Reproduction

Dr Badri Paudel
www.badripaudel.com

Male Reproductive System

Overview of Reproductive System

- Primary sex organs (gonads)
  - Produce gametes (testes or ovaries) -
  - Gametogenesis - spermatogenesis or oogenesis
- Secondary sex organs
  - Male - ducts, glands, penis deliver sperm cells
  - Female - uterine tubes, uterus and vagina receive sperm and nourish developing fetus
- 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

Adolescence

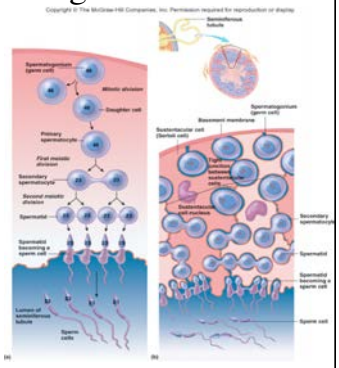
- Puberty
- Burst of hormones activate maturation of the gonads: testes
- Begins: 9 – 14 yrs of age
- Abnormally early = precocious puberty
- Delayed = eunuchoidism

General Physical Changes

- Enlargement of the external and internal genitalia
- Voice changes
- Hair growth
- Mental changes
- Changes in body conformation and skin
- Sebaceous gland secretions thicken/increase → acne

Spermatogenesis

• Spermatogonia produce 2 kinds of daughter cells
  – Type A remain outside blood-testis barrier and produce more daughter cells until death
  – Type B differentiate into primary spermatocytes
    • Cells must pass through BTB to move inward toward lumen - new tight junctions form behind these cells
    • meiosis I → 2 secondary spermatocytes
    • meiosis II → 4 spermatids



Spermatogenesis

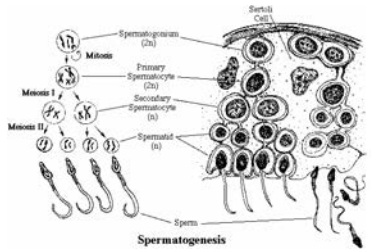
- Sperm are produced within the seminiferous tubules.
- Interspersed within the tubules are large cells which are the sustentacular cells (Sertoli's cells), which support and nourish the other cells.

Spermatogenesis

- Early in embryonic development, primordial germ cells enter the testes and differentiate into spermatogonia
- Spermatogonia are diploid cells, each with 46 chromosomes (23 pairs) located around the periphery of the seminiferous tubules.
- At puberty, hormones stimulate these cells to begin dividing by mitosis. Some remain at the periphery as spermatogonia.
- Others become primary spermatocytes. Because they are produced by mitosis, primary spermatocytes, like spermatogonia, are diploid and have 46 chromosomes.

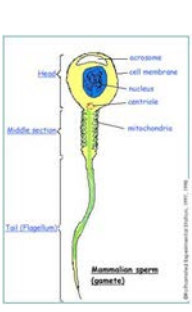
Spermatogenesis

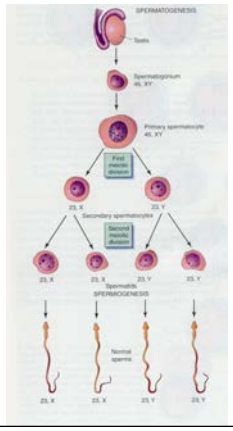
- Each primary spermatocytes goes through the first meiotic division, meiosis I, to produce two secondary spermatocytes, each with 23 chromosomes (haploid). Just prior to this division, the genetic material is replicated so that each chromosome consists of two strands, called chromatids, that are joined by a centromere
- During meiosis I, one chromosome, goes to each secondary spermatocyte. In the second meiotic division, meiosis II, each secondary spermatocyte divides to produce two spermatids. There is no replication of genetic material in this division, but a single-stranded chromatid goes to each cell.
- As a result of the two meiotic divisions, each primary spermatocyte produces four spermatids.
- each spermatid has 23 chromosomes (haploid), one from each pair in the original primary spermatocyte.
- During spermatogenesis there are two cellular divisions, but only one replication of DNA so that each spermatid has 23 chromosomes (haploid), one from each pair in the original primary spermatocyte.



Spermatogenesis

- The final step in the development the spermatids formed from spermatogenesis become mature spermatozoa, or sperm.
- The mature sperm cell has a head, midpiece, and tail. The head, also called the nuclear region, contains the 23 chromosomes surrounded by a nuclear membrane. The tip of the head is covered by an acrosome, which contains enzymes that help the sperm penetrate the female gamete. The midpiece, metabolic region, contains mitochondria that provide adenosine triphosphate (ATP). The tail, locomotor region, uses a typical flagellum for locomotion.





Spermatogenesis

- The sperm are released into the lumen of the seminiferous tubule and leave the testes. They then enter the epididymis where they undergo their final maturation and become capable of fertilizing a female gamete.
- Sperm production begins at puberty and continues throughout the life of a male.
- The entire process, beginning with a primary spermatocyte, takes about 74 days. After ejaculation, the sperm can live for about 48 hours in the female reproductive tract.

This sperm is fusing with an egg to produce an organism with a new combination of genes.

Brain-Testicular Axis

- Testicular regulation involves three sets of hormones:
  - **GnRH** - gonadotropin-releasing hormone
    - Secreted by hypothalamus
    - Stimulates secretion of anterior pituitary secretion hormones (FSH/ LH)
  - **FSH and LH** - Follicle stimulating hormone and leuteinizing hormone
    - LH aka as Interstitial Cell Stimulating Hormone
    - Secreted by anterior pituitary
    - Directly stimulate the testes
      - FSH - stimulates formation of ABP (androgen binding protein) by nurse cells
      - LH - stimulates interstitial cells to secrete testosterone
  - **Testosterone**
    - Secreted by cells of Leydig (Interstitial cells of seminiferous tubules)
    - Exert negative feedback on hypothalamic and ant. pituitary hormones
    - Stimulates spermatogenesis by binding to ABP and development of secondary sex characteristics

Hormonal Regulation of Testicular Function

- Feedback inhibition on the hypothalamus and pituitary results from:
  - Rising levels of testosterone
  - Increased inhibin

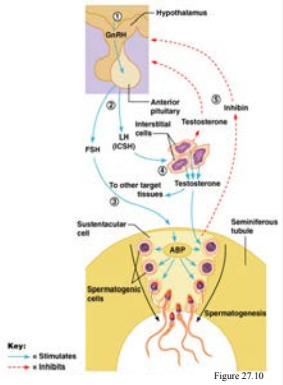
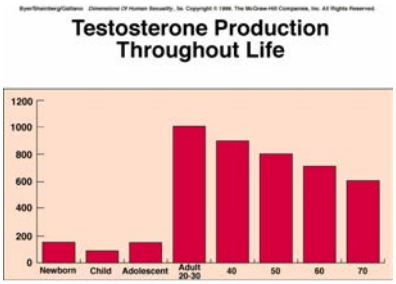


Figure 27.10



Testosterone

- Most from interstitial cells of testes with small amounts from adrenal glands and sustentacular cells
- Causes enlargement and differentiation of male genitals and reproductive duct system
- Necessary for sperm cell formation
- Required for descent of testes
- Hair growth on certain parts of the body
- Skin is rougher and coarser
- Quantity of melanin increases
- Increases rate of secretion of sebaceous glands
- Hypertrophy of larynx
- Increases metabolic rate
- Increases red blood cell count
- Increases protein synthesis, rapid bone growth
- Causes closure of epiphyseal plates

Mechanism and Effects of Testosterone Activity

- Testosterone is synthesized from cholesterol
- It must be transformed to exert its effects on some target cells
  - Prostate – it is converted into dihydrotestosterone (DHT) before it can bind within the nucleus
    - Requires the enzyme 5alpha-reductase
  - Neurons – it is converted into estrogen to bring about stimulatory effects
    - Reqires the enzyme *aromatase*
- Testosterone targets all accessory organs and its deficiency causes these organs to atrophy

Accessory Glands

- **Seminal vesicles**
  - Empty into ejaculatory duct
  - Produce about 60% of semen
  - Secretion contains fibrinogen
  - High pH
- **Prostate gland**
  - Produces about 30% of semen
  - Thin, milky secretion, high pH
  - Contain clotting factors, and fibrinolysin
- **Bulbourethral glands**
  - Contribute about 5% to semen
  - Mucous secretion. Just before ejaculation
  - Helps neutralize pH of female vagina

Semen or Seminal Fluid

- 2-5 mL of fluid expelled during orgasm
  - 60% seminal vesicle fluid, 30% prostatic, 10% sperm
    - normal sperm count 50-120 million/mL
- Other components of semen
  - fructose - energy for sperm motility
  - fibrinogen causes clotting
    - enzymes convert fibrinogen to fibrin
  - fibrinolysin liquefies semen within 30 minutes
  - prostaglandins stimulate female peristaltic contractions
  - spermine is a base stabilizing sperm pH at 7.2 to 7.6

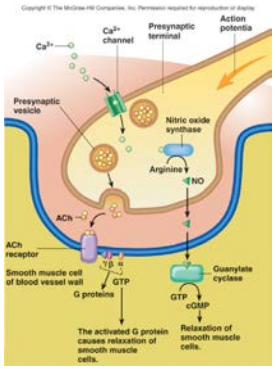
Semen

- Secretions of all three accessory glands plus sperm cells referred to as **semen**.
- **Emission**: discharge of semen into prostatic urethra
- **Ejaculation**: forceful expulsion of semen from urethra. Caused by peristalsis
- Temporary coagulation as fibrinogen becomes fibrin then fibrinolysin breaks up the coagulation. Sperm swim up vagina

Emission and Ejaculation

- **Emission**: accumulation of sperm cells and secretions of the prostate gland and seminal vesicles in the urethra
- Controlled by sympathetic centers in spinal cord
  - Peristaltic contractions of reproductive ducts
  - Seminal vesicles and prostate release secretions
- Accumulation in prostatic urethra sends sensory information through pudendal nerve to spinal cord
- Sympathetic and somatic motor output
  - Sympathetic: constriction of internal sphincter of urinary bladder so semen and urine do not mix
  - Somatic motor: to skeletal muscles, urogenital diaphragm and base of penis causing rhythmic contractions that force semen out of urethra: **ejaculation**

Neural Control of Erection



Female Reproductive Physiology

Establishing the Ovarian Cycle

- During childhood, ovaries grow and secrete small amounts of estrogens that inhibit the hypothalamic release of GnRH
- As puberty nears, GnRH is released; FSH and LH are released by the pituitary, which act on the ovaries
- These events continue until an adult cyclic pattern is achieved and menarche occurs

Ovarian Cycle

- Monthly series of events associated with the maturation of an egg
- Follicular phase – period of follicle growth (days 1–14)
- Luteal phase – period of corpus luteum activity (days 14–28)
- Ovulation occurs midcycle

Sexual Cycle

- Averages 28 days, ranges from 20 to 45
- Hormone cycle: hierarchy of control
  - hypothalamus→ pituitary → ovaries → uterus
- Follicular phase (2 weeks)
  - menstruation occurs during first 3 to 5 days of cycle
  - uterus replaces lost endometrium and follicles grow
- Luteal phase (2 weeks)
  - corpus luteum stimulates endometrial thickening
  - endometrium lost without pregnancy

Hormonal Interactions During the Ovarian Cycle

- Day 1 – GnRH stimulates the release of FSH and LH
- FSH and LH stimulate follicle growth and maturation, and low-level estrogen release
- Rising estrogen levels:
  - Inhibit the release of FSH and LH
  - Prod the pituitary to synthesize and accumulate these gonadotropins
- Estrogen levels increase and high estrogen levels have a positive feedback effect on the pituitary, causing a sudden surge of LH

Hormonal Interactions During the Ovarian Cycle

- The LH spike stimulates the primary oocyte to complete meiosis I, and the secondary oocyte continues on to metaphase II
- Day 14 – LH triggers ovulation
- LH transforms the ruptured follicle into a corpus luteum, which produces inhibin, progesterone, and estrogen

Hormonal Interactions During the Ovarian Cycle

- These hormones shut off FSH and LH release and declining LH ends luteal activity
- Days 26-28 – decline of the ovarian hormones
  - Ends the blockade of FSH and LH
  - The cycle starts anew

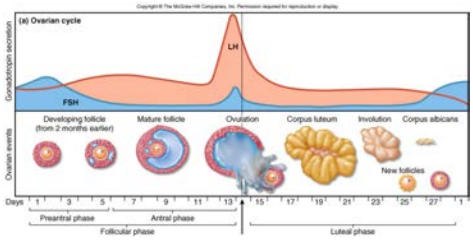
Follicular Phase

- The primordial follicle, directed by the oocyte, becomes a primary follicle
- Primary follicle becomes a secondary follicle
  - The theca folliculi and granulosa cells cooperate to produce estrogens
  - The zona pellucida forms around the oocyte
  - The antrum is formed

Follicular Phase

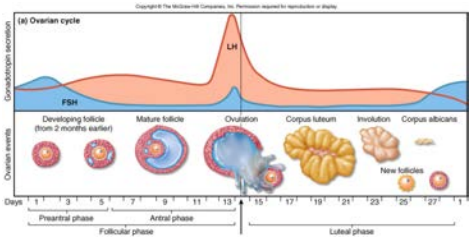
- The secondary follicle becomes a vesicular follicle
  - The antrum expands and isolates the oocyte and the corona radiata
  - The full size follicle (vesicular follicle) bulges from the external surface of the ovary
  - The primary oocyte completes meiosis I, and the stage is set for ovulation

Ovarian Cycle - Follicular Phase



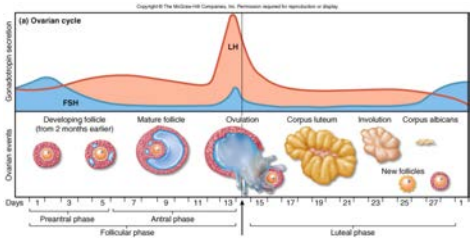
- Menstruation (day 1) to ovulation(14) (variable)
- Difficult to predict date of ovulation
- Contains menstrual and preovulatory phases

Ovarian Cycle - Preantral Phase



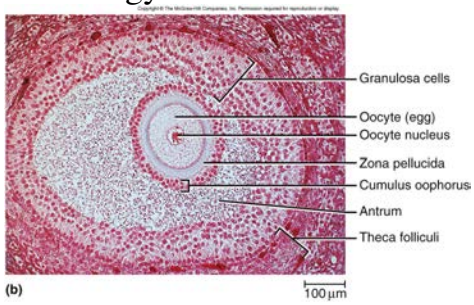
- Discharge of menstrual fluid (days 1-5)
- Before follicle develops antrum
  - primordial and primary follicles

Ovarian Cycle - Antral Phase



- Day 6 to 14, one dominant follicle advances to mature (graafian) follicle; secretes estrogen

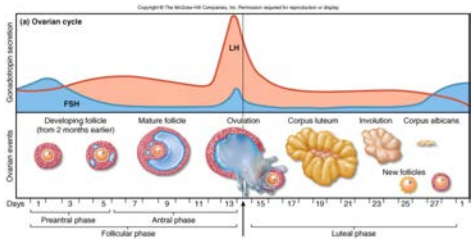
Histology of Ovarian Follicles



Ovulation

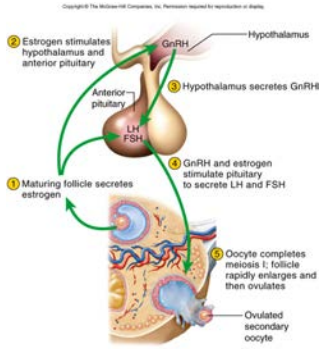
- Ovulation occurs when the ovary wall ruptures and expels the secondary oocyte
- Mittelschmerz – a twinge of pain sometimes felt at ovulation
- 1-2% of ovulations release more than one secondary oocyte, which if fertilized, results in fraternal twins

Ovarian Cycle - Ovulation



- Mature follicle ruptures, releases oocyte influenced by LH

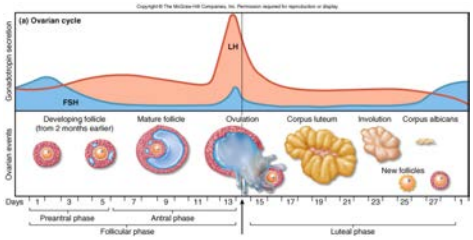
Pituitary-Ovarian Axis



Luteal Phase

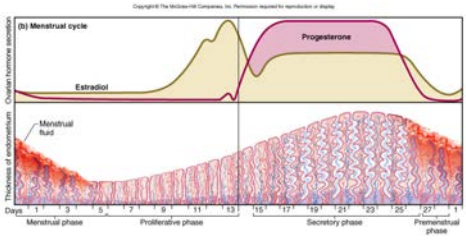
- After ovulation, the ruptured follicle collapses, granulosa cells enlarge, and along with internal thecal cells, form the corpus luteum
- The corpus luteum secretes progesterone and estrogen
- If pregnancy does not occur, the corpus luteum degenerates in 10 days, leaving a scar (corpus albicans)
- If pregnancy does occur, the corpus luteum produces hormones until the placenta takes over that role (at about 3 months)

Ovarian Cycle - Luteal Phase



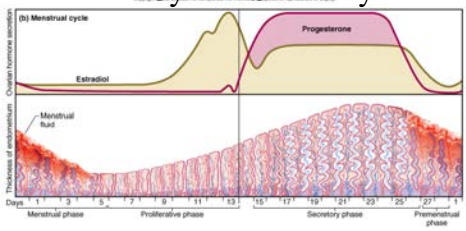
- Corpus luteum - forms from ruptured follicle, under influence of LH; secretes progesterone

Menstrual Cycle - Proliferative



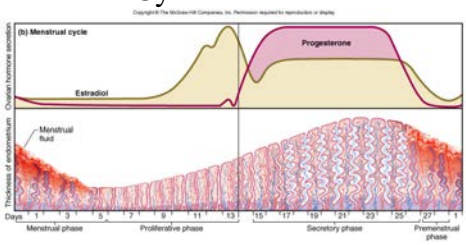
- Day 6-14 rebuild endometrial tissue
  - mitosis occurs in stratum basalis
  - result of estrogen from developing follicles

Menstrual Cycle - Secretory Phase



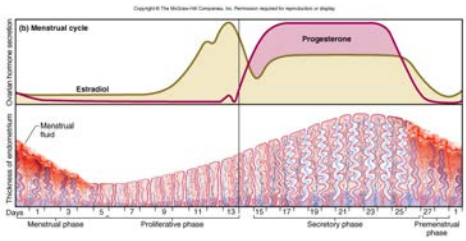
- Further thickening of endometrium due to secretion and fluid accumulation -- not mitosis
- Due to progesterone stimulation of glands

Menstrual Cycle Premenstrual Phase



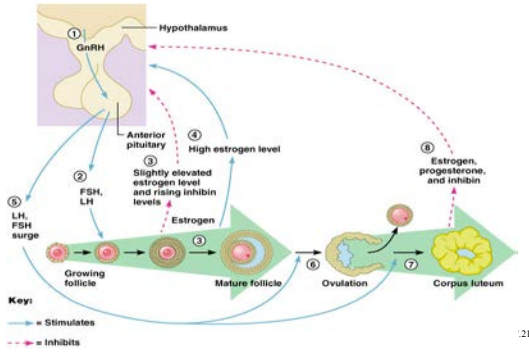
- Involution of corpus luteum, progesterone falls
  - spiral arteries constrict causes endometrial ischemia
  - stratum functionalis sloughs

Menstrual Cycle - Menstrual Phase



- Blood, serous fluid and endometrial tissue are discharged

Feedback Mechanisms in Ovarian Function



Uterine (Menstrual) Cycle

- Series of cyclic changes that the uterine endometrium goes through each month in response to ovarian hormones in the blood
- Days 1-5: Menstrual phase – uterus sheds all but the deepest part of the endometrium
- Days 6-14: Proliferative (preovulatory) phase – endometrium rebuilds itself
- Days 15-28: Secretory (postovulatory) phase – endometrium prepares for implantation of the embryo

Menses

- If fertilization does not occur, progesterone levels fall, depriving the endometrium of hormonal support
- Spiral arteries kink and go into spasms and endometrial cells begin to die
- The functional layer begins to digest itself
- Spiral arteries constrict one final time then suddenly relax and open wide
- The rush of blood fragments weakened capillary beds and the functional layer sloughs

Gonadotropins, Hormones, and the Ovarian and Uterine Cycles

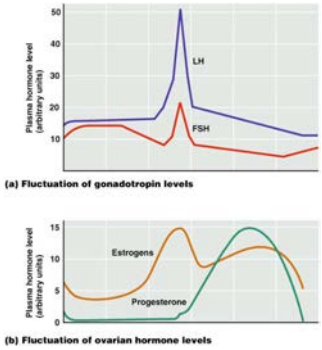


Figure 27.22a, b

Gonadotropins, Hormones, and the Ovarian and Uterine Cycles

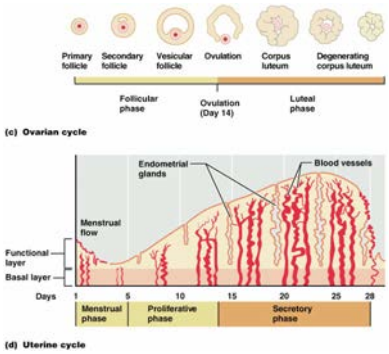


Figure 27.22c, d

Extrauterine Effects of Estrogens and Progesterone

- Estrogen levels rise during puberty
- Promote oogenesis and follicle growth in the ovary
- Exert anabolic effects on the female reproductive tract
  - Uterine tubes, uterus, and vagina grow larger and become functional
  - Uterine tubes and uterus exhibit enhanced motility
  - Vaginal mucosa thickens and external genitalia mature

Estrogen-Induced Secondary Sex Characteristics

- Growth of the breasts
- Increased deposition of subcutaneous fat, especially in the hips and breasts
- Widening and lightening of the pelvis
- Growth of axillary and pubic hair

From Egg to Embryo

- Pregnancy – events that occur from fertilization until the infant is born
- Conceptus – the developing offspring
- Gestation period – from the last menstrual period until birth
- Preembryo – conceptus from fertilization until it is two weeks old
- Embryo – conceptus during the third through the eighth week
- Fetus – conceptus from the ninth week through birth

Accomplishing Fertilization

- The oocyte is viable for 12 to 24 hours
- Sperm is viable 24 to 72 hours
- For fertilization to occur, coitus must occur no more than:
  - Three days before ovulation
  - 24 hours after ovulation
- Fertilization – when a sperm fuses with an egg to form a zygote

Sperm Transport and Capacitation

- Fates of ejaculated sperm
  - Leak out of the vagina immediately after deposition
  - Destroyed by the acidic vaginal environment
  - Fail to make it through the cervix
  - Dispersed in the uterine cavity or destroyed by phagocytic leukocytes
  - Reach the uterine tubes
- Sperm must undergo capacitation before they can penetrate the oocyte

Acrosomal Reaction and Sperm Penetration

- An ovulated oocyte is encapsulated by:
  - The corona radiata and zona pellucida
  - Extracellular matrix
- Sperm binds to the zona pellucida and undergoes the acrosomal reaction
  - Enzymes are released near the oocyte
  - Hundreds of acrosomes release their enzymes to digest the zona pellucida

Acrosomal Reaction and Sperm Penetration

- Once a sperm makes contact with the oocyte's membrane:
  - Beta protein finds and binds to receptors on the oocyte membrane
  - Alpha protein causes it to insert into the membrane

Acrosomal Reaction and Sperm Penetration

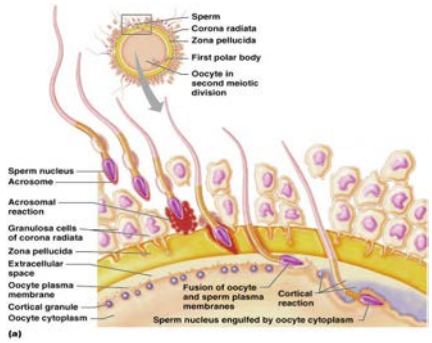


Figure 28.2a

Blocks to Polyspermy

- Only one sperm is allowed to penetrate the oocyte
- Two mechanisms ensure monospermy
  - Fast block to polyspermy – membrane depolarization prevents sperm from fusing with the oocyte membrane
  - Slow block to polyspermy – zonal inhibiting proteins (ZIPs):
    - Destroy sperm receptors
    - Cause sperm already bound to receptors to detach

Implantation

- Viability of the corpus luteum is maintained by human chorionic gonadotropin (hCG) secreted by the trophoblasts
- hCG prompts the corpus luteum to continue to secrete progesterone and estrogen
- Chorion – developed from trophoblasts after implantation, continues this hormonal stimulus
- Between the second and third month, the placenta:
  - Assumes the role of progesterone and estrogen production
  - Is providing nutrients and removing wastes

Hormonal Changes During Pregnancy

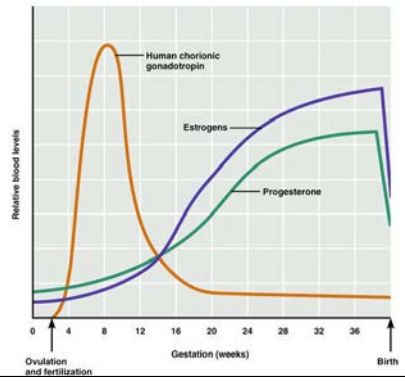


Figure 28.6

Parturition: Initiation of Labor

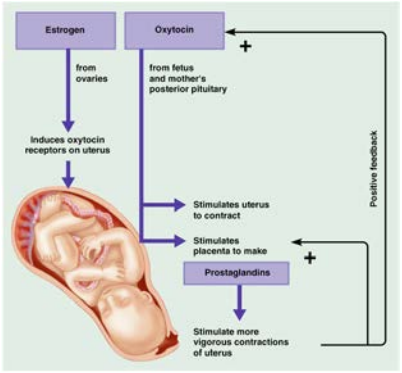
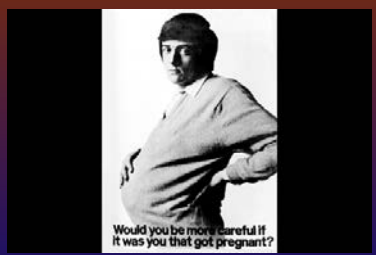


Figure 28.16

Contraception



Risk and Responsibility

- If intercourse occurs the day before ovulation, the chance of pregnancy is about 30%.
- If intercourse occurs the day of ovulation, the chance of pregnancy is about 15%.
- Over the course of one year, couples who do not use contraception have a 90% chance of pregnancy.

Women Men, and Birth Control: Who Is Responsible?

- Traditionally has been the women's responsibility.
- Attitudes are changing.
- In addition to use of a condom men can help take contraceptive responsibility by.

Women Men, and Birth Control: Who Is Responsible?

- 1. Exploring ways of making love without intercourse;
- 2. Helping to pay doctor or clinic bills and sharing the cost of pills, implants, or other birth control supplies;

Women Men, and Birth Control: Who Is Responsible?

- 3. Checking on supplies, helping to keep track of the woman's menstrual cycle, and helping his partner with her part in the birth control routine;
- 4. In long-term relationships, if no (or no more) children are wanted, having a vasectomy.

Birth Control and Contraception

- What is the difference
  - Birth Control: Preventing birth from taking place
    - IUD
    - Emergency contraceptive pills
    - RU-486
    - Surgical Abortion

Birth Control and Contraception

- Contraception: Preventing conception (preventing the sperm and the egg from uniting)
  - Barrier methods
    - Condoms, diaphragms
  - Spermicides
  - Hormonal methods
    - Pill
    - Shot (depo)
    - Implants

Methods of Contraception and Birth Control

- Choosing a Method
  - The best method is the one you will use consistently and correctly
  - Know the reliability of method
  - Know the advantages and disadvantages
  - Side effects
  - Risks

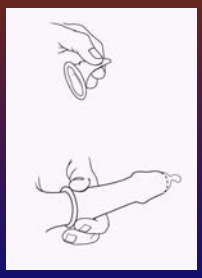
Methods of Contraception and Birth Control

- Abstinence
  - Choosing not to have intercourse
- Outercourse
  - Sexual activity without penetration

Methods of Contraception and Birth Control

- Hormonal Methods
  - The pill
  - Implants
  - Injections

Condom



- 98% effective
- Protects against some STDs

Female Condom

- 95% effective
- Protects against some STDs
- Noisy
- Use extra lubrication

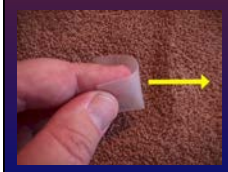
Diaphragm

- 95% effective
- Requires fitting, manual dexterity
- Leave in place 6 hours after intercourse
- Use with contraceptive jelly/cream



Foam

- 80-85% effective
- Works immediately
- Effective for an hour
- Over the counter
- No douching for 6 hours after intercourse
- 20% have burning (reaction)

Film

- 80-85% effective
- Works 10 min after insertion
- Effective for an hour
- Over the counter
- No douching for 6 hours after intercourse
- 20% have burning (reaction)

Suppository

- 80-85% effective
- Works 10 min after insertion
- Effective for an hour
- Over the counter
- No douching for 6 hours after intercourse
- 20% have burning (reaction)

Spermicides

- Nonoxynol-9
- Use in combination with barrier methods of contraception
  - Foam
  - gel
  - Film
  - Creams, jellies and suppositories

The Pill

- Combination of estrogen and progestin (some progestin only)
- Inhibits ovulation
- Thickens the cervical mucous
- Changes the lining of the uterus to inhibit implantation of the fertilized ovum
- Alter the rate of ovum transport
- 99.5 % effective (if used correctly) 92 %

Implants

- Progestin only (Norplant)
- Prevents ovulation
- More effective than the Pill

Implant

- Advantages
  - Convenience
  - Eliminate user error
  - No menses or very light
  - Decreased cramping

IUD

- Intrauterine device
- Copper and plastic (Copper T-380A) 10 years
- Plastic and Progesterone (progestasert IUD) 1 year
- 90-96 % effective in use
- Increased risk of PID

IUD

- 98-99% effective
- Lasts 10 years
- Heavier, crampier periods
- Risk of infection/PID
- Risk of ectopic pregnancy
- Good candidate:
  - multiparous
  - monogamous

Injectable Contraceptives

- Depo-Provera (DMPA) Progesterone
  - Can stop menses
  - Side effects include
    - Spotting, wt. gain, headaches, breast tenderness, dizziness, loss of libido and depression
- Lunelle Progestin and estrogen
  - Similar to the pill in all aspects

DMPA

- 99% effective
- Lasts 3 months
- IM injection
- Amenorrhea, spotting
- Weight gain
- Ovulation returns in 4.5 months
- Average 10 months to conception

Rhythm

- Avoid unprotected IC day #9-19
- 70-80% effective
- Assumes ovulation about day #14

Fertility Awareness Methods

- Calendar or rhythm method
  - Midway in cycle
- Basal body temperature (BBT) method
  - Increase in body temperature
- Cervical Mucous Method
  - Clear slippery mucous
- Symptothermal method
  - Combination of BBT and Cervical Mucous methods

Withdrawal

- 80-90% effective
- Always available
- Requires motivation, sense of timing
- Some sperm present in pre-ejaculatory fluid
- Psychological issues

Tubal Ligation & Vasectomy

- Surgical sterilization
- Permanent, irreversible
- >99% effective

Sterilization

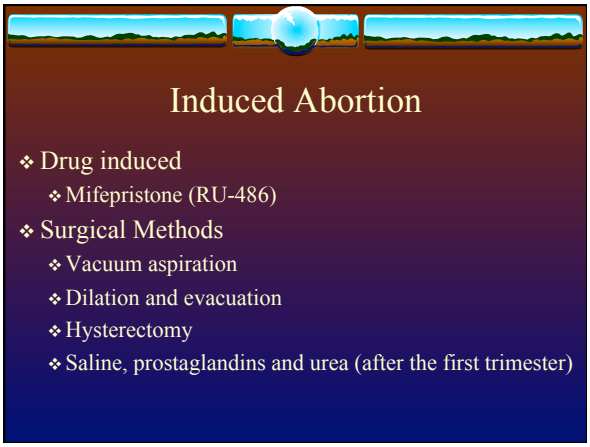
- For Women
  - Tubal ligations
    - Cut and seal the fallopian tubes
  - Hysterectomy
    - Removal of the uterus
- For Men
- Vasectomy
  - Vas deferens are cut and sealed

Emergency Contraception

- Emergency Contraception Pill (ECP)
- Copper IUD

Abortion

- Spontaneous abortion (miscarriages)
- Induced abortion


Induced Abortion
Drug induced
Mifepristone (RU-486)
Surgical Methods
Vacuum aspiration
Dilation and evacuation
Hysterectomy
Saline, prostaglandins and urea (after the first trimester)