal P4 content or mRNA abundance of enzymes for ET or PG systems in cows with high or low P4 at lutectomy

Dispersed luteal cells incubated with LH, AA, or ET-1 (or combinations)

↓

No difference in basal or LH stimulated P4 secretion

↓

ET-1 inhibition of P4 secretion greater in LOW P4 compared to high P4 cows

Cows injected with P4 every 12 h for 48 h beginning at lutectomy

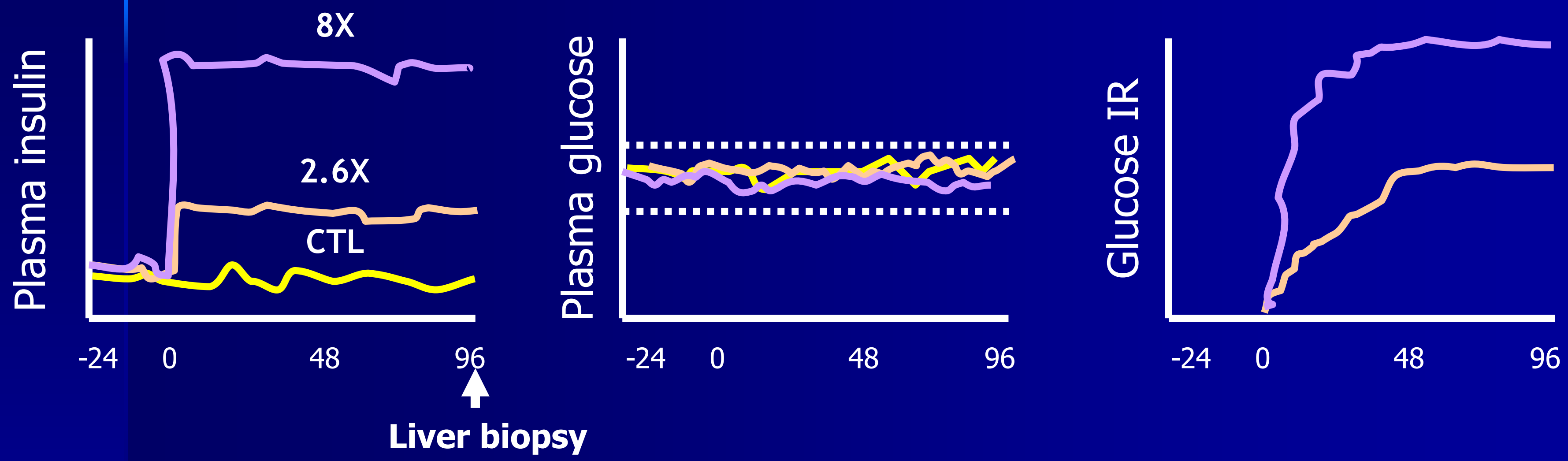
↓

P4 maintained at lower concentrations in LOW vs HIGH cows

Rhinehart, 2007

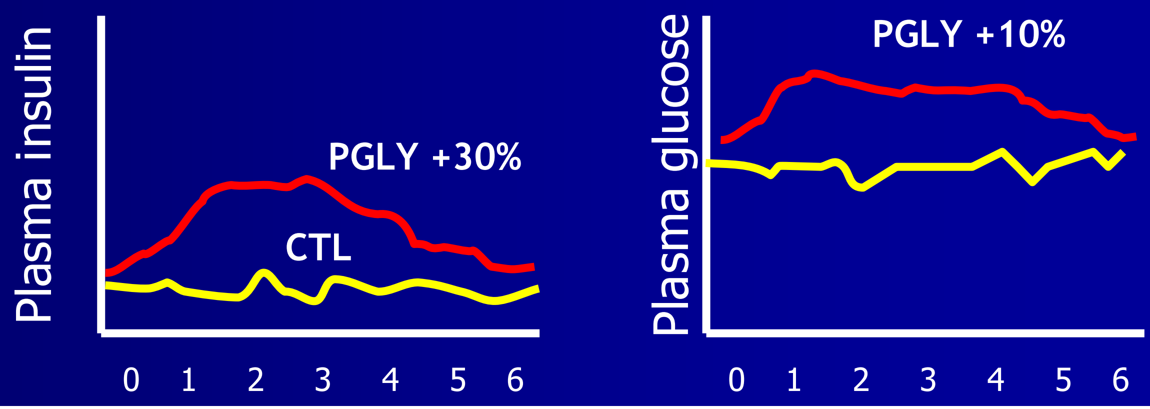
Regulation of P4 metabolism

Hyperinsulinemic-euglycemic clamps D10-14 pp (Butler et al., 2003 & 2004)



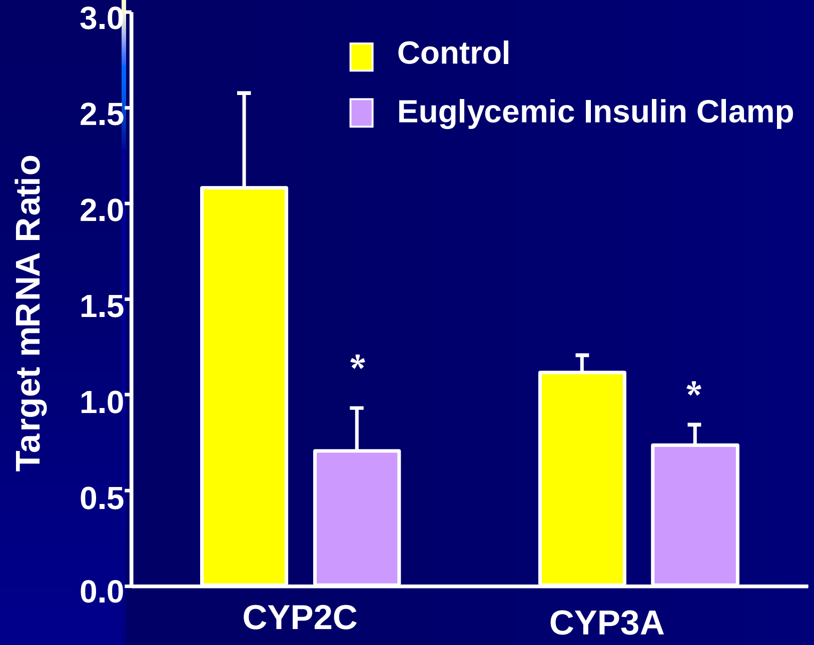
Propylene glycol drenched daily from D-10 to +30 relative to parturition. Biopsies D 25.

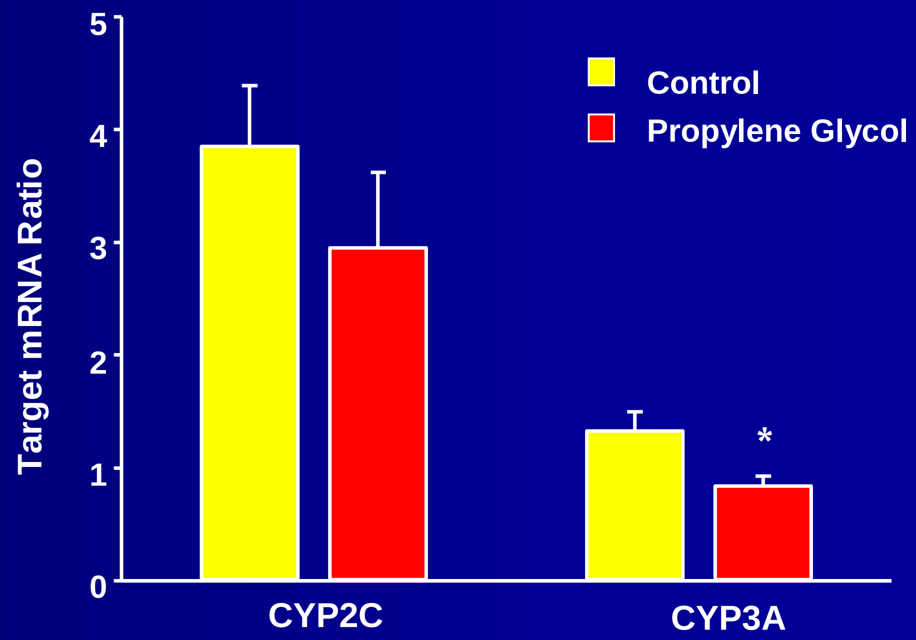
Butler et al. (2006)



P4 catabolic enzymes

Cytochrome P450 2C and 3A mRNA abundance

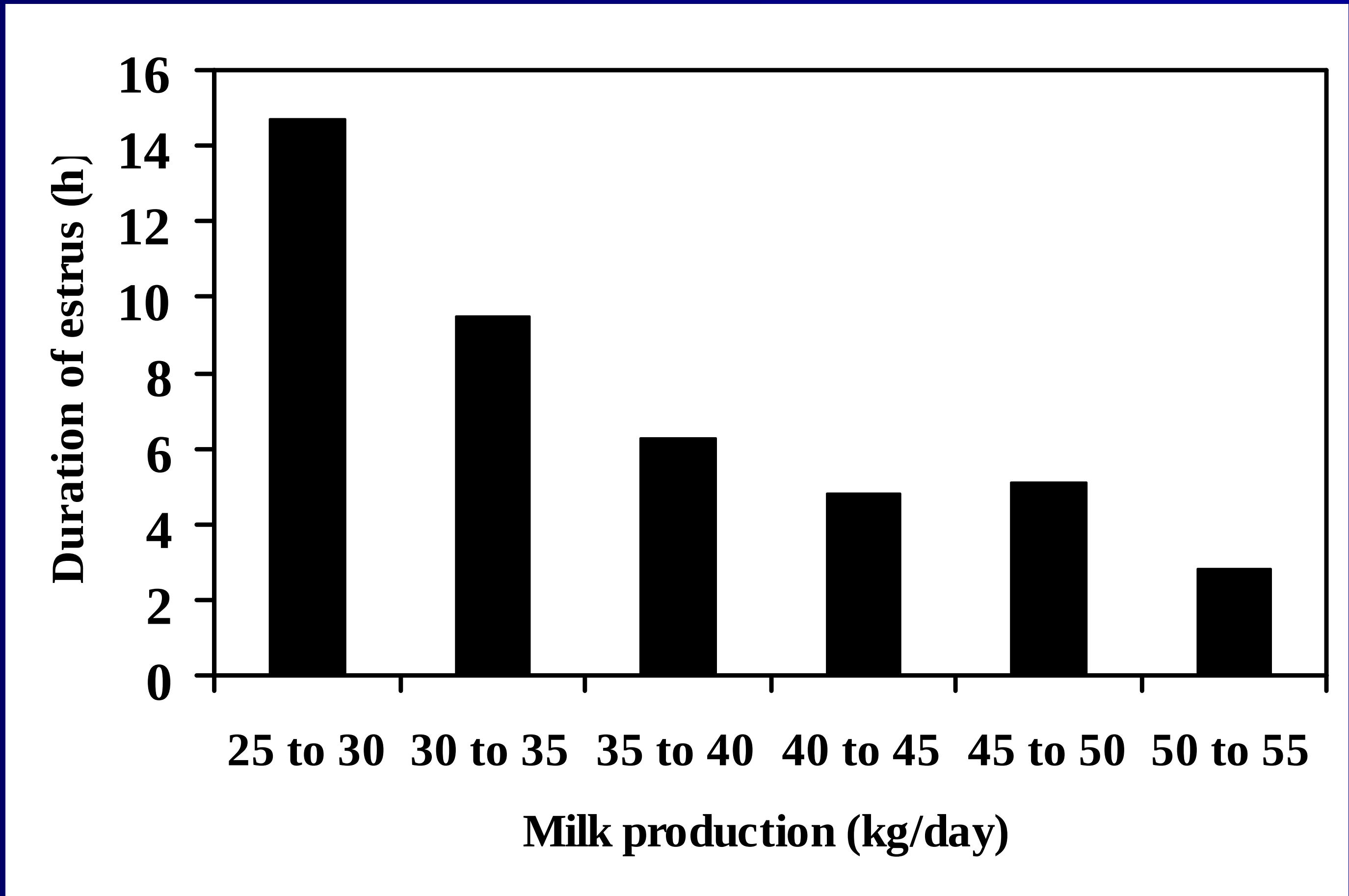




- Greater DMI increases P4 metabolism
- Greater DMI usually associated with favourable fertility outcomes??
- Plasma insulin increases when EB status improves
- When greater DMI increases plasma insulin, P4 metabolism reduced

Lemley et al. (2008). JDS 91:641-645

Influence of milk production on oestrus duration



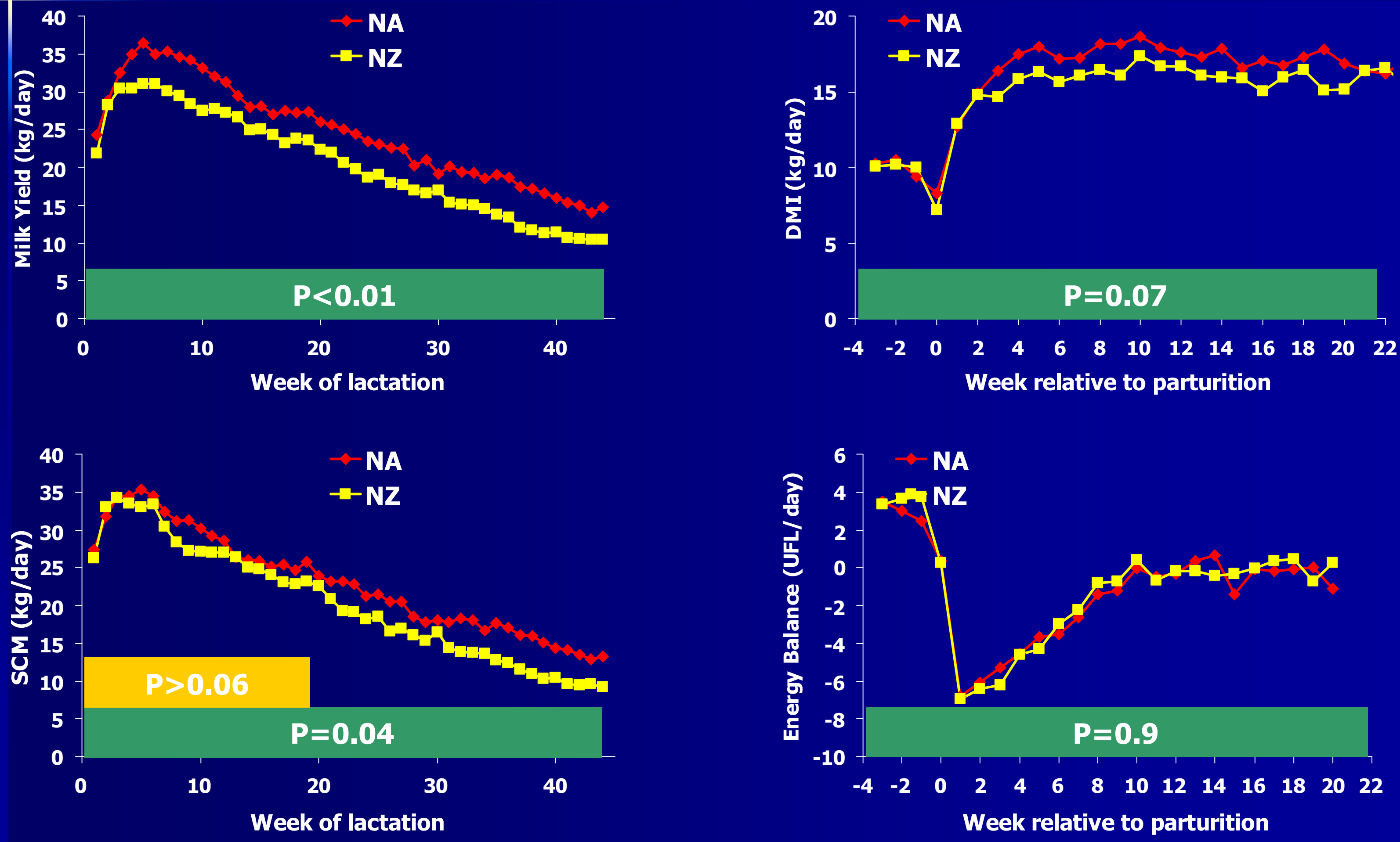
Wiltbank et al. (2006) Theriogenology 65:17-29

Strain of Holstein-Friesian cow

- Moorepark strain comparison study
  - NA genetics
    - Selected for increased milk yield
  - NZ genetics
    - Selected for milk solids, feed efficiency and survivability in pasture based system
- 10 NA and 10 NZ cows
  - DMI/EB, endocrine and metabolic profiles
  - Reproductive hormone profiles
  - Embryo quality
  - Responsiveness to homeostatic challenges

Strain of Holstein-Friesian cow

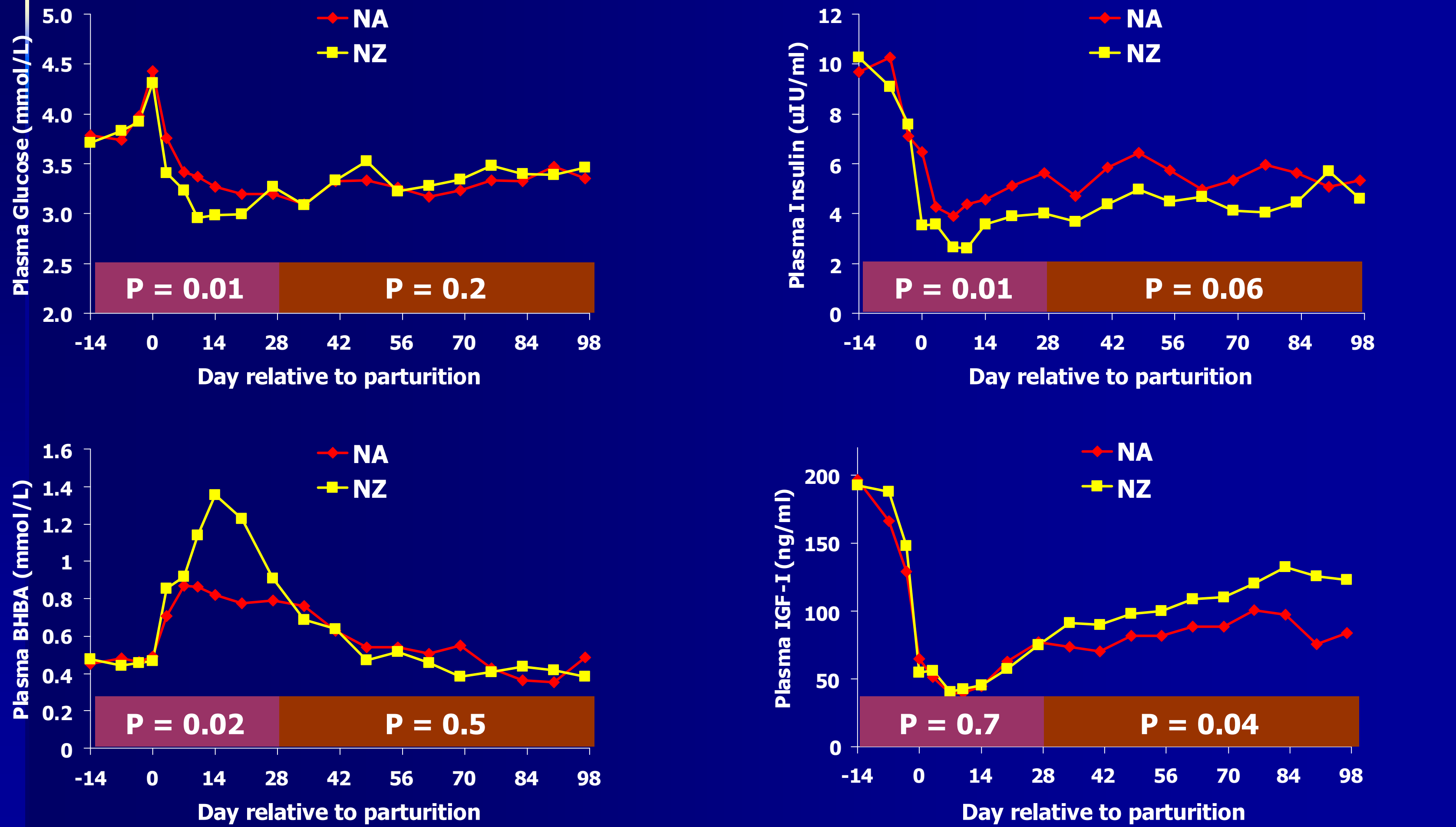
Production and Bioenergetic status



Patton et al. (2008) Animal 2:969-978

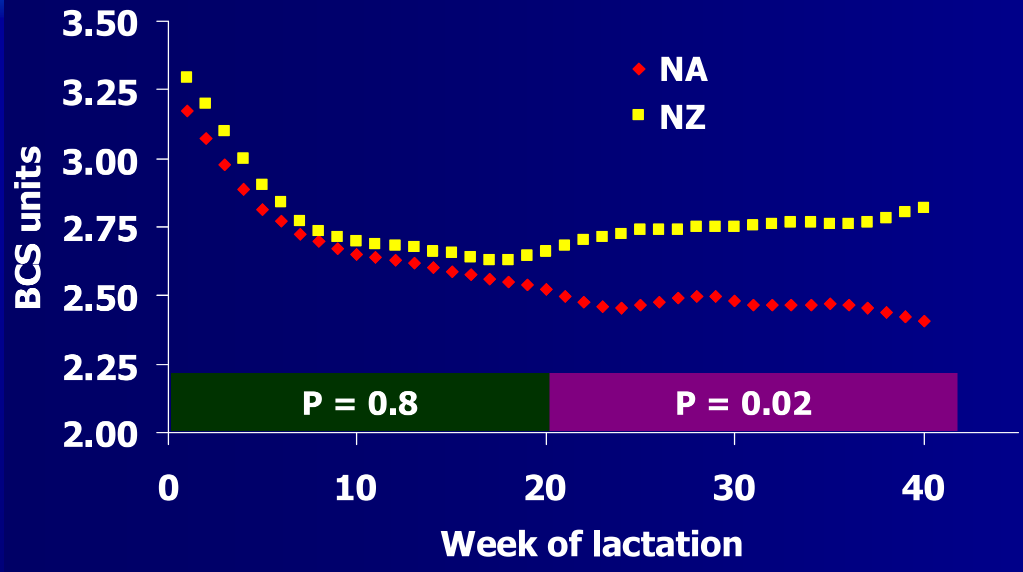
Strain of Holstein-Friesian cow

Hormones and Metabolites



Patton et al. (2008) Animal 2:969-978

Strain of Holstein-Friesian cow
BCS and nutrient partitioning



<u>Response to IVGTT</u>

No difference in early lactation

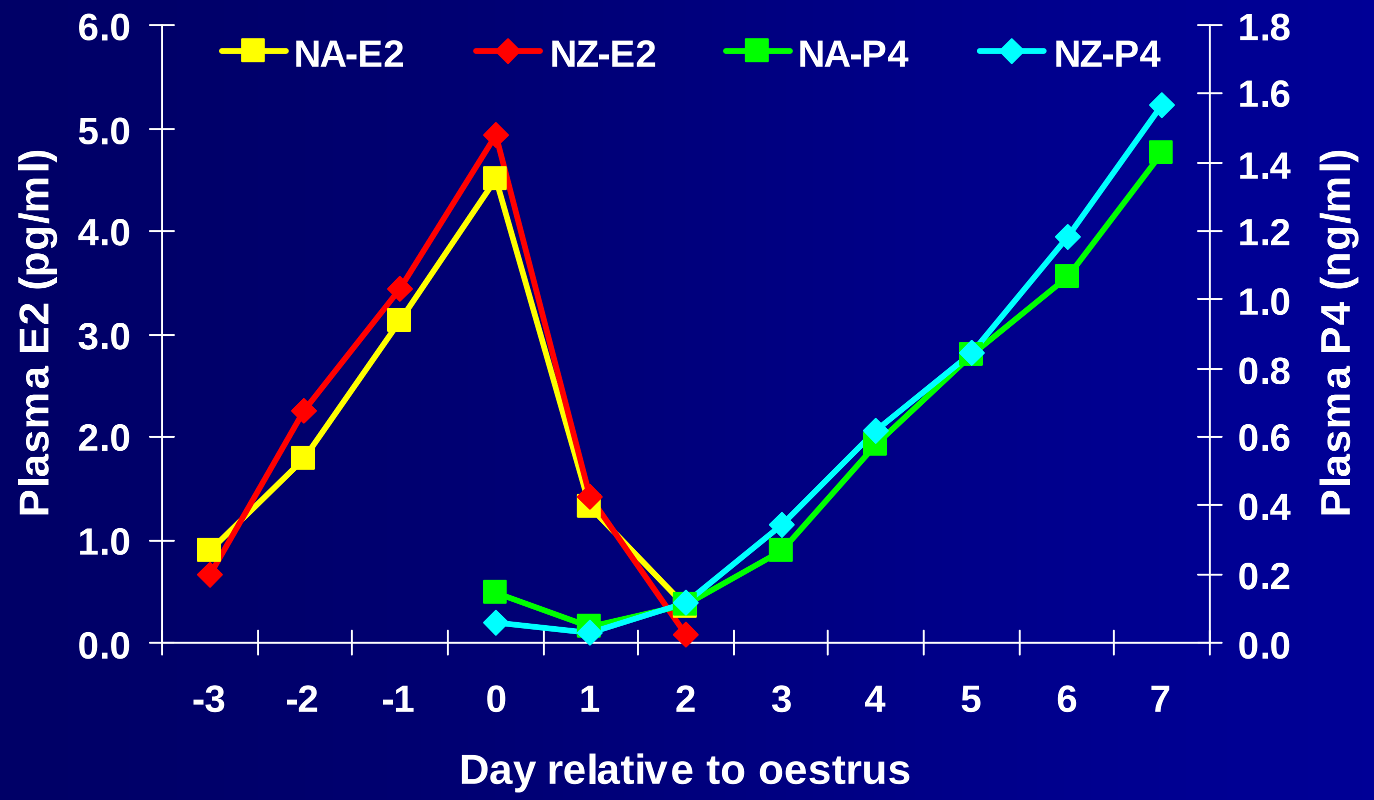
Greater clearance rate and shorter t1/2 in mid-lactation for NZ strain

Likely involved in mid-lactation BCS replenishment (IGF-I?)

Patton et al. (2008) Animal 2:969-978

Strain of Holstein-Friesian cow

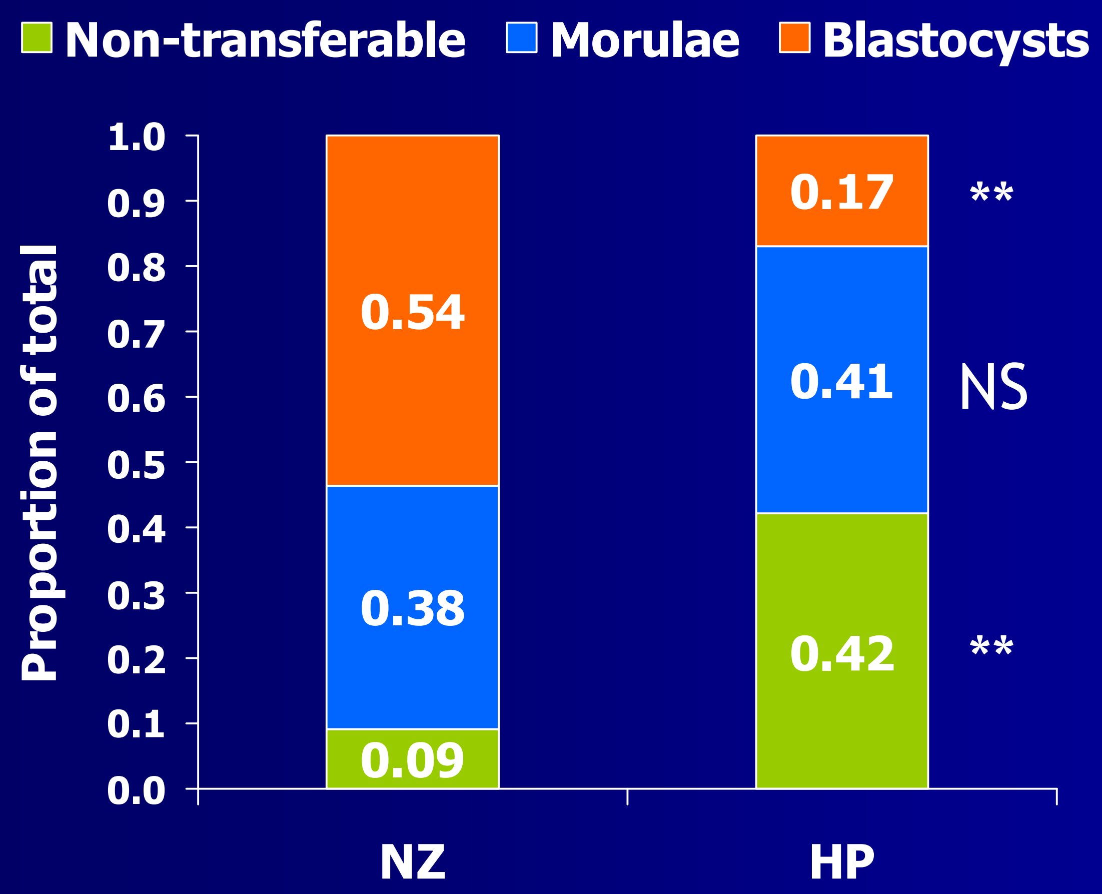
Circulating steroid concentrations

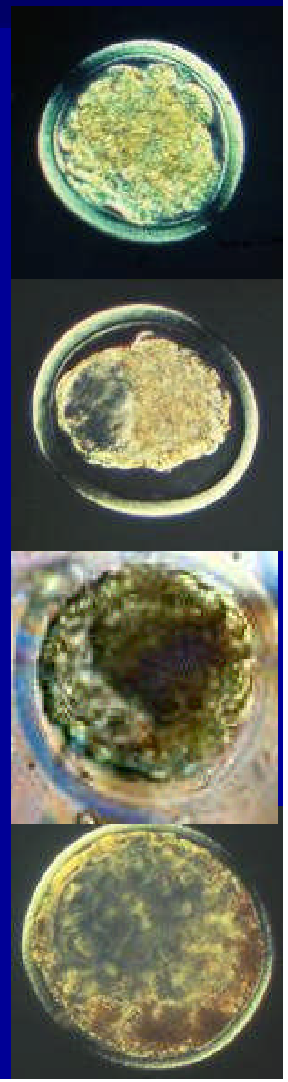


de Feu et al. (2008) Theriogenology: In Press

Strain of Holstein-Friesian cow

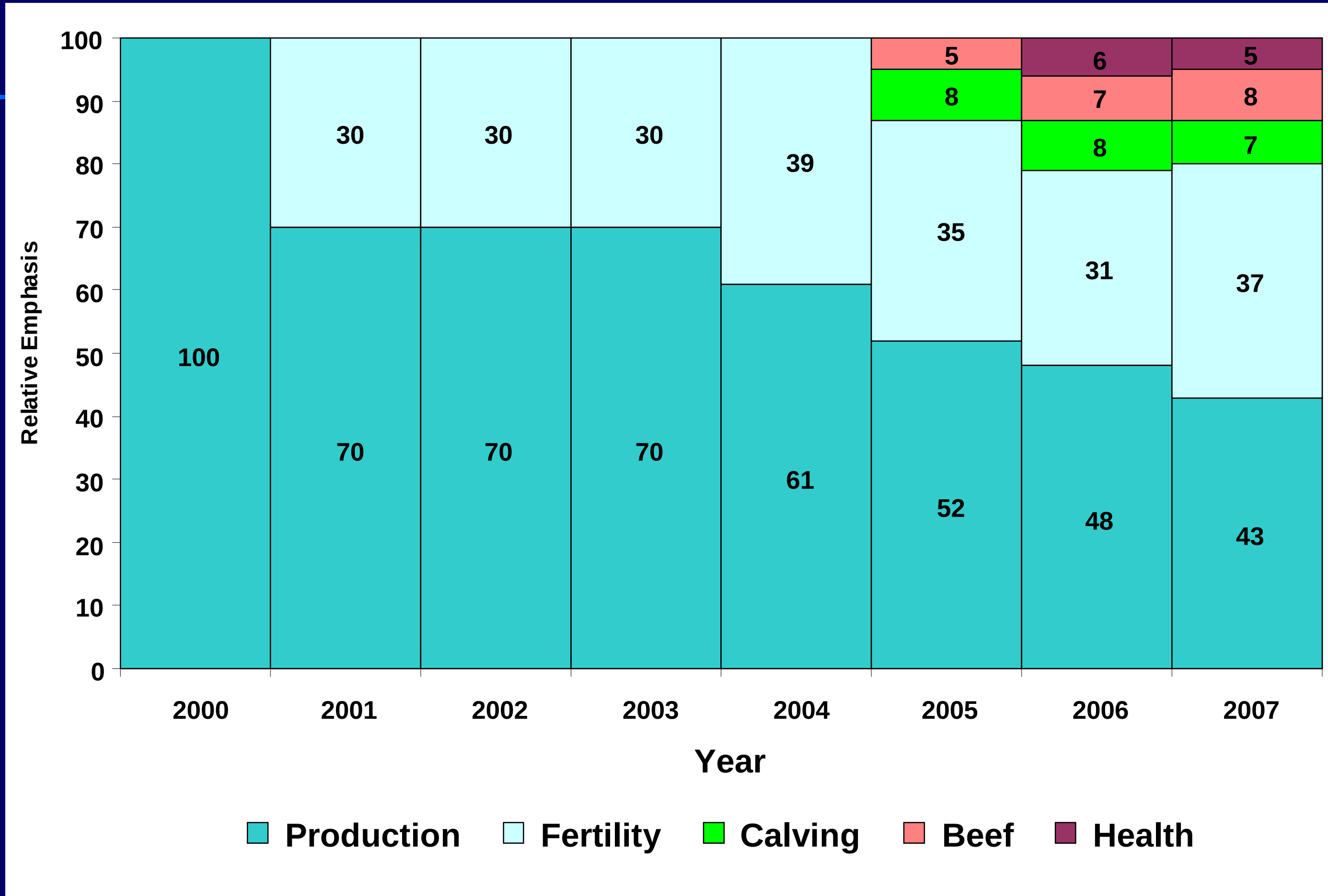
Embryo Quality





de Feu et al. (2008) Theriogenology: In Press

Economic Breeding Index (IRL)



Single Trait Selection → Balance Breeding Objective

Genetic selection for improved fertility

- New traits to consider
  - Energy balance/BCS (Berry et al., 2003)
    - Voluntary recording/industry recording?
  - Interval to first ovulation
    - Milk P4 (Petersson et al., 2007)
  - Interval to first observed heat
    - Voluntary recording/industry recording?
  - Endocrine indicators of metabolic status
    - IGF-I
    - Insulin
  - Juvenille predictors?
    - Metabolic?
    - Reproductive hormones?

Genomic selection for improved fertility

- Examine SNP markers (>50K) on thousands of bulls
- Identify SNP's associated with desirable reproductive traits in daughter offspring
  - Calving interval
  - Non-return rate
  - Conception rate
- Requirements
  - Large DNA database
  - Good phenotypic data on offspring
  - Huge computational power
- Already in use in a number of countries

Conclusions

- Selecting solely for increased milk production has resulted in undesirable genetics for fertility
  - Genetics widely dispersed
- Exquisite co-ordination of metabolism necessary to meet genetic potential for milk yield <u>**AND**</u> successfully conceive in desired timeframe
  - Some cows adjust well, some cows don't
- Selection, management and nutritional approaches to maximise postpartum DMI and minimize NEB should benefit fertility
  - Hormones and metabolites will follow
- Genomic selection holds promise to hasten genetic progress for all traits of interest