Animal Science 434

Lecture 11: The Luteal Phase of the Estrous and Menstrual Cycle

- **Preovulatory Follicle**
  - Steroid synthesis
    - Progesterone
    - Collagenase
  - Theca interna

- **Corpus Hemorrhagicum**
  - Present 1-3 days following ovulation
  - Blood vessels in follicle wall rupture
  - Walls collapse
  - Cells intermix
  - Old basement membrane becomes connective tissue of CL

- **Luteal Tissue**
  - Large cells from granulosa
  - Small cells from theca interna

- **Functional Corpus Luteum**
  - Increases in size
    - Papilla forms
  - Composed of cells from the granulosa and theca interna
  - Progesterone production increases
  - A small cavity may be present where the follicular antrum was present
Functional Capability of CL

• the number of luteal cells
  – large cells undergo hypertrophy (3 fold)
  – small cells undergo hyperplasia (5 fold)
• vascularization of CL
  – Initiated by angiogenic factors from follicle
  – Vascularity affects CL steroid synthesis and delivery of hormones
• Insufficient CL function
  – Failure to maintain pregnancy
  – Important in domestic animals

Molecular Mechanism of LH on Luteal Cell
(cAMP second messenger)
Luteolysis

- Uterus
- PGF$_{2\alpha}$
- Oxytocin

Luteolysis in Cows, Ewes, Sows

- Normal Uterus
- Total Hysterectomy
  - CL Normal Lifespan
  - CL Lifespan Longer Similar to Gestation Length

- Contralateral Hysterectomy
  - CL Normal Lifespan
  - CL Lifespan Longer
  - >30 days

Prostaglandin F2α Control of Luteolysis

Prostaglandin synthesis by uterine endometrium is released into the uterine vein.

- Corpus Luteum
- Uterine Vein
- Progesterone from CL stimulates production of uterine PGF$_{2\alpha}$ after day 15 in cow
- PGF$_{2\alpha}$ is picked up by ovarian artery through counter current exchange and delivered back to the ovary where it causes lysis of the CL

Blood Supply to Uterus and Ovary in the Mare

- Blood Supply to Uterus and Ovary
- CL Normal Lifespan
- CL Maintained
  - 50% of CL’s Maintained
  - 50% of CL’s Maintained
Relationship of Oxytocin and PGF2α

- decreased blood flow
- cellular response
  - apoptosis
  - progesterone synthesis
- immune response
  - Lymphocytes
  - Macrophages
**Molecular Mechanism of PGF (Ca²⁺ Second Messenger)**

- **Receptor**
- **G-protein**
- **PLC**
- **PIP₁**
- **IP₃**
- **DAG**
- **Ca²⁺**
- **Protein Kinase C**
- **Ca²⁺**
- **Endoplasmic Reticulum**
- **Apoptosis**
- **Cholesterol**
- **PGF**
- **Receptor**
- **G-protein**
- **Ca²⁺**
- **PLC**
- **PIP₁**
- **IP₃**
- **DAG**
- **Ca²⁺**
- **Protein Kinase C**
- **Ca²⁺**
- **Endoplasmic Reticulum**
- **Apoptosis**
- **Cholesterol**
- **PGF**
- **Receptor**
- **G-protein**
- **Ca²⁺**
- **PLC**
- **PIP₁**
- **IP₃**
- **DAG**
- **Ca²⁺**
- **Protein Kinase C**
- **Ca²⁺**
- **Endoplasmic Reticulum**
- **Apoptosis**
- **Cholesterol**

**Luteolysis**

- **decreased blood flow**
- **cellular response**
  - apoptosis
  - progesterone synthesis
- **Immune response**
  - Lymphocytes
  - Macrophages

**Menstrual Cycle**

- **Anterior Pituitary Hormones**
- **FSH**
- **LH**
- **Ovarian Hormones**
- **Estriol**
- **Ovulation**
- **Corpus Luteum**
- **Corpus Albinus**
- **Uterine Endometrium**
- **Recruitment**
- **Selection**
- **Dominance**
- **Recruitment**

**Luteolysis in the Primate**

- Does not require the uterus
- CL lifespan in the human is 12-14 days unless pregnancy occurs
  - In the absence of pregnancy, CL self destructs
  - Possible intra-ovarian oxytocin receptors and PGF₂α production
- Menstruation
  - Drop in P₄ and E₂
  - Endometrial PGF₂α, vasoconstriction, necrosis
  - Endometrial inflammation and tissue degeneration

**Manipulating Ovulation**

- Hormonal induction of ovulation
  - PGF₂α
  - GnRH
  - Progestins
- Superovulation
  - FSH
  - eCG
**Principle of PGF$_{2\alpha}$ Use**

- Regress active corpus luteum
  - Only effective on a day 5 - 17 CL
  - Not effective on days:
    - 1 - 4 (CL not responsive)
    - 18 - 21 (CL already regressed)

**Induction of Ovulation with PGF$_{2\alpha}$**

- Ovulation
- Follicular Size
- Day After Ovulation

**Ovsynch**

- GnRH
- PGF$_{2\alpha}$
- GnRH

- 7 Days
- 36 - 48 hours
- Timed AI 8 - 18 hours

- Eliminate current follicular wave
- Luteolysis
- Ovulates dominant follicle
Induction of Ovulation with PGF$_{2\alpha}$

**Follicular Size**

- **Progesterone**
- **Ovulation**
- **Dominance**
- **Selection**
- **Recruitment**
- **Day After Ovulation**

9 16 21

**Progesterone**

- **GnRH**
- **PGF$_{2\alpha}$**
- **Eliminate current follicular wave**
- **Ovulates dominant follicle**

**Ovulation**

7 36 - 48

**Timed AI**

8 - 18 hours
Use of Progestogens

**Principle:**
Maintain the cow under the influence of progesterone until corpus luteum regresses, remove progesterone - animal respond to progesterone with estrus and ovulation 2-5 days later. This does not regress the CL!!!!

**Administration:**
- Injection
- Feed
- Implant
- Pessary or Control Internal Drug Release (CIDR)

**Progestens Effect on Ovulation**

**Stimulating Follicular Development**

- eCG or FSH
- PGF $\alpha$