

## The Physiology of Pregnancy Loss: Female Factors

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## Points at Which Failure Can Occur

Live offspring = number of ovulations x % fertilization rate x % embryonic survival x % fetal survival x % survival during the birth process

## Embryonic and Fetal Mortality

- How Much Mortality Occurs?
- When Does Mortality Occur?
- What Are Some of the Causes?
- When Do the Causes Occur?
- Is There Anything We Can Do About It?

## Patterns of Embryonic and Fetal Loss Vary with Species, Herds and Breeds

Cattle – Most losses by Day 8.  
Dairy cows – 12 to 14% of pregnancies on Day 28 to 30 are lost by Day 45 to 60.  
Beef cattle – no more than 5% late losses.  
Sheep – Throughout pregnancy – 3 to 4% every 20 days.  
Goats – More in last third of pregnancy.

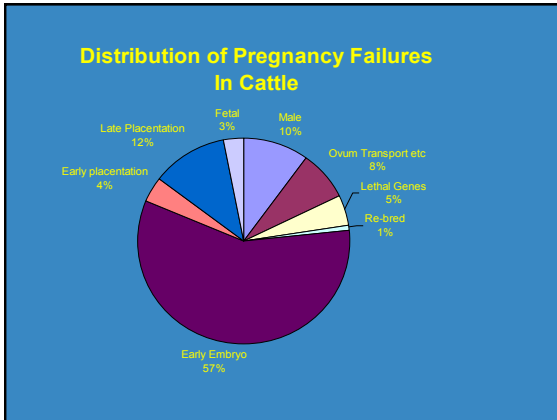
## Herd Variation Example in Dairy Cows

Eight Herds on Ov-Synch Protocols

Range – 7.6 to 21.6% lost between 30 and 60 days post-insemination

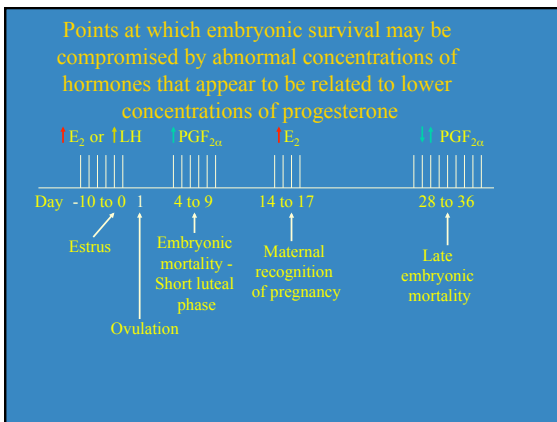
## Estimates from the Early Literature

- Fertilization Failure - 0 to 40%
- Overall Loss of Embryos
  - 10 to 40 percentage points
  - 15% to first service
  - 28.5% in repeat breeders

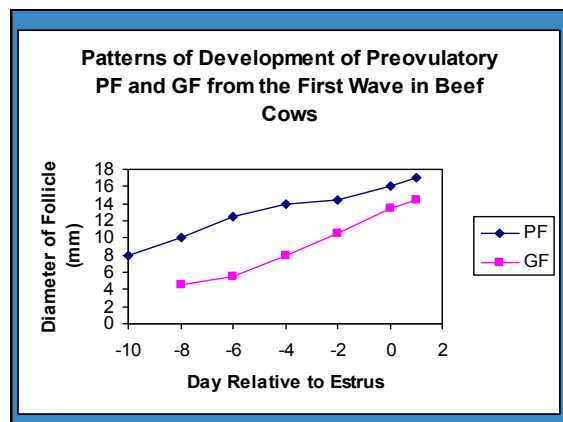
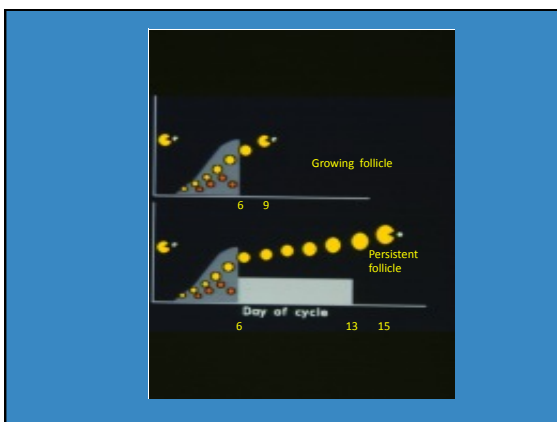


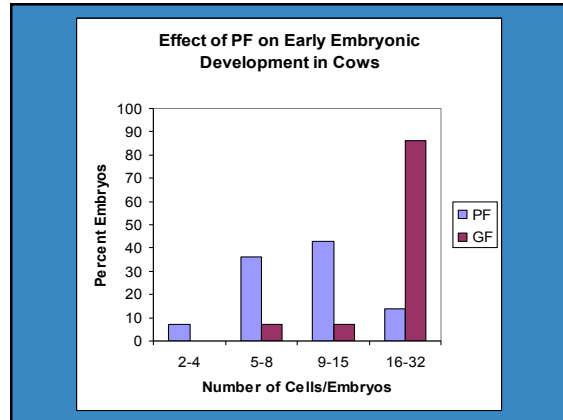
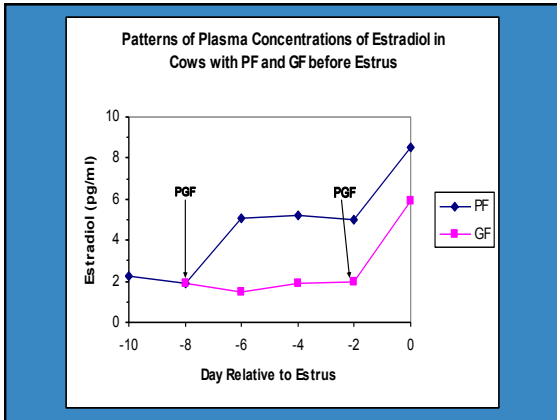
### What Are Some of the Causes of Embryonic Death?

- Persistent (or Immature) Follicle Ovulated
- Short Life Span of the Corpus Luteum
- Low Progesterone
  - Early - Days 4 to 8
  - At Maternal Recognition - Days 14 to 18
  - During Placentation - Days 28 to 42
- Genetic Defects in the Embryo
- Other Factors



### How Aged Follicles Affect Fertility (Or Why Was Ov-Synch Developed for Dairy Cows?)





### Effect of persistent follicles on early embryos

Status of embryos recovered on day 6 after mating:

Proportion of Good or Excellent Embryos

| Type of follicle | ≥ 16-cell stage | Morulae |
|------------------|-----------------|---------|
| Growing          | 73%             | 86%     |
| Persistent       | 14%             | 14%     |

### How Aged Follicles Affect Fertility

### How Immature Follicles Affect Fertility

### Where is adequate estradiol important, the ovary or the uterus?

- Donor cows - Greater estradiol just before ovulation → more embryos and fewer unfertilized oocytes
- Recipient cows - Greater estradiol just before ovulation → established more pregnancies from ET

*Jinks et al. J. Anim. Sci. 91:1176, 2012*

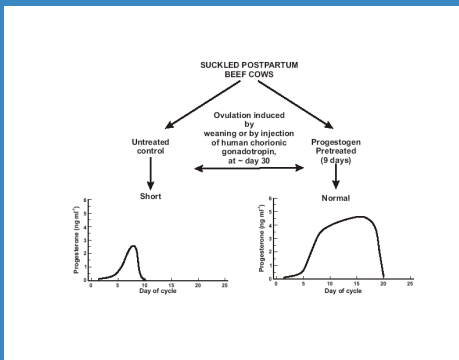
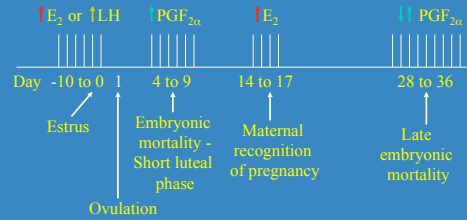
## Importance of Preovulatory Estradiol

Estradiol in:

| Donor | Recipient | N   | Pregnancy at Day 27 |
|-------|-----------|-----|---------------------|
| Low   | Low       | 78  | 45 %                |
| Low   | High      | 80  | 65 %                |
| High  | Low       | 91  | 43 %                |
| High  | High      | 101 | 61 %                |

Jinks et al. J. Anim. Sci. 91:1176, 2012

Points at which embryonic survival may be compromised by abnormal concentrations of hormones that appear to be related to lower [progesterone]



## With a Short Cycle:

Fertilization can occur.

Prostaglandin  $F_2\alpha$  is secreted at days 4 to 9 and causes a short cycle.

The  $PGF_2\alpha$  is embryotoxic to the morula stage, so that supplemental progesterone can not save the embryo!

## With a Normal Cycle:

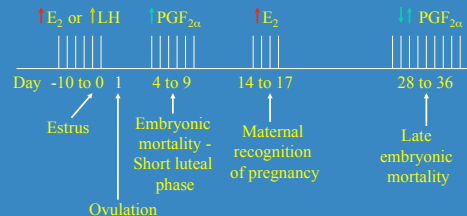
Fertilization can occur.

$PGF_2\alpha$  is secreted at days 14-17, not earlier.

$PGF_2\alpha$  is not embryotoxic after the morula stage.

Thus the embryo is not interfered with, and a normal pregnancy can occur.

Points at which embryonic survival may be compromised by abnormal concentrations of hormones that appear to be related to lower [progesterone]



### Embryonic Death (%) During Maternal Recognition of Pregnancy

Irish Study (N = 158 Beef Heifers):

Loss d 14 (n=47) to d 30 (n=111)

0

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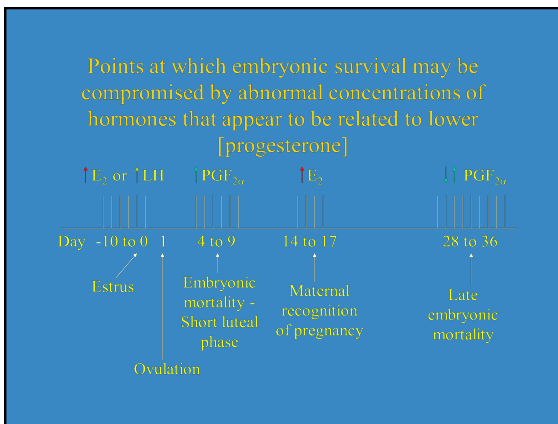
West Virginia Study (60 Beef Females)

| Follicular Waves After Breeding | Conception Rate (%) |
|---------------------------------|---------------------|
| Two                             | 70                  |
| Three                           | 96                  |

0.05 p <

### Relationship of Conception Rate to Progesterone and Estrogen on Days 14 through 17 After AI in 101 Lactating Beef Cows

|                                                          | Conception Rate (%) |
|----------------------------------------------------------|---------------------|
| <b>Progesterone</b>                                      |                     |
| Low ¼                                                    | 54                  |
| Medium ¼                                                 | 56                  |
| High ¼                                                   | 73                  |
| <b>Estrogen (Groups P &lt; 0.05; Linear P &lt; 0.01)</b> |                     |
| Low ¼                                                    | 77                  |
| Medium ¼                                                 | 60                  |
| High ¼                                                   | 42                  |



### Late Embryonic/Early Fetal Death (%) in Dairy Cows Bred at Timed AI

|                                       |                                       |       |
|---------------------------------------|---------------------------------------|-------|
| • Florida - Moreira et al. 2001       | <u>d 32 to d 74</u>                   | 13.7  |
| • OvSynch                             |                                       |       |
| • Kansas - Cartmill et al. 2001       | <u>d 28 to d 56</u>                   | 46    |
| • OvSynch                             |                                       | 24    |
| • CIDR w/OvSynch                      | <u>d 28 to d 38-56</u> <u>d 27-30</u> |       |
|                                       | <u>to d 40-50</u>                     |       |
| • Cyclic Cows                         | 26                                    | 11.5* |
| • Anestrous Cows                      | 33                                    | 25.6  |
| • Wisconsin - Vasconcelos et al. 1997 | <u>d 28 to d 98</u>                   | 22    |
| • AI at GnRH                          |                                       | 17    |
| • AI 24 h > GnRH                      |                                       |       |
| • West Virginia (N=211)               | <u>Week 5 to Week 9</u>               |       |

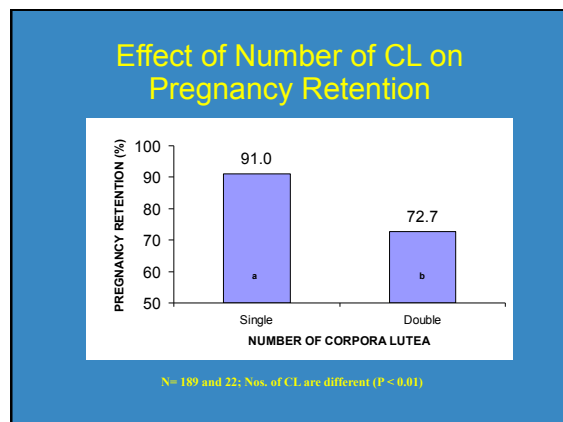
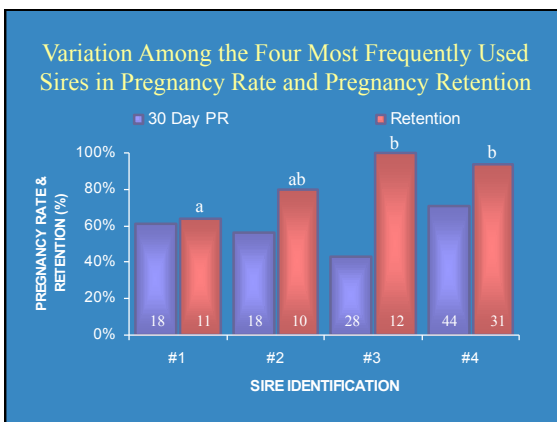
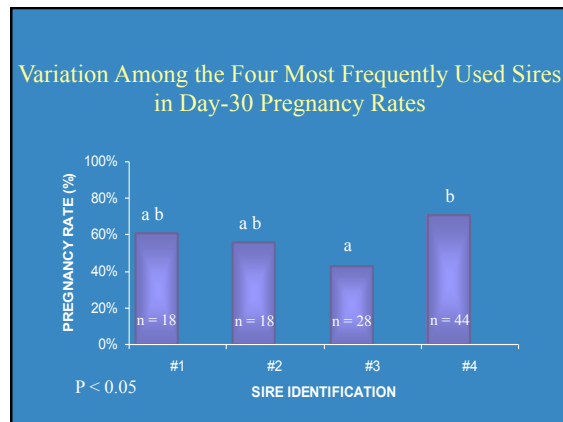
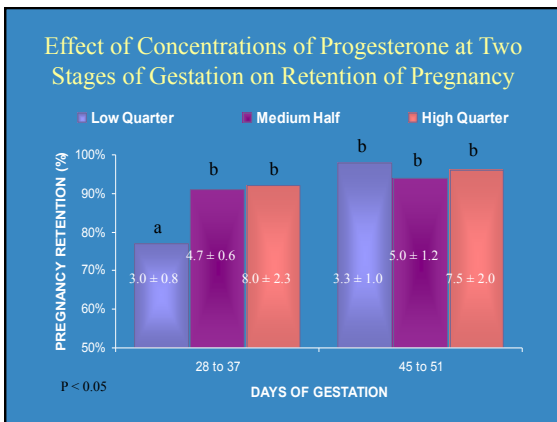
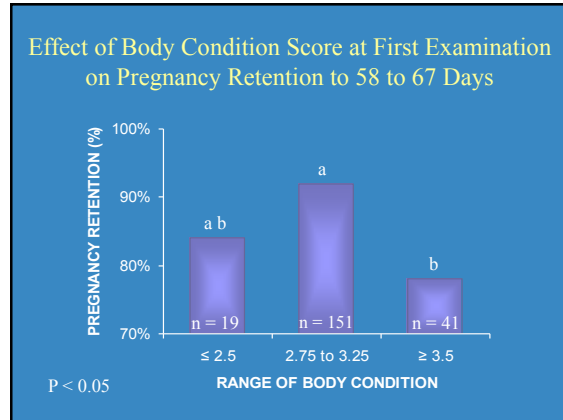
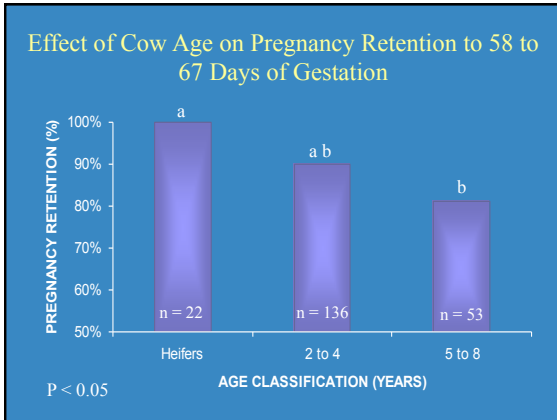
### Late Embryonic/Fetal Death (%) in Beef Heifers

- Kansas Study d 29-33 to d 60-90
  - 525 Pregnant Heifers 4.2
- Irish Study d 30 to Term
  - 72 Pregnant Heifers 4.2

### Late Embryonic/Fetal Death (%) in Lactating Dairy Cows

West Virginia Study (N=211)

|                        | <u>Week 5 to Week 9</u> |
|------------------------|-------------------------|
| AI and Natural Service | 11                      |
| Causes?????            |                         |



### Take-home Messages

Females in estrus at fixed AI are more fertile.

Concentrations of estrogen just before and at time of insemination are important.

Avoid persistent or immature follicles. Both cause more embryo deaths.

Longer durations of progestogen treatment ( $\geq 14$  days) can lead to persistent follicles. Breeding heifers at second estrus, will  $\uparrow$  fertility.

High concentrations of estrogen during maternal recognition of pregnancy may contribute to losses.

### Take-home Messages

#### Preparation of uterus and ovaries

Exposure of prepubertal heifers and anestrous cows to a progestogen for 5 or more days will induce normal luteal function, so a developing embryo can establish pregnancy.

Animals must be in good body condition to respond to progestogen and show estrus.

Programs without progestogen pretreatment or induction of a functional corpus luteum will not be effective in anestrous females.

### Take-home Messages

#### Placentation is a critical period

Low progesterone or elevated estrogen during days 30 to 35 of gestation can contribute to pregnancy loss.

Late embryonic losses are increased in animals that were induced to ovulate a small follicle by treatment with GnRH.

#### Fetal losses

Losses after onset of placentation are minimal in beef animals that are free of disease.

# Questions?