HORMONES
Endocrine System
Review

- When does the udder form?
- When is the udder able to produce milk?
- Why the difference?

- Growth of the gland has already occurred before lactation can be induced
  - Hormonally controlled from puberty through pregnancy
  - Already have basic ductal system with alveoli that now can be induced to produce milk
Lactogenesis

- Dependent upon a specific set of hormones
  - Lactogenic Complex of hormones
    - Insulin
    - Glucocorticoids
    - Prolactin
- Mammary tissue from most states of a non-lactating mammary gland also can be made to undergo some degree of lactogenesis
  - Administration of high amounts of LC hormones
    - Even in non-pregnant animals
Lactogenic Complex of Hormones: Insulin

- Required in vitro to cause a lactogenic-like response in mammary tissue
- Causes non-secretory epithelia to undergo cell division
- Role in vivo is unknown
  - Mammary cells in vivo undergo large burst of cell division in late pregnancy
  - IGF-1 may be the primary mitogen involved in cell division leading to lactogenesis
  - Both insulin and IGFs may be involved in glucose uptake by the mammary cells
    - Critical for lactose synthesis
Lactogenic Complex of Hormones: Prolactin (In vitro)

- Added to cultures containing insulin and glucocorticoids
  - Causes transcription of casein and α-lactalbumin genes, translation of milk protein mRNAs, milk protein secretion, and synthesis of lactose and milk fat
- Prolactin produced in pituitary gland
  - Hypophysectomy = removal of pituitary
Lactogenic Complex of Hormones: Prolactin (In vivo)

- Hypophysectomy during pregnancy completely suppresses subsequent lactation after delivery.

- In ovariectomized - adrenalectomized - hyphophysectomized rats the minimal hormone requirement to induce lactogenesis is prolactin + glucocorticoids.

- In most species, levels are low during pregnancy and only increase prepartum around the time of the second stage of lactogenesis.
Lactogenic Complex of Hormones: Prolactin (In vivo)

- In nonruminants, prolactin suppression during late gestation completely suppresses lactogenesis.
- In lactating goats, hypophysectomy results in an immediate decline in milk production. Administration of prolactin with thyroxine and glucocorticoid reinitiates milk production, which can then be maintained with growth hormone.
- In cattle, if prolactin is blocked 12 days prepartum through 10 days postpartum, milk yield decreases 45% during the first 10 days of lactation. Milk yield increases as lactation progresses, even if prolactin continues to be suppressed.
Lactogenic Complex of Hormones: Prolactin (In vivo)

- In most species, prolactin receptors in the mammary gland are low during pregnancy and increase during the second stage of lactogenesis.
  
  - Availability of blood prolactin concentrations and the responsiveness of the mammary epithelial cells to prolactin (receptors) increase at the start of copious milk secretion.
Lactogenic Complex of Hormones: Glucocorticoids (In vitro)

- Glucocorticoids required in vitro for full initiation of milk secretion
- Several roles:
  - Seem to be involved in development of rough endoplasmic reticulum and other structural changes required for massive protein synthesis
  - May be directly involved in transcription of the casein and α-lactalbumin genes
Lactogenic Complex of Hormones: Glucocorticoids (In vivo)

- Adrenalectomy blocks casein synthesis
- Mammary glucocorticoid receptors increase 3 fold in the second half of pregnancy in mice
  - Synergize with prolactin to initiate lactation
  - Effects of administration of ACTH (adrenocorticotropic hormone from the pituitary gland) are mediated by its stimulation of glucocorticoid secretion
- Glucocorticoid concentrations in blood are fairly low during most of pregnancy, but increase markedly during the last few days prepartum
Lactogenic Complex of Hormones

- From in vitro studies on mid-pregnant mouse and rat mammary tissue culture:
  - Insulin alone causes cells to divide, but no cytological changes
  - Insulin + glucocorticoids results in RER and Golgi development, and cells can synthesize structural proteins; minimal milk protein and lactose synthesis
  - Insulin + prolactin results in transcription of milk protein genes, but little translation or milk protein synthesis
  - Insulin + glucocorticoid, followed by Insulin + prolactin or insulin + glucocorticoid + prolactin results in all of the cytological and enzymatic changes, and milk components are produced
Galactopoiesis

- Maintenance of lactation once it has been established
- Two key components contribute to the maintenance of lactation
  - *Galactopoietic hormones and removal of accumulated milk*
- Much of the fundamental knowledge that we have on galactopoietic hormones comes from classic studies demonstrating that inhibition of hormone secretion will inhibit milk production
- Additional levels of galactopoietic hormones during lactation can enhance milk production, again depending on the species, stage of lactation, and particular hormone
Galactopoiesis

- Bovine somatotropin (bST, or bovine growth hormone) to lactating dairy cattle results in relatively dependable milk yield increases

- Galactagogue = any substance that administered to a lactating animal that increases milk production

- Systemic factors:
  - Galactopoietic hormones (e.g. growth hormone and suckling-induced prolactin secretion) which generally stimulate milk secretion
  - Competing physiological states (e.g. pregnancy) may inhibit lactation
Galactopoiesis

- Prolactin is the predominant galactopoietic hormone in nonruminants
  - Released at time of milk removal in ruminants and nonruminants
  - In the rat, growth hormone plays an important role, independent of the role of prolactin

- Growth hormone is the predominant galactopoietic hormone in ruminants
  - Inhibition of prolactin secretion or administration of prolactin to lactating cows has little effect on milk yields
  - In lactating sheep, both prolactin and growth hormone seem to be important for galactopoiesis
Fig. 2.5. Changes in concentrations of estradiol, progesterone, prolactin, and growth hormone in blood of cattle during the estrous cycle and pregnancy.
What Do Other Species Need?

- Hypophysectomized (pituitary gland removal) rats need prolactin and glucocorticoid.

- Hypophysectomized goats need prolactin, glucocorticoid, growth hormone, and thyroid hormone.
  - If prolactin suppressed pre-partum, initiation of lactation delayed.
  - If prolactin suppressed after lactation already established, it won’t change much.

- Hypophysectomized rabbits will produce milk again if prolactin alone is administered.
Who’s cooler – Kangaroos or Rabbits?
RbST

- bST – bovine somatotropin
- Produced in the pituitary gland
- R = Recombinant; artificial growth hormone
- Posilac (Monsanto) in 1994
  - Sold in 2008 to Eli Lilly and Company for $300 million
  - Can increase production by 10%
RbST Effects on Lactation

- Increased
  - Blood flow
  - Milk synthesis
  - Uptake and lactose synthesis
  - NEFA utilization for milk fat synthesis
  - Amino acid utilization for milk proteins
  - Maintenance of secretory cell number
RbST

- FDA, World Health Organization, and National Institutes of Health independently stated that dairy products and meat from BST-treated cows are safe for human consumption.

- No effect on humans.

- Less greenhouse gases.
Questions?
Have a great summer!!