Reproduktion

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Formål

- Beskrive centrale elementer i reproduktionen
  - Fremstille en model af disse elementer

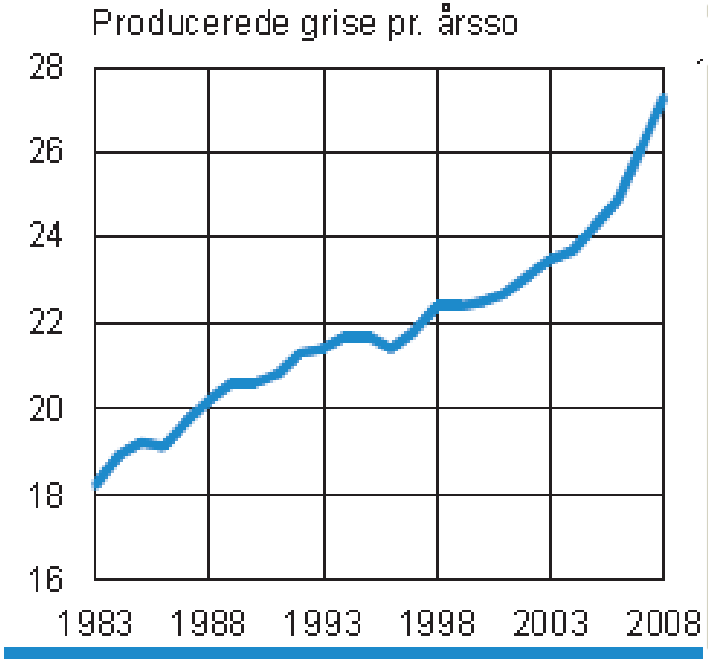
- Data og observationer fra forskning og praksis vedr. den højtydende ko i negativ energibalance

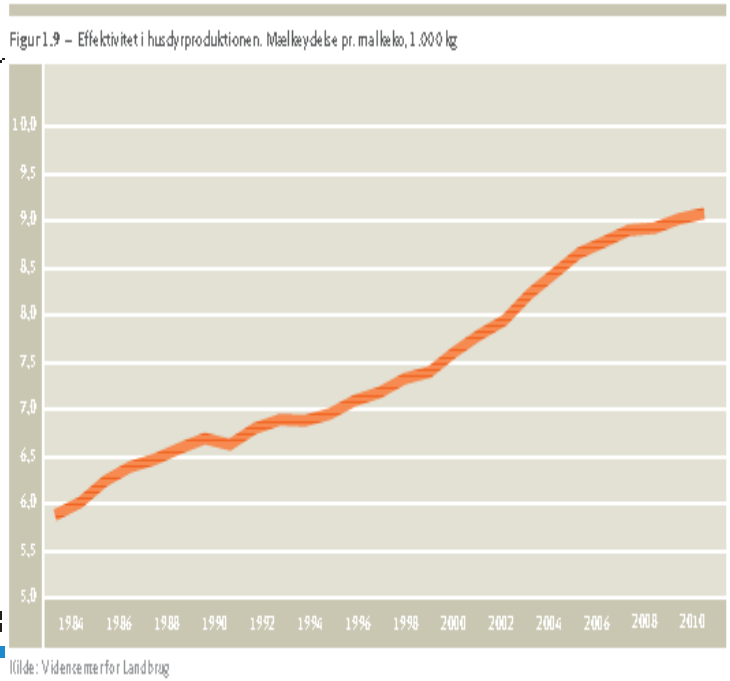
- Sammenstille model med data og observationer
  - analysere for årsager til dårlige reproduktionsresultater

Efficiency of reproduction

- Significant for economic output
  - •More calves
  - •More pigs
  - •More eggs
  - •Indirectly more milk
    - •Calving is starting a new lactation
- •Thus, efficiency in reproduction is important

Figur 3.6 Effektivitet i husdyrproduktionen





Kilde: Dansk Landbrugsrådgivning, Landscentret.

Reproduction

Coordination of processes very important

- Regulated by sex hormones
- Other factors
  - *Day length and season for some species (increasing or decreasing day length)*
  - ***Nutritional status (mobilization)***
    - » ***Metabolites and metabolic hormones***
  - ***Nutrition***
  - *Stress, infections, lameness …*

Hypothalamo-pituitary control of reproduction

- From pituitary
  - –Follicle stimulating hormone (FSH) is a gonadotropin
  - –Luteinizing hormone (LH) is a gonadotropin
  - –also growth hormone (GH) and prolactin and others

- From hypothalamus
  - –Gonadotropin releasing hormone (GnRH)
  - –Also growth hormone releasing hormone (GHRH) and others

- Pulse generator system – GnRH in pulses thus also LH and FSH in pulses

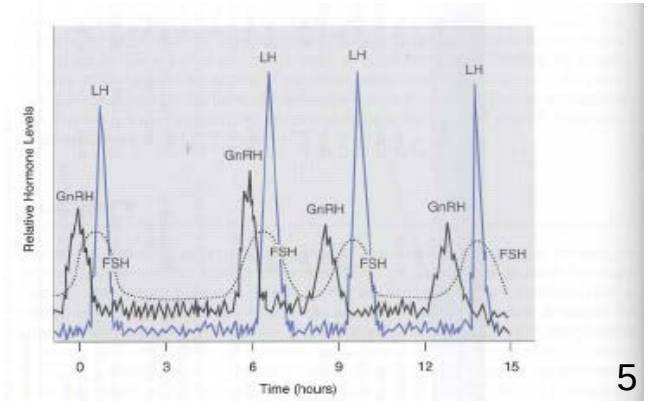
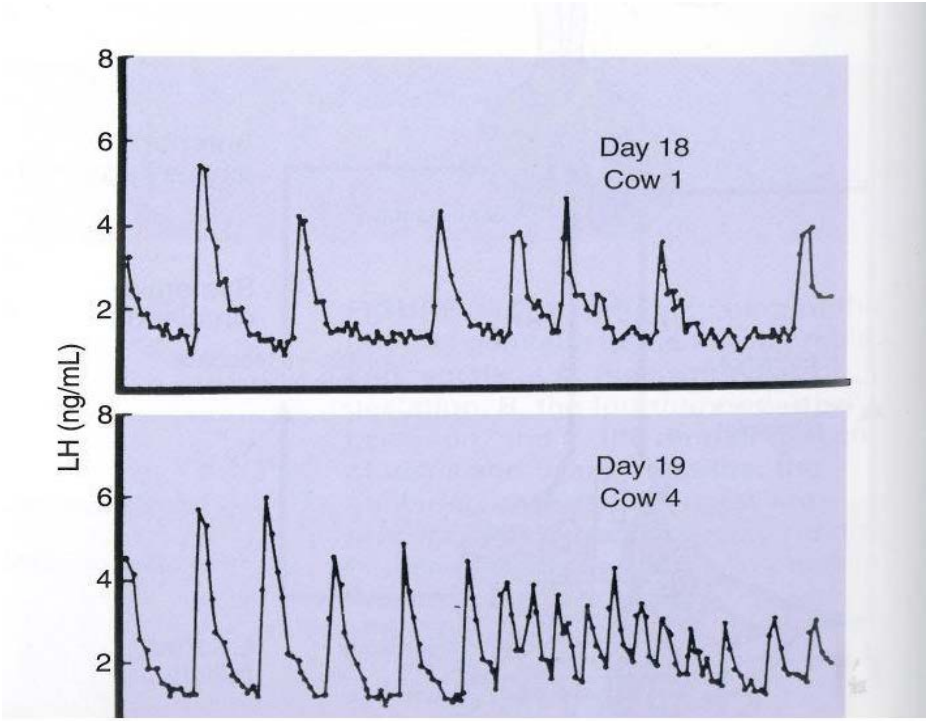


FIGURE 11–1 Episodic release of the hormones of reproduction in response to the release of gonadotropin-releasing hormone (GnRH). LH = luteinizing hormone; FSH = follicle-stimulating hormone. (SOURCE: Senger, 1997, p. 170. Used with permission.)

What is then controlling pulsativity?

Ovary comes into play

- Pulses affected by
  - Estrogen – positive feed-back on hypothalamus,
  - Progesteron – negative feed-back on hypothalamus, decreases pulse frequency (progest. absence will increase frequency)



LH in two cows

Luteal phase
-Dominated by progesteron control
-> pulativity decreased

Follicular phase
-Dominated by estrogen control/ absence of progest.
->pulativity increased

Let’s draw…

- First small reproduction model including
  - Hypothalamus
  - Pituitary
  - Ovary

- Draw boxes with the glands/organs
- Put arrows with affecting hormones

First small reproduction-model

- Hypothalamus - pituitary - ovary

- Control and feed-back
- Positive feed-back of estrogen on GnRH
- Negative feed-back of progesteron on GnRH (or absence of positive estrogen feed-back)

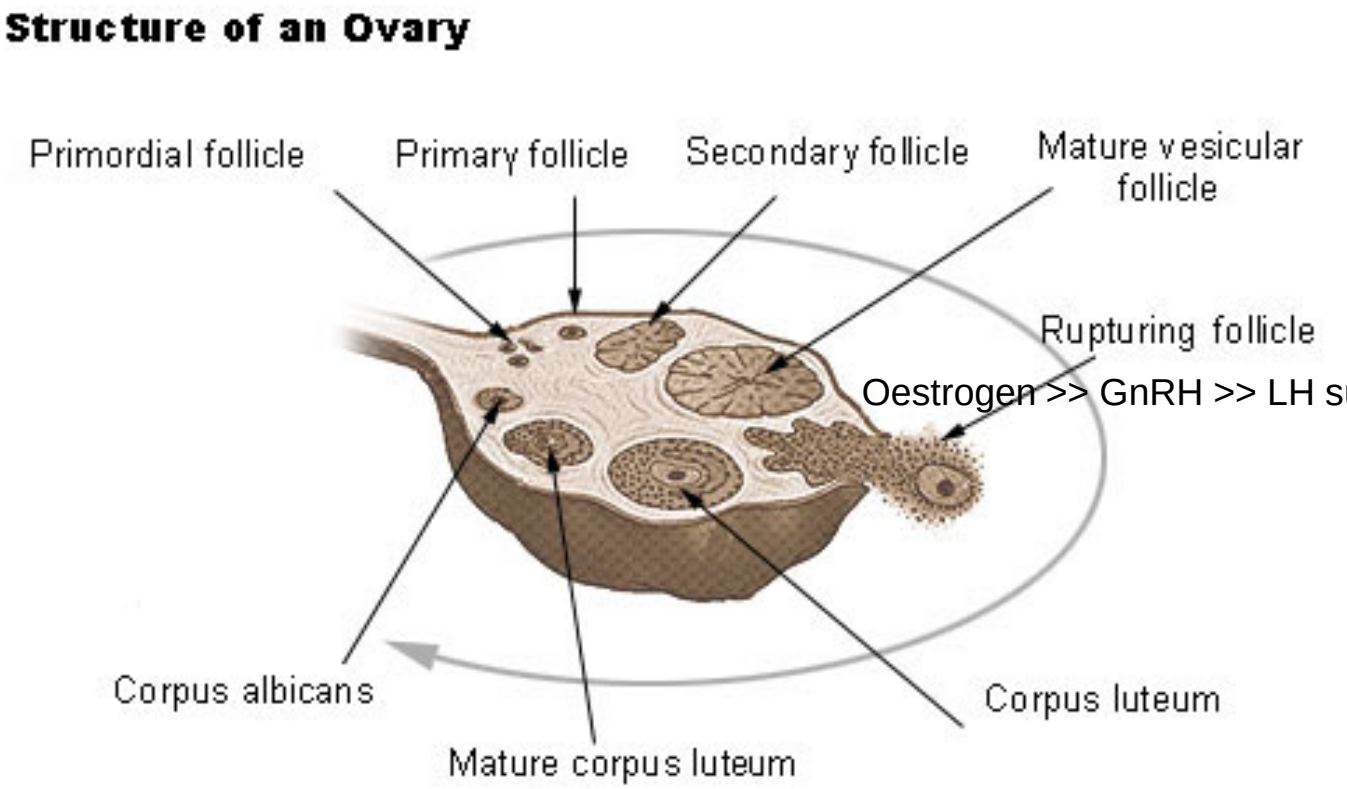
- Closer look at the ovary
  - Estrogen, progesteron, luteal phase and follicular phase

Follicular development

FSH stimulate follicular growth
LH causes the follicle to rupture

The follicle produces estrogen
Corpus luteum produces progesteron

Growing follicle = follicular phase
Corpus luteum dominating = luteal phase



Phases in 21 day estrus cycle

- Follicular phase
  - Proestrus 3 days (rapidly growing follicles)
  - Estrus 2 days (standing heat)
    - Ovulation (36-42 h after onset of estrus - late estrus)
- Luteal phase
  - Metestrus 4-5 days (early development of CL)
  - Diestrus 10-12 days (mature activity of CL)

Phases in estrus cycle

- 2 phases makes most sense in farm animals
  - Heat
  - Non-heat

Question

- Which hormone is responsible for “heat”
- From where

Cycle - 21 days in pigs and cows

- estrogen from follicles
- progesteron from corpus luteum

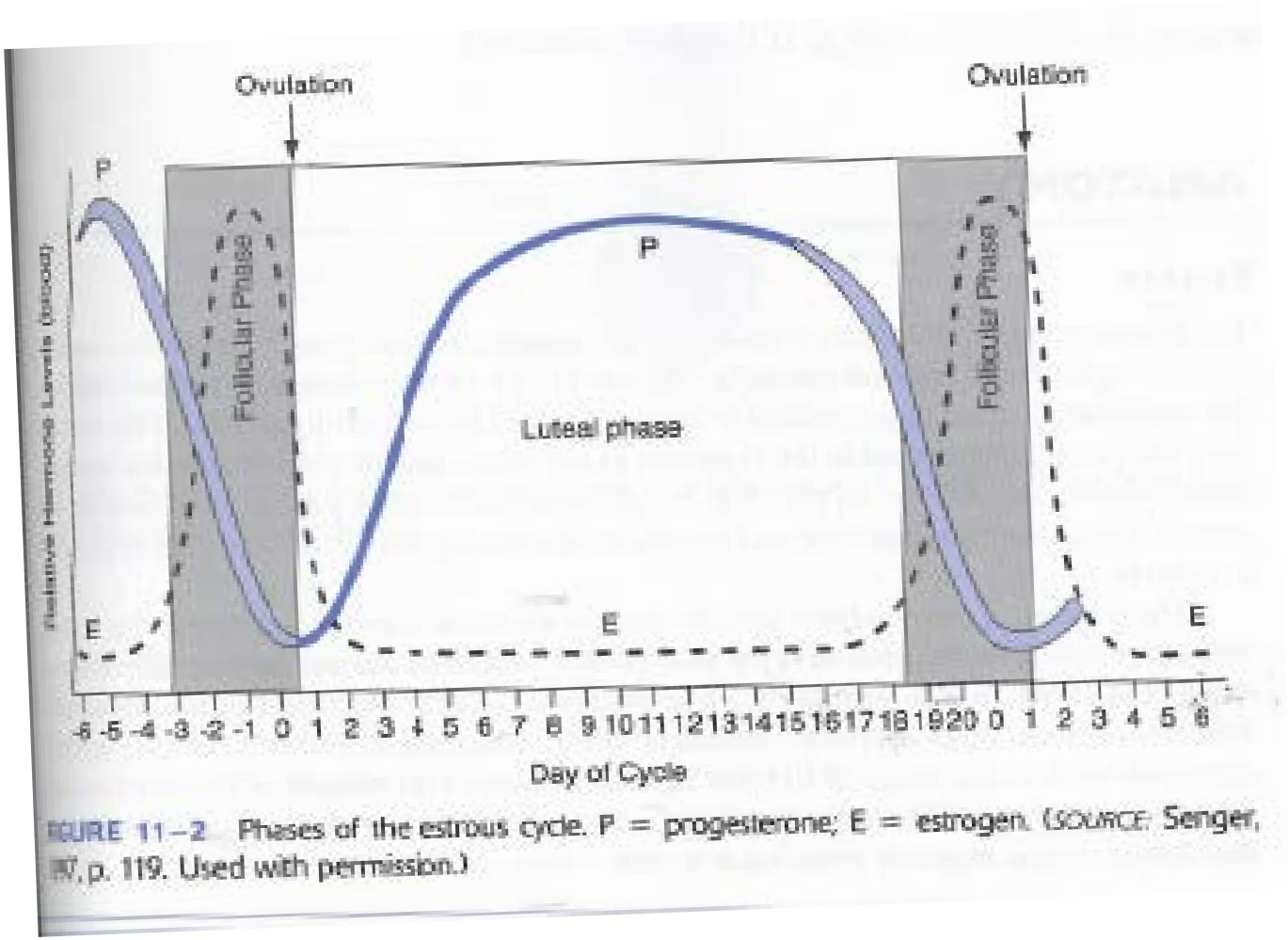
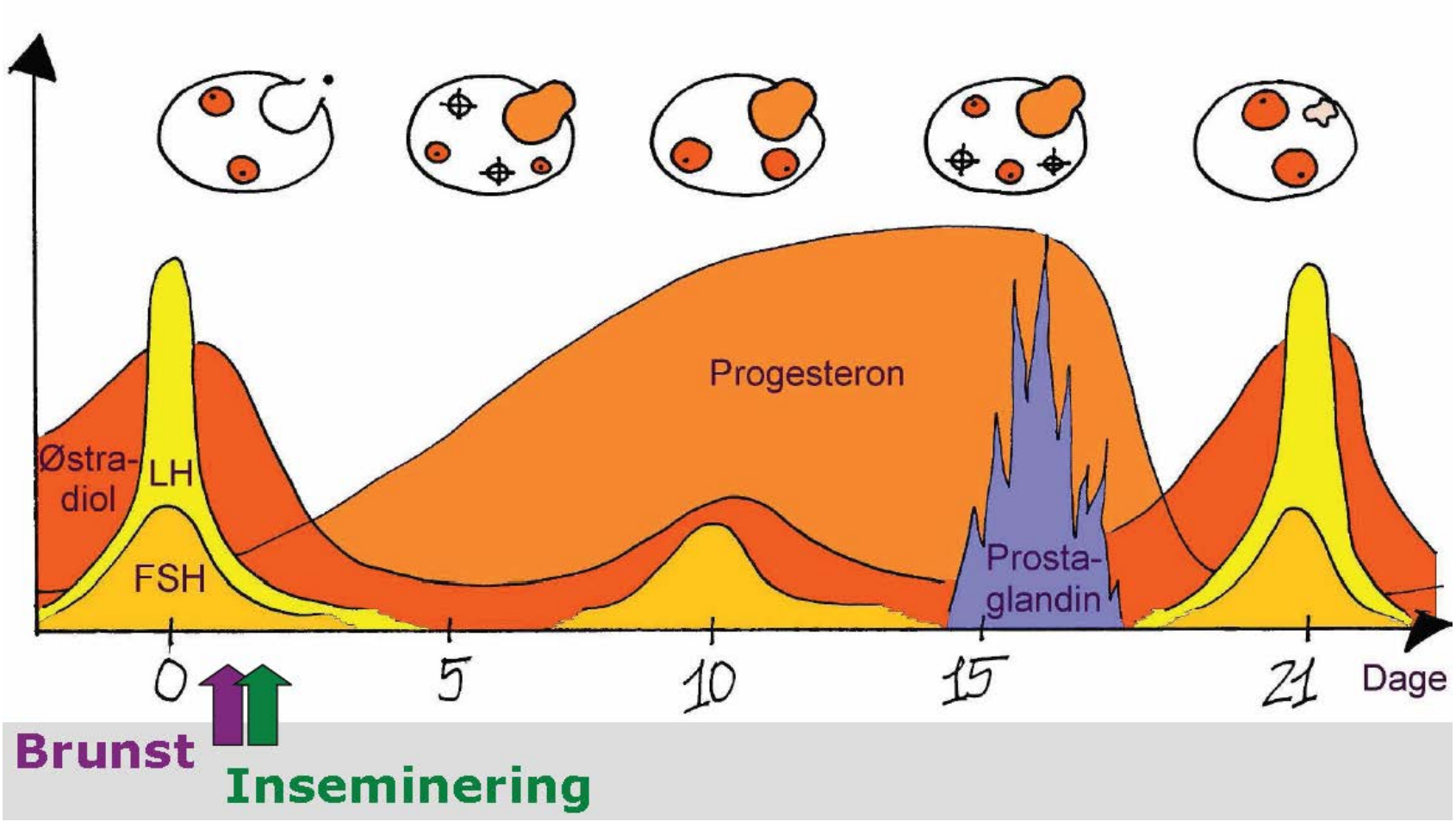
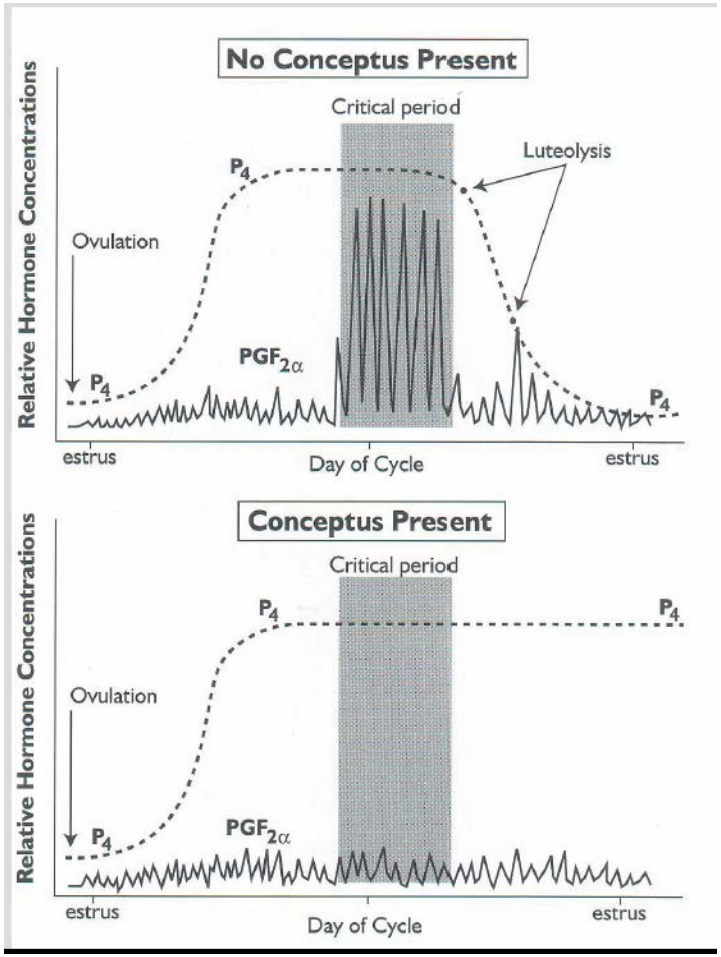


FIGURE 11–2 Phases of the estrous cycle. P = progesterone; E = estrogen. (SOURCE: Senger, [illegible]97, p. 119. Used with permission.)

Drægtighed eller ej -> prostaglandin





Erkendelse af drægtighed/
Signal fra foster

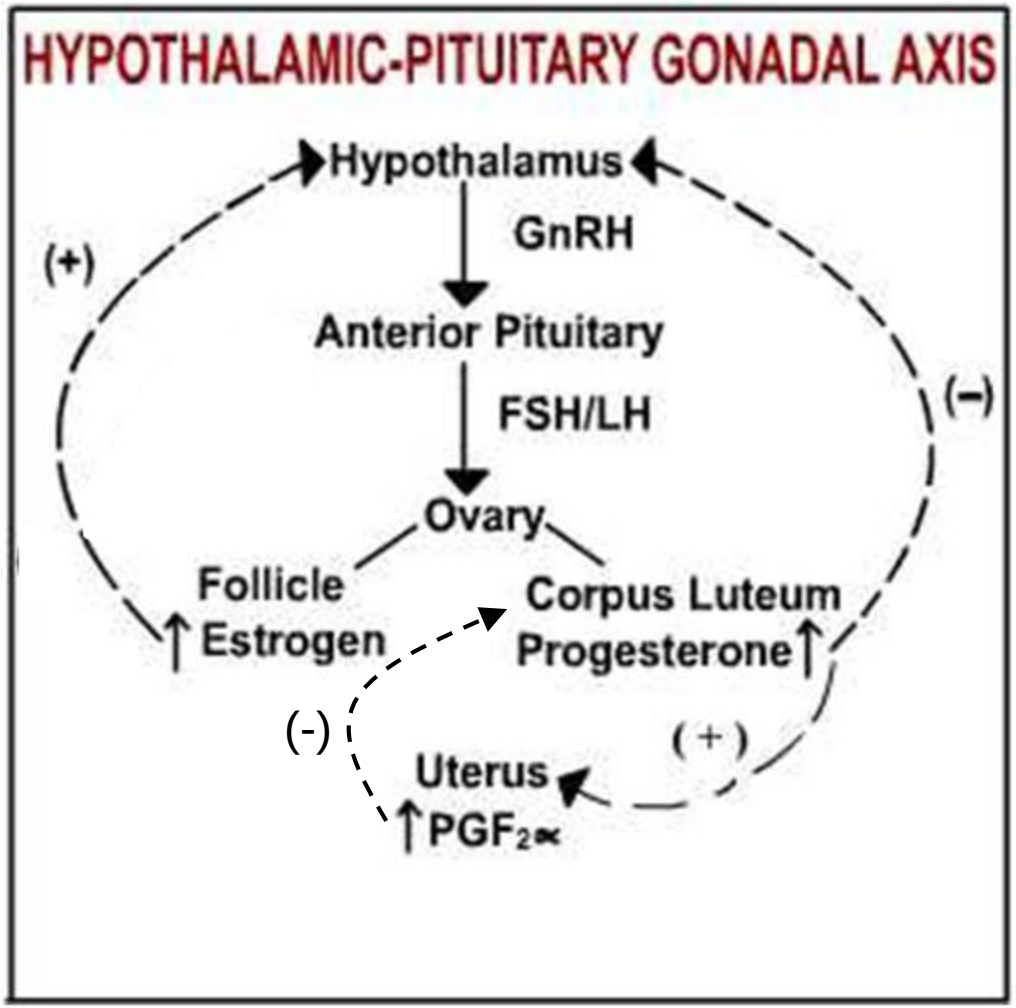
- Kvæg: ~dag 14-18
- Svin: ~dag 11-12

Regression of Corpus Luteum

- CL lifetime must be sufficiently long to allow fertilised oocytes to establish pregnancy
- CL lifetime must be relatively short to allow non-pregnant animals to start new follicle
- Prosteglandin (PGF2α) from uterus is the main CL killing factor

Expand reproduction model…

- Expand with uterus
- Expand with ovary
  - divided into follicle and corpus luteum


HYPOTHALAMIC-PITUITARY GONADAL AXIS
Hypothalamus
GnRH
Anterior Pituitary
FSH/LH
Ovary
Follicle
↑ Estrogen
Corpus Luteum
Progesterone ↑
Uterus
↑ PGF2∝
(+)
(-)
(-)
(+)

- If fertilized
  - Ova enter the uterus (3-4 days after fertilization)
  - Implantation
    - Sow: 12-20 days after fertilization
    - Cow: ~35 days after fertilization

- If not fertilized
  - New 21-day cycle

Establishment of pregnancy

- Fertilized oocyte develops into an embryo
- Develops to blastocyst stage in oviduct (5-6 days)
- Uterus finished inflammatory response and removal of sperms
- Nutrients available in the uterus for preimplantation embryos

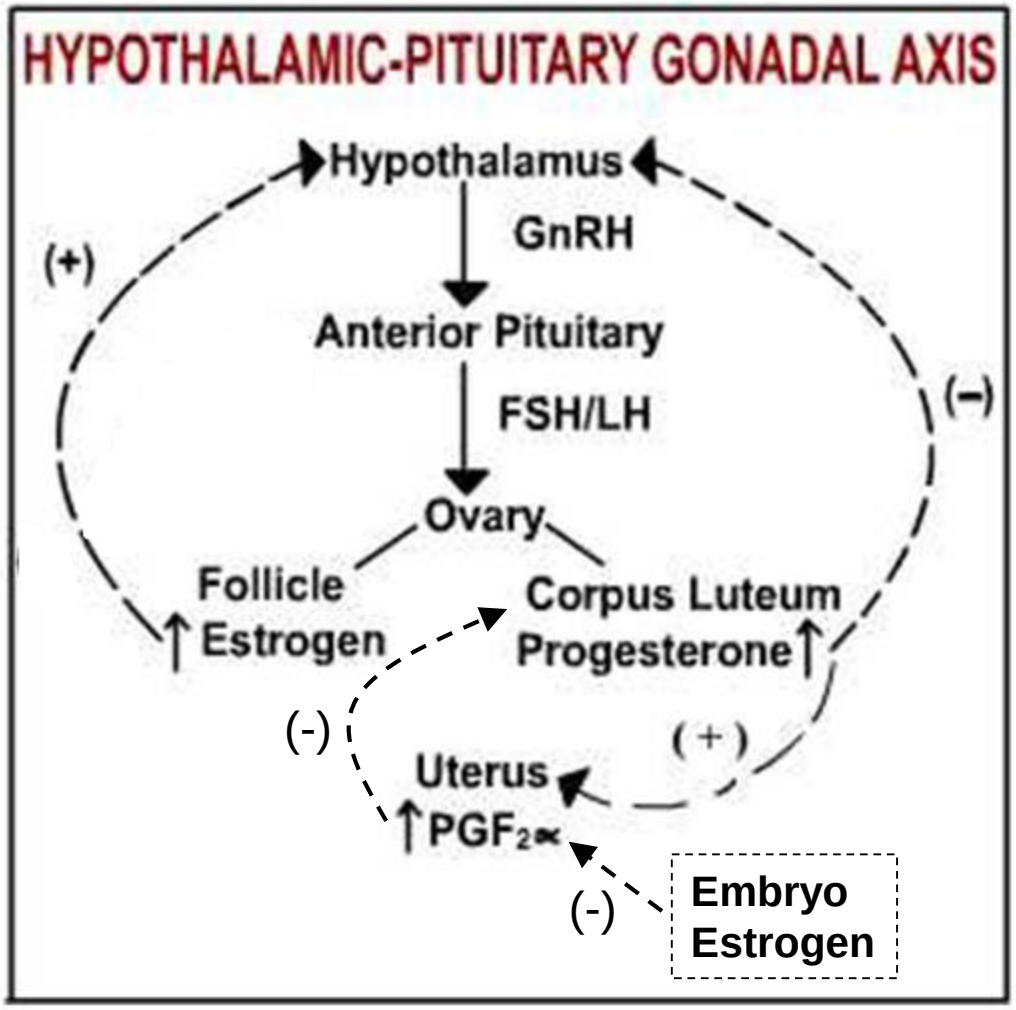
- CL has to be maintained
    - Uteral prosteglandin (PGF2α) has to be inhibited
        - estrogen from embryo inhibits PGF2α
- Recognition of pregnancy
    - Specific embryonic protein, trophoblastin
    - Movement of embryo(s) in uterine horns

- If no pregnancy >> new cycle

- After implantation the embryo is called a foetus

Expand reproduction model…

- Expand with embryo/fetus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(–)
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↑ Estrogen
Corpus Luteum
Progesterone ↑
(-)
(+)
Uterus
↑ PGF2∝
(-)
Embryo
Estrogen

Maintenance of pregnancy

Progesterone and estrogen are important pregnancy maintaining hormones

Placenta

- Production of progesterone (i.e. placenta also an endocrine gland)
- Production of estrogen
    - Interaction with the foetus in conversion of progesterone precursor to estrogen (placenta does not possess all necessary enzymes)

- Providing nutrients and oxygen for the foetus

Parturition

- Foetal adrenal cortex (binyrebark)
  - Cortisol >> release of PGF2α from uterus
    - Muscle contraction and relaxation of cervix

- PGF2α important for expulsion of placenta

Another story

- PGF2α is also used for estrus synchronization
  - Kills CL

Exercise
Pregnancy, parturition

- Mention key factors for establishment of pregnancy (implantation)
- Mention key factors for maintenance of pregnancy
- Mention the main roles of the placenta
- Mention key factors in parturition

The high yielding dairy cow

- **Reproduction model** (just done)

- Description of the high yielding dairy cow
  - Negative Energy Balance model (**NEB-model**)

- Can reproduction problems be explained by interaction between the two models?

Nutrition

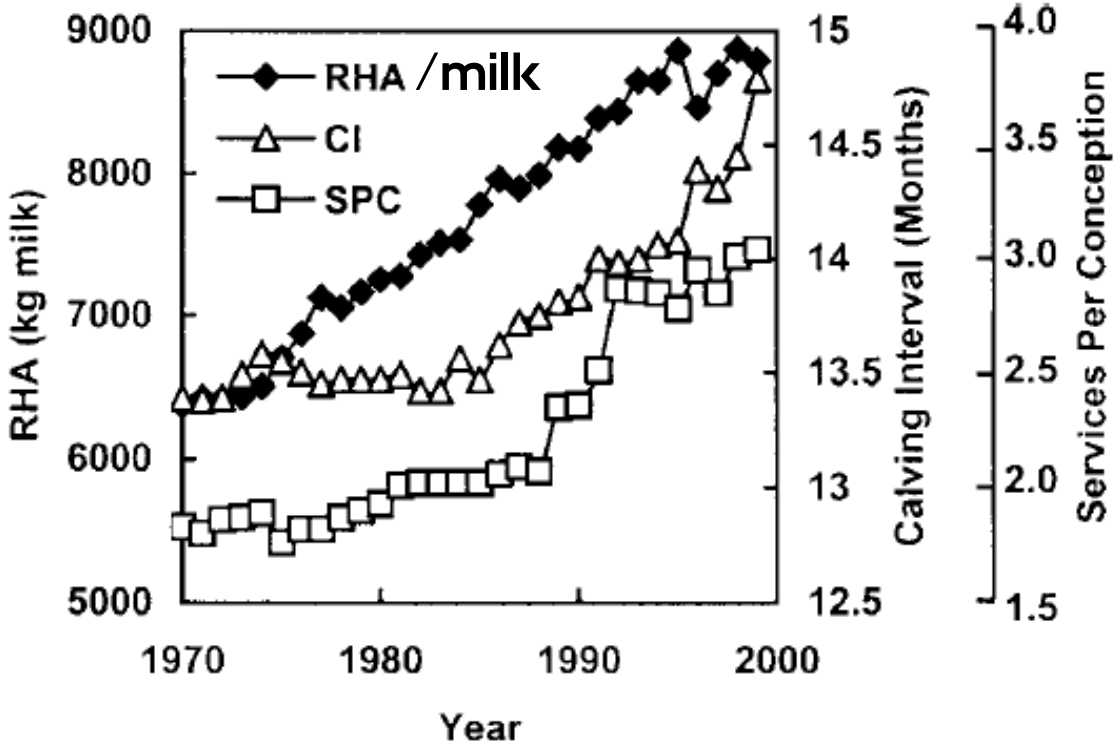
- Two review papers included:
  - Leroy et al. 2008. Nutrient prioritization in dairy cows early postpartum: Mismatch between metabolism and fertility? Reproduction in Domestic Animals, vol. 43, issue s2, pages 96-103
  - Walsh et al. 2011. A review of the causes of poor fertility in high producing dairy cows. Animal Reproduction Science, vol. 123, pages 127-138.

Køer – svagere brunsttegn

•Andel af køer der viser stående brunst er reduceret fra 80% til 50%
•Varighed af stående brunst er forkortet fra 15 til 5 timer

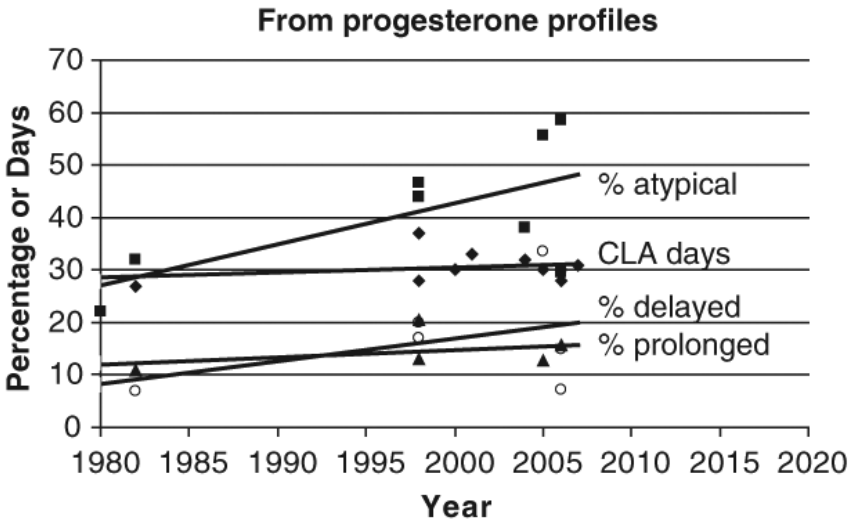
>> hjælpemidler til afsløring af brunst

Focus on high yielding dairy cows
Some evidence:
Development in milk and reproduction



Lucy, 2001, J. Dairy Sci. 84, 1277-1293

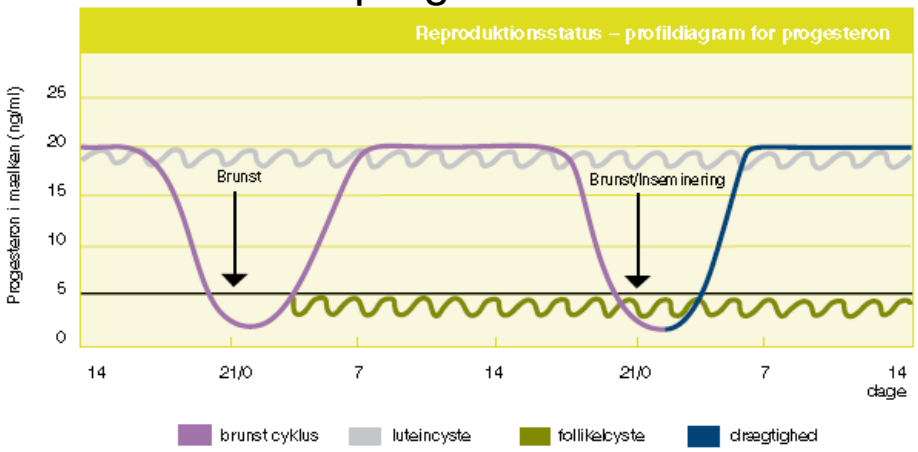
Analysis of progesterone profiles



- Pct. atypical profiles (■)
- Days from calving to commencement of luteal activity (CLA; ♦)
- Pct. delayed onset of luteal activity (▲)
- Pct. prolonged luteal phases (○)

Animal 2008, 2:1104-1111

Schematic progesterone



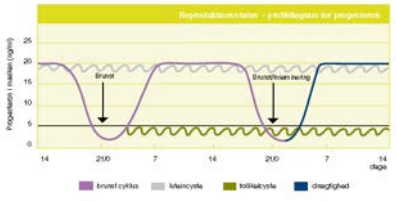
Leroy paper

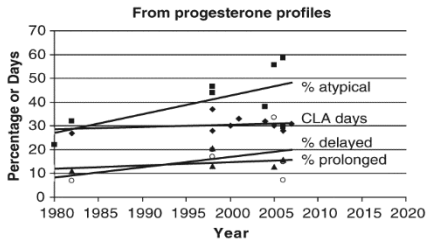
The process of becoming pregnant again after giving birth

- the ideal situation:
  - clearance of placenta
  - involution of uterus
  - resumption of ovarian activity
    - growth of healthy follicle enclosing a competent oocyte
    - estrus
    - ovulation
  - fertilization
  - uterine attachment of a viable embryo

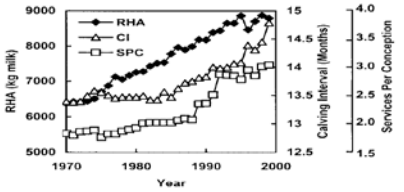
Subfertility syndrome

Two major sub-problems





- Abnormal estrus cycles
  - prolonged calving to first insemination interval
  - Instability within hypothalamo-pituitary-ovarian-uterine axis
    - reduced estrus expression or anestrus
    - cyst formation and delayed first ovulation



- Disappointing conception rates
  - Incl. high incidence of early embryonic loss

Evidence

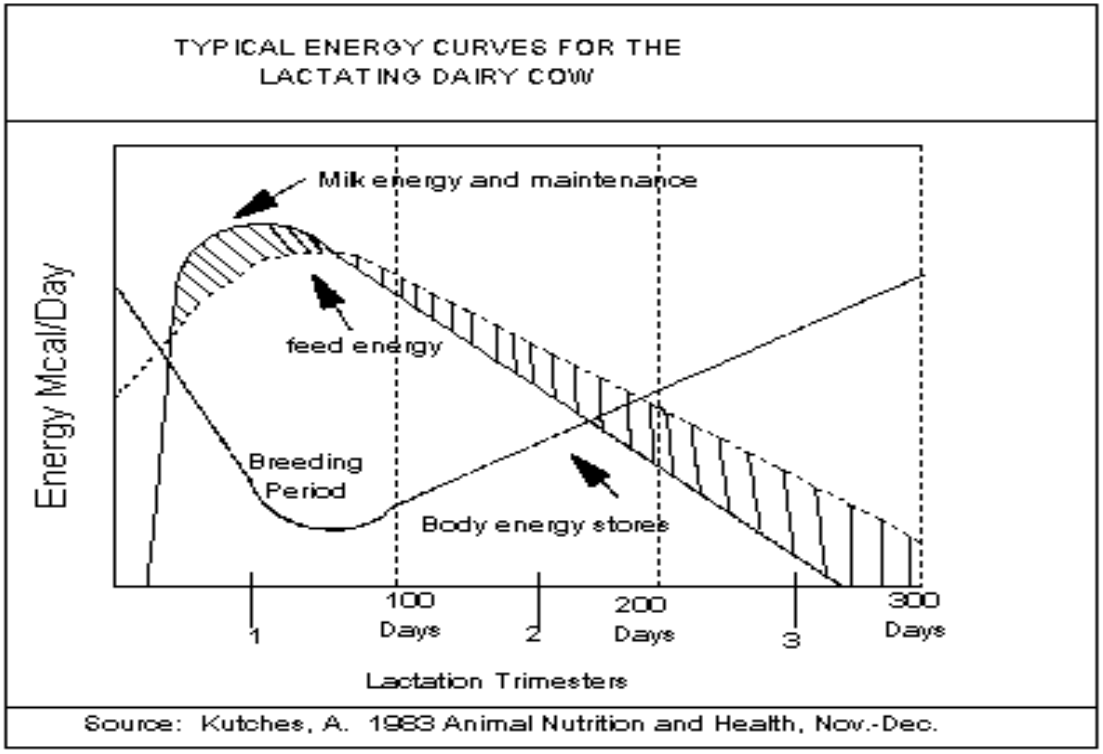
- From high milk merit cows
  - Lower blastocyst yield
  - Higher proportion of non-viable embryos
    - (70-80 % of total embryonic and foetal losses during early embryonic pre-attachment period)
- Heifer fertility unchanged
  - i.e. normal fertility in high milk merit cattle when lactational demands are not imposed
- Reason for reproduction problems: LACTATIONAL demands

Questions to be discussed:

- Why do modern dairy cows prioritize milk production at the expense of fertility?
- Does high milk yield conflict with good fertility in metabolic terms?

Lactation

- Cows in catabolic state in late pregnancy
- Lactation imposes additional demands for glucose, fatty acids and protein
- Unable to meet increased demands for energy by increasing feed intake >>> negative energy balance (NEB)



Lactation continued

- decreased insulin brings mobilization and partitioning to the udder.
- Hypoinsulemia promotes gluconeogenesis and triggers lipolysis
- Mobilised NEFA preserves glucose for the udder (for synthesis of lactose)
  - Ketone body formation from NEFA in liver >> risk of steatosis (fatty liver and disturbed liver function)

In high yielding cows everything goes to the udder for milk – even increase in feed intake will result in more milk and unchanged imbalance and mobilization

Biological mechanisms for milk production at the cost of body reserves

Firstly

- Udder independent of insulin for glucose uptake
  - Glucose transporter 1 (Glut 1) and Glut 3
- Most other tissues dependent on insulin
  - Glut 4
- This means that low insulin will favour the udder

Secondly

- Suppression of pancreatic function (due to high NEFA)

continued

Thirdly

- IGF1 production in liver suppressed
  - Negative feed-back of IGF1 at hypothalamus/pituitary removed
    - GH concentration increases
      - » Higher milk production and mobilization

Exercise – NEB-model

For the negative energy balance dairy cow:

- Which key hormones
  - Are they high or low – in which tissues/organs are they affecting
- Which key metabolites
  - Are they high or low – where do they come from/where do they go to

Interactions between the reproduction model and the NEB-model

At the hypothalamus level

- Metabolic input may have divergent effects
  - stimulating GHRH and inhibiting GnRH

At the ovarian level

- Decreased insulin-stimulated follicle growth
- Decreased IGF1-stimulated follicular growth

- Consequence:
  - Lower follicular/ovarian activity
    - Impaired ovulation
  - Cystic ovarian follicles

- Mobilization >> NEFA detrimental for follicle cell viability and function

Oocyte quality

- Carry over effects of impaired growth of primary follicles early postpartum to pre-ovulatory follicles 2-3 months later
  - Low estrogen and progesteron production and low oocyte quality

Embryo quality in high yielding cow

Dependent on

1. Gamete quality
2. Corpus luteum quality (progesterone conc.)
3. Uterine involution including endometrium repair and bacterial clean-up
4. Nutrition

Where does negative energy balance have an effect?

Ad 1. Already discussed – pre-ovulatory adverse conditions (e.g. negative energy balance) for oocyte may carry over to effects on embryo viability

Ad 2. NEB cows have lower progesterone

Ad 3. Delayed in NEB cows due to reduced immune response

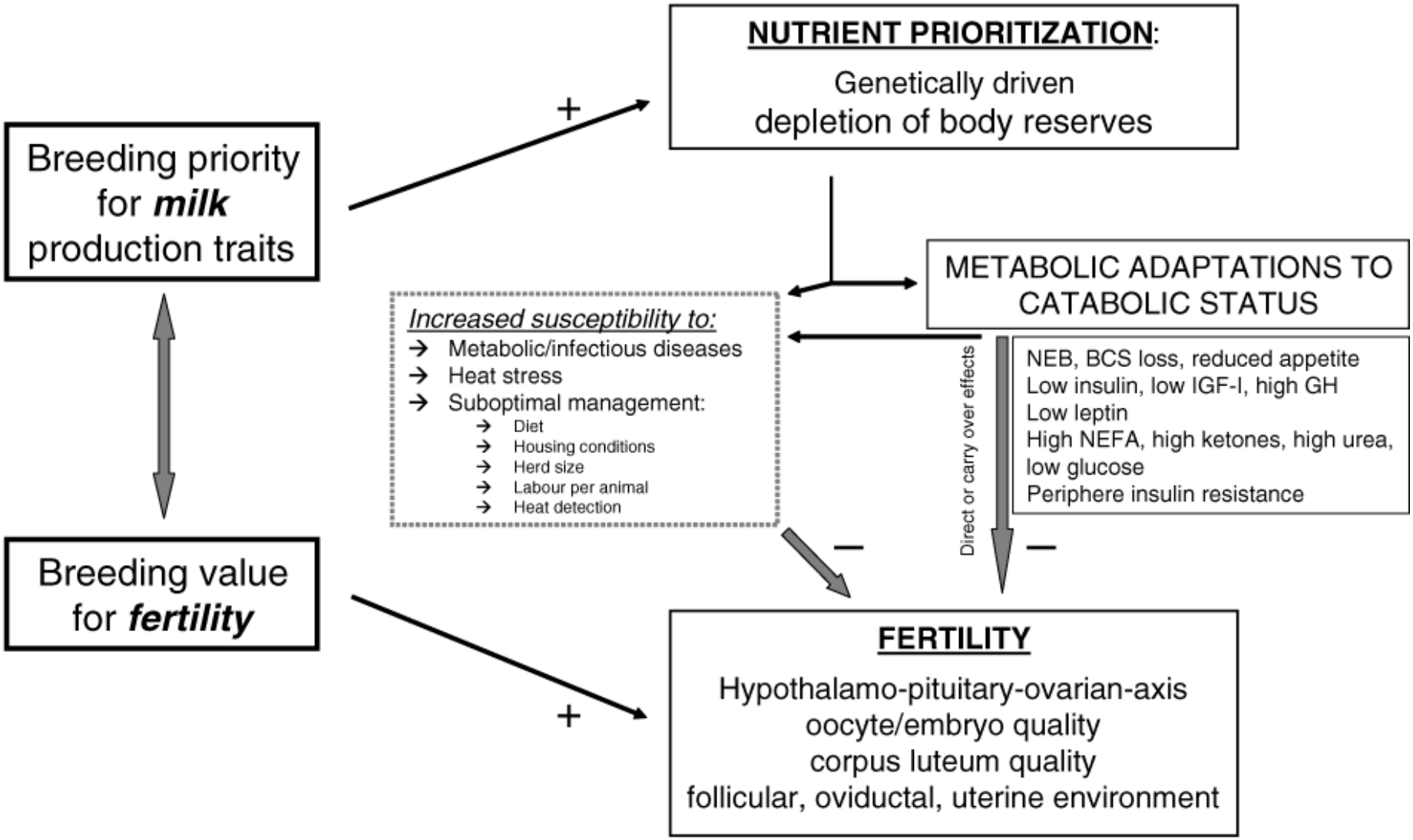
Ad 4. Diets are optimized for milk yield not for embryo quality and survival

Rehearse

Interaction between your “reproduction model” and your ”negative energy balance model” (NEB-model) in high producing dairy cow

- From your NEB-model try to predict disturbances in your reproduction-model

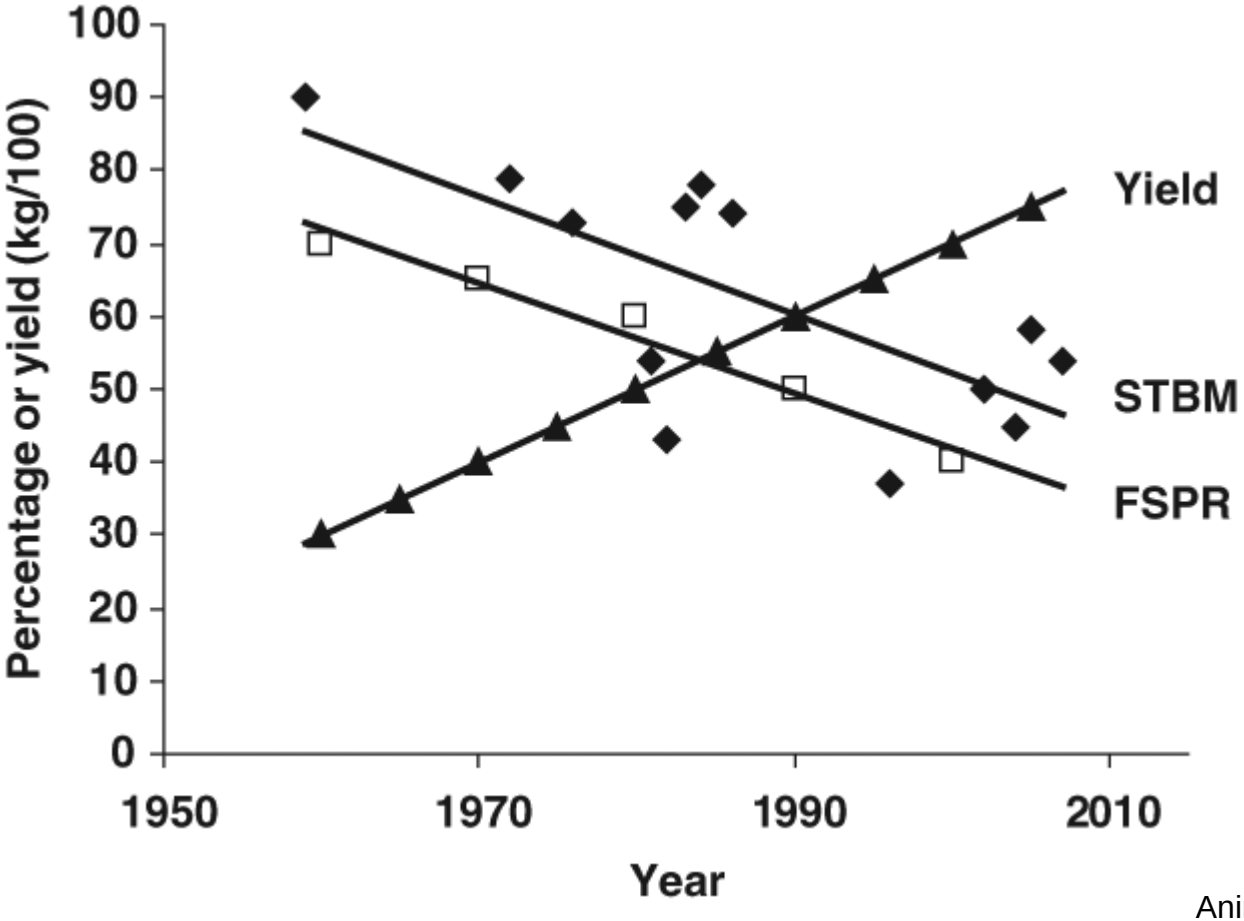
Interaction between genetic selection for milk production and fertility



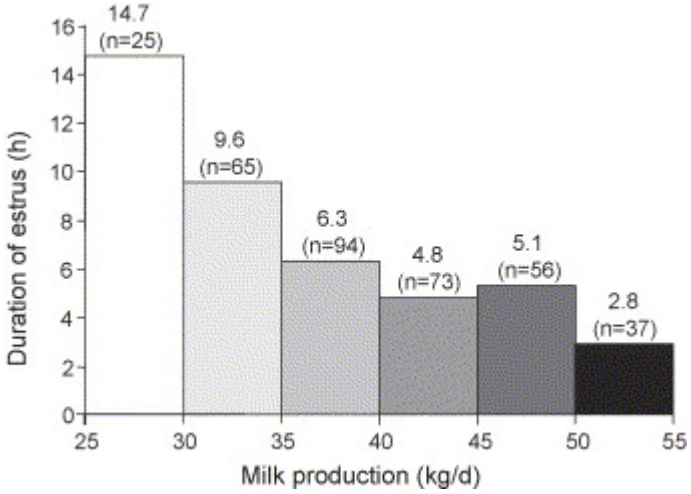
Leroy et al 2008, Reprod. Domest. Anim. 43, s2, 96-103

More evidence

•Percentage of animals standing-to-be-mounted (STBM; ⧫)
•first-service-pregnancy-rate (FSPR; □)
•average milk yield ()



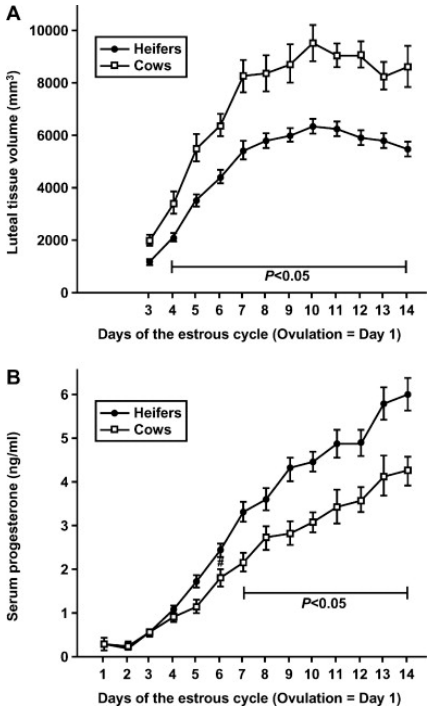
Animal 2008, 2:1104-1111

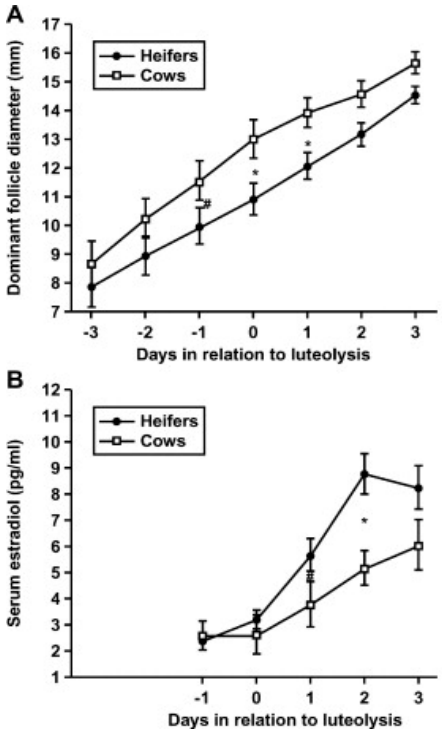


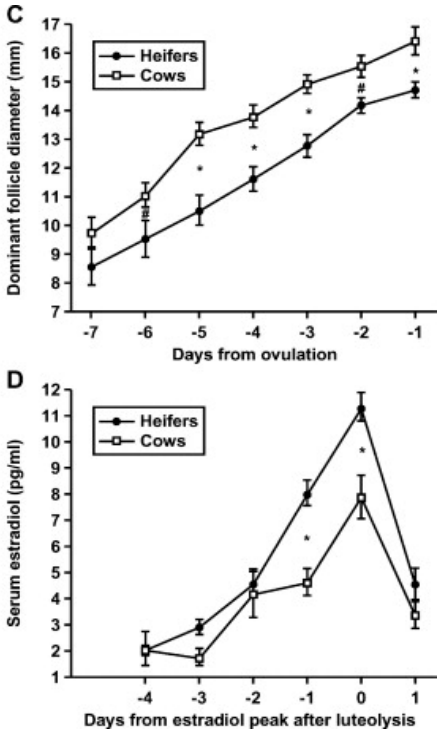
- Cows in heat
  - Heat signs decreased
  - Standing heat reduced
  - What hormone is responsible?
  - From where does it come?

Anim Reprod Sci, **81** (2004), pp. 209–223

Size of follicle and CL, and concentration of estrogen and progesterone in lact. and non-lact.



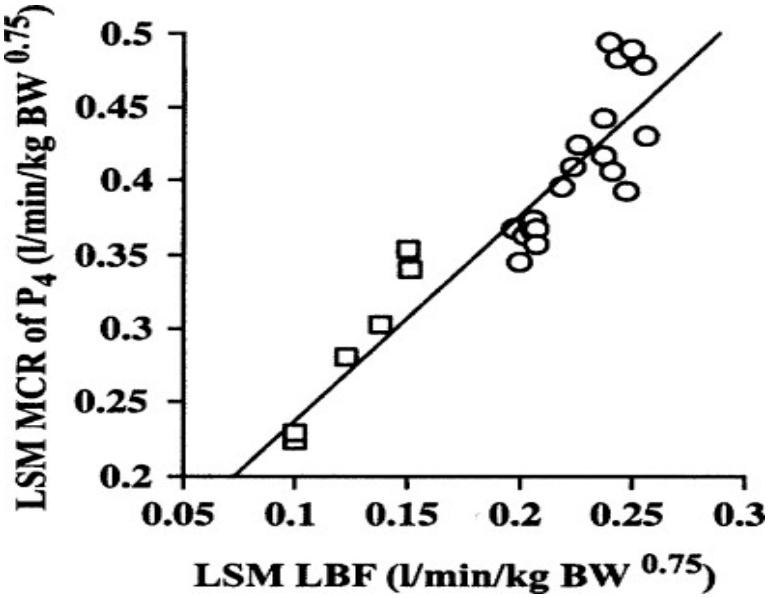




J Dairy Sci, **87** (2004), pp. 905–920

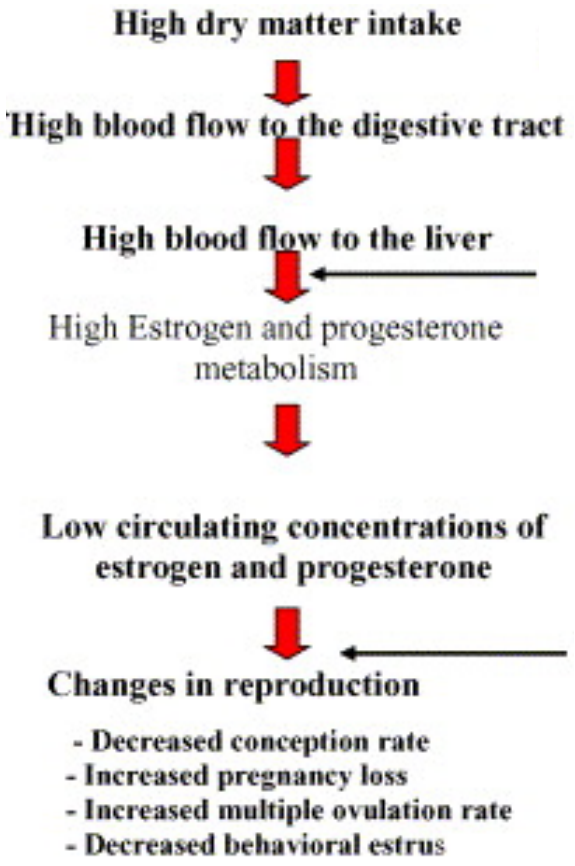
Feed intake, blood flow and clearance of estrogen and progesterone in lact. and non-lact.

Progesterone (P4) metabolic cleatance rate (MCR) vs liver blood flow (LBF)



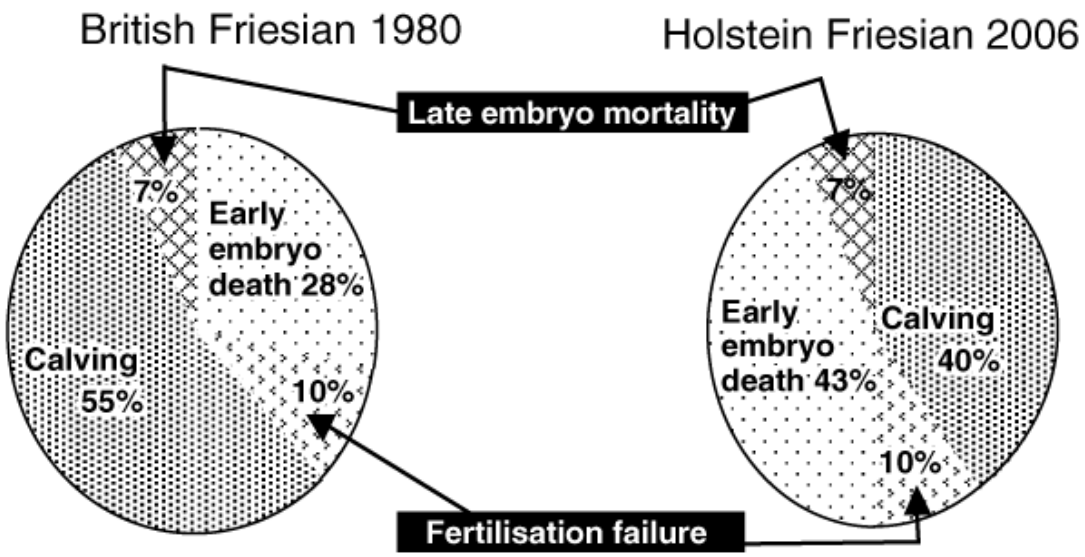
Journal of Dairy Science 2002, vol. 85, pages 2831-2842

Schematic of the potential physiological pathway that may produce the changes in reproductive physiology observed in high-producing lactating dairy cows.



Theriogenology
Volume 65, Issue 1, 7 January 2006, Pages 17-29

Embryonic and Early Foetal Losses in Cattle and Other Ruminants



Reproduction in Domestic Animals
pages 260-267, 9 JUL 2008 DOI: 10.1111/j.1439-0531.2008.01171.x
http://onlinelibrary.wiley.com/doi/10.1111/j.1439-0531.2008.01171.x/full#f1

What to do?

- It is the destiny of the high yielding dairy cow to produce milk
- Har I forslag?
  - Altså forslag der ikke har nedsat ydelse som sideeffekt?
- Forlænget laktation ?

Afslutning

- Beskrive centrale elementer i reproduktionen
  - Fremstille en model af disse elementer

- Bruge model samt data og observationer til at analysere for årsager til dårlige reproduktionsresultater