Learning Objectives for Reproduction

1. Male and female reproductive anatomy
2. Male and female gamete and sex hormone production and regulation
3. Changes that occur in sperm and egg before and during fertilization (chromosome number reduction)
4. Fetal Development
5. Adaptations to maternal body during pregnancy
6. Guest lecturer – Dr. Jason Ross (Estrus cycle and Porcine Reproduction)

Male Reproductive System

- **Testes (within the scrotum)** produce sperm
- Sperm are delivered to the exterior through a system of ducts
  - Epididymis, ductus deferens, ejaculatory duct, and the urethra

Overview of Reproductive System

- **Secondary sex characteristics**
  - develop at puberty to attract a mate
  - pubic, axillary and facial hair
  - scent glands, body morphology and low-pitched voice in males

The Scrotum

- Sac of skin and superficial fascia
  - Hangs outside the abdominopelvic cavity
  - Contains paired testes
    - 3°C lower than core body temperature (temperature necessary for sperm production)

The Scrotum

- Temperature is kept constant by two sets of muscles
  - **Smooth muscle** that wrinkles scrotal skin (dartos muscle)
  - Bands of **skeletal muscle** that elevate the testes (cremaster muscles)
The Testes

- **Blood supply**
  - testicular arteries
  - testicular veins
- **Spermatic cord encloses:**
  - nerve fibers
  - blood vessels
  - lymphatics

Spermatic Ducts

- Epididymis (head, body and tail)
  - 6 m long coiled duct
  - site of sperm maturation and storage (fertile for 60 days)
- Ductus deferens (peristalsis during orgasm)
  - 45 cm long
- Ejaculatory duct
  - 2 cm

Seminal Vesicles
- Viscous alkaline seminal fluid
  - Fructose, ascorbic acid, coagulating enzyme and prostaglandins
  - 70% of the volume of semen

Prostate
- Milky, slightly acid fluid
  - Contains citrate and enzymes
  - Plays a role in the activation of sperm

Accessory Glands

- **Bulbourethral Glands**
  - Prior to ejaculation - thick, clear mucus
  - Lubricates the glans penis
  - Neutralizes traces of acidic urine in the urethra
Semen

- Mixture of sperm and accessory gland secretions
- Contains nutrients
- Protects and activates sperm
- Facilitates sperm movement
- Prostaglandins in semen
  - Decrease the viscosity of mucus in the cervix
  - Stimulate reverse peristalsis in the uterus

Semen

- Alkalinity neutralizes acid in the male urethra and female vagina
- Antibiotic chemicals destroy certain bacteria
- Only 2–5 ml of semen are ejaculated, containing 20–150 million sperm/ml

Sertoli cell function

- Nourish developing spermatozoa
- Intracellular junctions form blood-testes barrier
- Produce inhibin – represses FSH
- Secrete androgen-binding protein (ABP)
- Produce mullerian duct-inhibiting substance (MIS)

Leydig Cell Function

- Secrete androgens
  - Testosterone
  - Dihydrotestosterone
  - Androstenedione
  - Dihydroepiandrosterone

Sustentacular = sertoli
Interstitial = leydig

Spermatozoon
Meiosis events:
1. Introduce genetic variability
2. Reduction of chromosome number

Testicular hormones
- Leydig: FSH increases LH receptor number
- Leydig: LH increases Testosterone (T) synthesis
- Sertoli: FSH stimulates production of androgen-binding protein (ABP)
- ABP binds T, thus increasing concentration in Testes
- Increased T stimulates spermatogenesis

Testosterone Functions
- Differentiation of fetal male internal genitalia
- Spermatogenesis
- Development of secondary sexual characteristics
- Libido
- Muscle development, skeletal growth
- Red blood cell production
**Female Reproductive System**

- Produce and deliver gametes
- Provide nutrition and room for fetal development
- Give birth
- Nourish infant

---

**Secondary Sex Organs**

- **Female Duct system**
  - uterine tubes, uterus, vagina
- **External genitalia**
  - clitoris, labia minora, and labia majora
  - accessory glands beneath skin provide lubrication

---

**Uterine Tubes**

- **Ampulla**
  - Usual site of fertilization
- Ciliated fibriae of infundibulum move oocyte into uterine tube
- Oocyte is carried along by peristalsis and ciliary action
- Nonciliated cells nourish the oocyte and the sperm

---

**Uterus**

- **Cervix**: narrow neck, or outlet; projects into the vagina
- **Fundus**: rounded superior region
- **Isthmus**: narrowed inferior region
- **Cervical glands secrete mucus**
  - block sperm entry except during midcycle
Vagina
- Birth canal and organ of copulation
- Extends between the bladder and the rectum from the cervix to the exterior
- Urethra embedded in the anterior wall

Oogenesis and Sexual Cycle
- Sexual cycle - events recurring every month when pregnancy does not occur
  - Ovarian cycle = events in ovaries
  - Menstrual/estrous cycle = parallel changes in uterus
- Reproductive cycle - events occurring between fertilization and birth

Ovarian Cycle
- Monthly series of events associated with the maturation of an egg
- Two consecutive phases
  - Follicular phase: period of follicle growth
  - Ovulation occurs midcycle
  - Luteal phase: period of corpus luteum activity

Follicular Phase
- Primordial follicle becomes primary follicle
  1. The primordial follicle is activated
     - Squamouslike cells become cuboidal
  2. Follicle enlarges to become a primary (1°) follicle

Follicular Phase
3. Primary follicle becomes a secondary follicle
   - Stratified epithelium (granulosa cells) forms around oocyte
   - Granulosa cells and oocyte guide one another’s development
4. Secondary follicle becomes a late secondary follicle
   - Theca and granulosa cells cooperate to produce estrogens
   - Zona pellucida forms around the oocyte
   - Fluid begins to accumulate
Follicular Phase

5. Late secondary follicle becomes a vesicular follicle
   - Antrum forms and expands to isolate the oocyte with its corona radiata on a stalk
   - Vesicular follicle bulges from the external surface of the ovary
   - The primary oocyte completes meiosis I

E2 synthesis: two-cell model

(a) Fluctuation of gonadotropin levels: Fluctuating levels of pituitary gonadotropins (follicle-stimulating hormone and luteinizing hormone) in the blood regulate the events of the ovarian cycle.
Function/Targets of E2

Main E2 target is reproductive tract
1. Vaginal mucous increased
2. Increased blood flow
3. Genital swelling
4. Growth of Uterus

Menstruation in mammals?

• Loss of endometrial lining through blood flow limited to primates
• Other species resorb the lining
• Menstrual cycle/Estrous cycle

Estrous v Estrus

• Estrous = the cycle
• Estrus – stage of the estrous cycle when animals are in behavioral heat (high estrogen)

Ovulation

• Ovary wall ruptures and expels the secondary oocyte with its corona radiata
• Mittelschmerz: twinge of pain sometimes felt at ovulation
• Mono- or Poly-ovulatory

Luteal Phase

• Ruptured follicle collapses
• Granulosa cells and internal thecal cells form corpus luteum
• Corpus luteum secretes progesterone and estrogen

Luteal Phase

• If no pregnancy, the corpus luteum degenerates into a corpus albicans
• If pregnancy occurs, corpus luteum produces hormones until the placenta takes over
Maternal Recognition of Pregnancy

Cow: Interferon Tau
Pig: Estrogen
Horse: Conceptus/unknown protein

- secreted by blastocyst within 9 days of conception
- prevents involution of corpus luteum
- detected by pregnancy tests

Hormone Levels and Pregnancy

Uterine (Menstrual/Estrous) Cycle

• Cyclic changes in endometrium in response to ovarian hormones
• Three phases
  1. Menstrual/resorption phase
  2. Proliferative (preovulatory) phase
  3. Secretory (postovulatory) phase (most constant in length)

Uterine Cycle

• Menstrual/resorbtive phase
  - Ovarian hormones are at their lowest levels
  - Gonadotropins are beginning to rise
  - Stratum functionalis is shed and the menstrual flow occurs
Uterine Cycle

- Proliferative phase
  - Estrogen levels prompt generation of new functional layer and increased synthesis of progesterone receptors in endometrium
  - Glands enlarge and spiral arteries increase in number

- Secretory phase
  - Progesterone levels prompt
    - Further development of endometrium
    - Glandular secretion of glycogen
    - Formation of the cervical mucus plug

Uterine Cycle

- Menstrual phase
  - Shedding of the functional layer of the endometrium

- Proliferative phase
  - Rebuilding of the functional layer of the endometrium

- Secretory phase
  - Begins immediately after ovulation
  - Enrichment of the blood supply and glandular secretion of nutrients prepare the endometrium to receive an embryo

If fertilization does not occur
  - Corpus luteum degenerates
  - Progesterone levels fall
  - Spiral arteries kink and spasm
  - Endometrial cells begin to die
  - Spiral arteries constrict again, then relax and open wide
  - Rush of blood fragments weakened capillary beds and the functional layer sloughs

Sexual reproduction

- each offspring has 2 parents and receives genetic material from both
- provides genetic diversity
- foundation for survival and evolution of species

Two Sexes

- Male and female gametes (sex cells) combine their genes to form a fertilized egg (zygote)
  - one gamete has motility (sperm)
    - parent producing sperm considered male
    - has Y chromosome
  - other gamete (egg or ovum) contains nutrients for developing zygote
    - parent producing eggs considered female
    - in mammals female also provides shelter for developing fetus (uterus and placenta)
Oocyte – 2 meiotic divisions

#1 Begins in fetal development – primordial follicles
Completed at time of ovulation

#2 Occurs at fertilization

Very few follicles will complete both divisions

Meiotic division

- Cell division without replication
- Chromosomal reduction
  - 46 diploid → 23 haploid
- Provides half genetic material from each parent

Pregnancy lengths

<table>
<thead>
<tr>
<th>Species</th>
<th>Gestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human</td>
<td>266</td>
</tr>
<tr>
<td>Mouse/hat</td>
<td>21</td>
</tr>
<tr>
<td>Cat/dog</td>
<td>65-70</td>
</tr>
<tr>
<td>Pig</td>
<td>114</td>
</tr>
<tr>
<td>Goat</td>
<td>145</td>
</tr>
<tr>
<td>Sheep</td>
<td>150</td>
</tr>
<tr>
<td>Cow</td>
<td>284</td>
</tr>
<tr>
<td>Elephant</td>
<td>~640</td>
</tr>
</tbody>
</table>
Hormones of Pregnancy

• Estrogens
  — increases to 30 times normal before birth
  — corpus luteum is source until placenta takes over
  — causes uterine, mammary duct and breast enlargement

Hormones of Pregnancy

• Progesterone
  — secreted by placenta and corpus luteum
  — suppresses secretion of FSH and LH preventing follicular development
  — prevents menstruation, thickens endometrium
  — stimulates development of acini in breast

Organ development in utero

Role of Sex Chromosomes

• Our cells contain 23 pairs of chromosomes
  — 22 pairs of autosomes
  — 1 pair of sex chromosomes (XY males: XX females)
    • males produce 50% Y carrying sperm and 50% X carrying
    • all eggs carry the X chromosome
  • Sex of child determined by type of sperm that fertilizes mother’s egg

Wolffian ducts – male
Mullerian ducts - female

• Genetic male:
  — Testosterone and Mullerian inhibiting substance
• Testosterone
  — promotes development of Wolffian ducts
• MIS
  — causes regression of mullerian ducts

Wolffian ducts – male
Mullerian ducts - female

• Absence of MIS
• Mullerian ducts proliferate forming uterus, uterine tubes, upper 2/3 of vagina
• By week 8: full development into female genitalia
• Absence of androgens (T), wolffian ducts degenerate
5- to 6-week embryo: sexually indifferent stage

**Sex-determining region Y - SRY gene**

---

7- to 8-week male embryo

---

Developmental problems

- Every 4.5 minutes a baby with a birth defect is born
- 15-25% genetic reasons
- 4% - maternal condition
- 3% - maternal infections
- 1-2% - deformations (u. cord)
- 65% unknown etiology

---

Male pseudohermaphrodite (XY)

Androgen Insensitivity Syndrome (AIS)
- Has testes (usually in body cavity)
- but female external genitalia (can be ambiguous)
- Testicular feminization in men is X-linked
- Lack androgen receptor for male sexual development
- Body doesn’t respond to androgen being produced

---

Female pseudohermaphrodite

Have ovaries - but male external genitalia
Female XX

Congenital Adrenal Hyperplasia - adrenal glands overproduce testosterone

Cattle:

**Anastomosis** – interconnection of blood vessels
- Male hormone pass into female in twin pregnancy
- Exchange of blood cells from male to female
- stimulates male duct development
- Infertile female - **Freemartin**
Anestrus – without cyclicity

- Pregnancy
- Lactation
- Presence of offspring
- Season
- Stress
- Pathology
- Nutritional Status

Gestational Anestrus

- Progesterone (from CL/placenta) inhibits GnRH
- Prevents FSH/LH secretion; no follicle development

Seasonal Anestrus

- Means to give birth when environment is favorable
- Pre-attachment embryo survival low during high temp’s (Heat stress)
- Fall conception – moderate temp’s
- Birth during spring – nutritional conditions better (e.g. for lactation)
- This is controlled by photoperiod

Seasonal Anestrus - Mare

- Cycles in spring
- Conceives before summer
- Long pregnancy (11 mo)
- Foal born in spring, optimum time for birth

Seasonal Anestrus - Sheep

- Cycles in fall
- Short pregnancy (5 mo)
- Lamb born in spring, optimum time for birth
Lactational Anestrus

- Cyclicity completely suppressed in sow with milking
- On weaning; sow displays estrus; ovulates within 4-8 days
- Suckled cow; cyclicity delayed by 60 days after birth
- Suckling session <2 per day
- >2 sucking sessions per day = postpartum anestrus
- Thus, two suckling sessions per day is threshold

Postpartum Anestrus

- Negative energy balance
- Absence of GnRH pulses from hypothalamus
- Inadequate secretion of gonadotrophins
- Inactive ovaries

Acyclicity in women

- Amenorrhea – absence of menses over long period of time
- Athletes, anorexic patients
- Lactational amenorrhea – ovarian inactivity in women
- High prolactin, decrease in GnRH frequency and amplitude, decrease in LH/FSH
- Effective contraceptive <6 months