

Outline

Fertilization
Gametes

Germ Cells
Meiosis

Male Reproductive Tract
Spermatogenesis

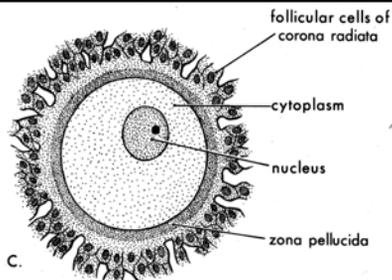
Female Reproductive Tract
Oogenesis

Menstrual Cycle
Hormones

Fertilization

Gametes – Oocyte, Sperm
Acrosomal reaction
Cell Fusion
Cortical reaction
Completion of Meiosis – 2nd polar body released
Pronuclear fusion
Zygote = fertilized egg

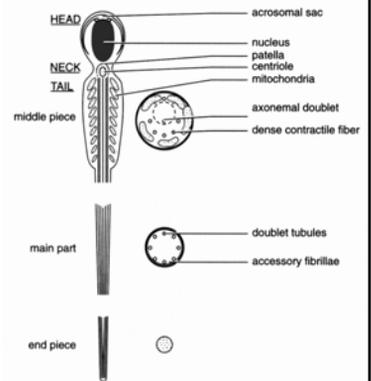
Oocyte



Corona radiata, follicle cells
Zona pellucida, acellular – 3 primary glycoproteins (ZP1, 2, 3)
Cortical Granules – vesicles, hydrolytic enzymes, polysaccharides
Female pronucleus

From KL Moore, 1977

Sperm Anatomy



Head (nucleus - meiosis completed)

Acrosome

Neck (junction)

Tail (middle piece; end piece) – mitochondria, microtubule system

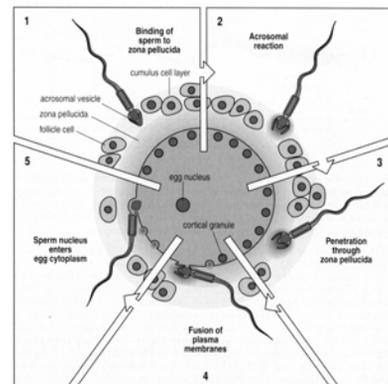
From Brookes and Zietman, 1998

Sperm – Egg Fusion

Sperm swimming penetrates the Corona Radiata
Sperm binding to the zona pellucida – ZP3 is critical
Binding induces the Acrosomal Reaction
Membrane fusion
Everts Acrosomal sac - releases hydrolytic enzymes (acrosin is a membrane bound serine protease)
Cell membrane fusion
Prevention of polyspermy
fast block - membrane depolarization
slow block - Ca⁺⁺ mediated cortical granule vesicle fusion with membrane; hydrates perivitelline space, zona pellucida elevates
Metabolic activation of egg - Ca⁺⁺ mediated – increase intracellular pH

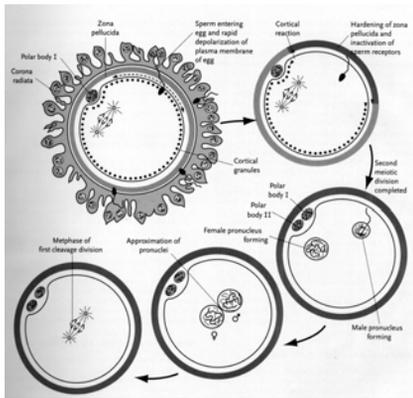
Acrosome reaction

From L. Wolpert, 1998

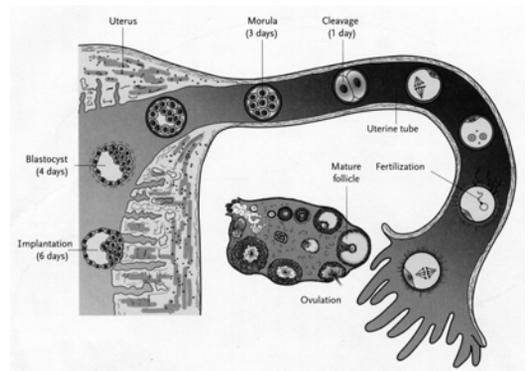


From BM Carlson, 1999

Fertilization



Fertilization occurs in the ampulla of the uterus

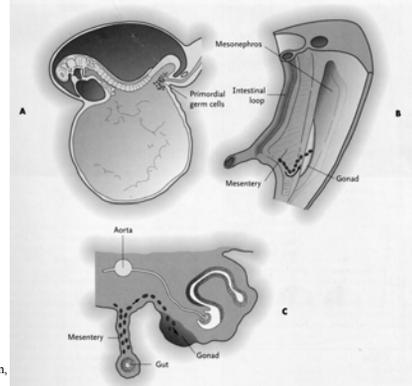


From BM Carlson, 1999

Gametogenesis

- Spermatogenesis, oogenesis
- Germ cells originate from yolk sac of embryo (parent)
- Migration into genital ridge
- Primary sex cords (compact strands of tissue)
- Mitosis
- Female - ovary, sex cords cells → ovarian follicle
- Male - testis, sex cord cells → Sertoli cells of the seminiferous tubules
- Sex cord cells are essential for gametogenesis.

Gametogenesis – Germ Cells



From BM Carlson, 1999

Meiosis

Meiosis occurs during gametogenesis

1 round of DNA replication → 2 divisions

2n (diploid) → 4n (diploid) → 2n (haploid) → 1n (haploid)

Ploidy = # of each unique chromosome set

n = number of copies of each unique DNA set

46 Chromosomes - 22 pairs - autosomes, 2 sex chromosomes

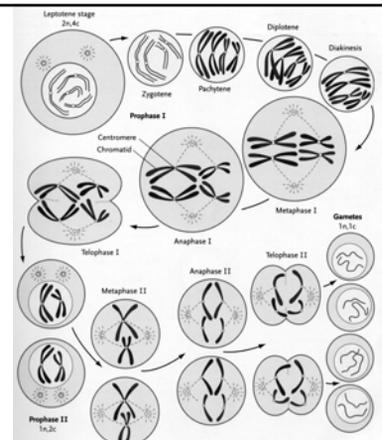
female is XX

male is XY

Nomenclature: 46,XX or 46,XY

Recombination occurs during meiosis

Meiosis

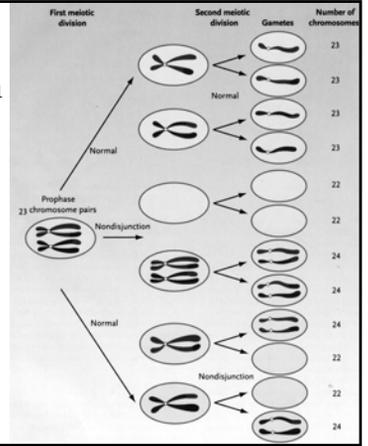


From BM Carlson, 1999

Anomalies

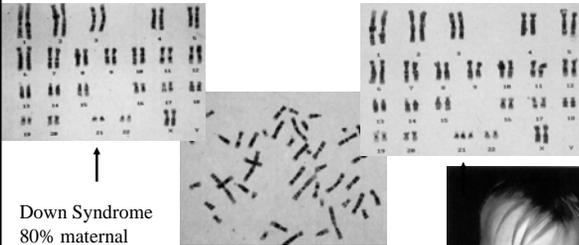
Non-Disjunction - Mis-segregation of chromosomes
 Aneuploidy = any deviation from 46,XX or 46,XY
 Aneuploidy of entire genome = triploidy, tetraploidy
 in humans this is rare and lethal
 Aneuploidy of single chromosome:
 hypodiploid (e.g. monosomy)
 hyperdiploid (e.g. trisomy)

Nondisjunction



From BM Carlson, 1999

Karyotype / Trisomy 21

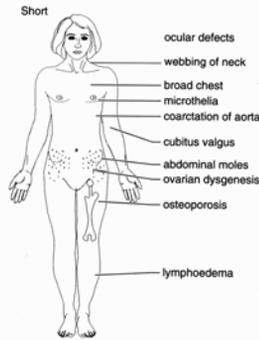


Down Syndrome
 80% maternal
 Over 300 Characteristics:
 Flat facial features
 Protruding tongue
 Cardiac defects
 Mental deficiencies

From Brookes and Zietman, 1998

Turner's Syndrome 45,XO

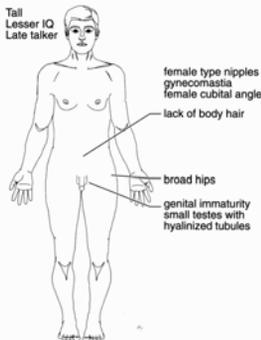
From Brookes and Zietman, 1998



Female
 Monosomy
 1:5000
 75% paternal X is missing
 Short stature
 Ovarian dysgenesis
 Broad chest



Klinefelter's Syndrome 47,XXY or 48,XXXY



Male
 Sterile
 Breasts
 Testicular atrophy

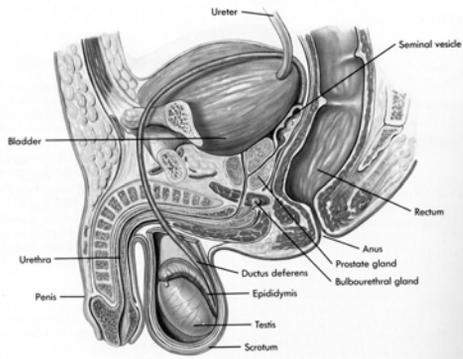
From Brookes and Zietman, 1998



Male Reproductive Tract

Testis (seminiferous tubules) – differentiation
 Epididymis – biochemical maturation
 Ductus deferens (vas deferens)
 Ejaculatory duct and inputs:
 seminal vesicle
 prostate gland
 bulbourethral gland
 Urethra - out the penis
 Ejaculate – 25 to 250 million sperm
 Capacitation - final step of maturation
 acrosome changes induced in the female genital tract

Male Reproductive Tract

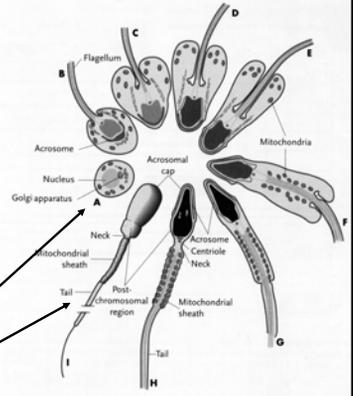


From Seeley, Stephens and Tate, 1989

Spermatogenesis

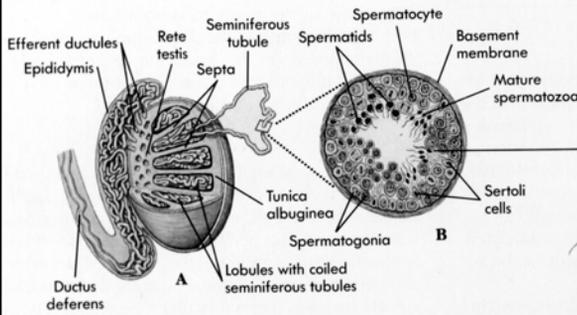
Before puberty:
Spermatogonia multiply
Puberty → Meiosis
Meiosis: equal division
Spermatogonia
type A – stem cell
type B – differentiation
I° spermatocyte - meiosis I
II° spermatocyte - meiosis II

Spermiogenesis
Spermatids
Spermatozoa



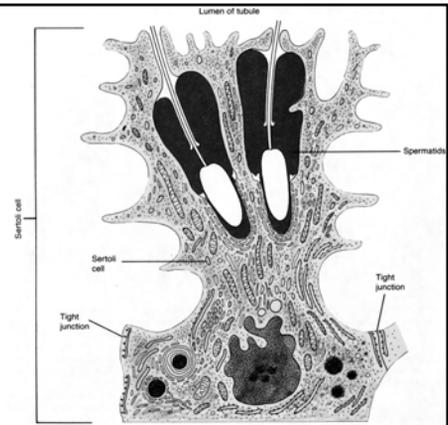
From BM Carlson, 1999

Seminiferous Tubules



From Seeley, Stephens and Tate, 1989

Sertoli Cells

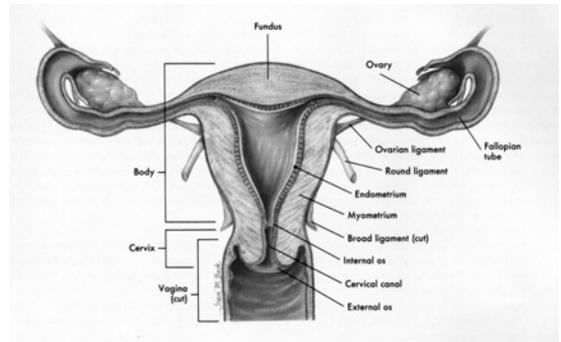


From SI Fox, 1984

Female Reproductive Tract

Ovary - Oogenesis
Uterine (Fallopian) Tube
Fimbriare (finger like projections of Infundibulum)
Infundibulum
Ampulla – Fertilization
Isthmus
Uterus - endometrium, myometrium, perimetrium
Cervix
Vagina

Female Reproductive Tract

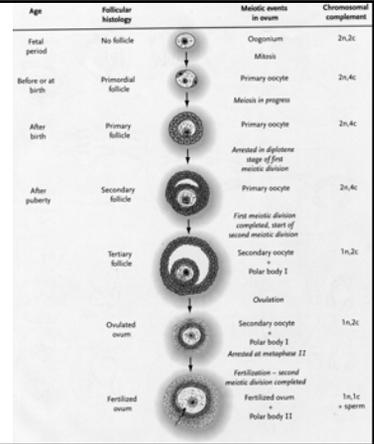


From Seeley, Stephens and Tate, 1989

Oogenesis

Oogonia – mitosis to 5th month, 7 million at birth
Atresia of oogonia degeneration: Puberty - 40,000; Ovulated - 400
 Meiosis - initiated in newborn
 1st Block of Meiosis → 1st prophase – called **Primary oocyte**
 Primary oocyte – Large nucleus → **germinal vesicle**
 After Puberty - 1st meiosis completed just prior to ovulation
 Unequal meiosis → **secondary oocyte** and **1st polar body**
 2nd block of meiosis is at metaphase of 2nd division
 Fertilization releases 2nd block

Oogenesis

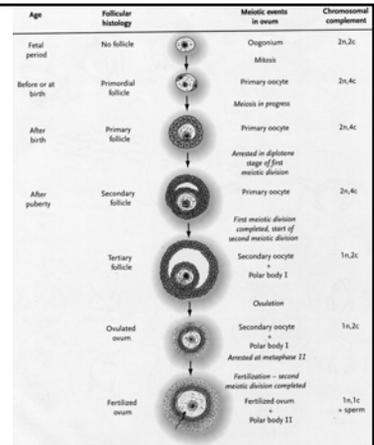


From BM Carlson, 1999

Follicle

Follicle cells (from sex cords) surround the Primary oocyte
 The Follicle is the oocyte plus follicle cells
 Primordial follicle - **follicle cells** partially surround oocyte
 Primary follicle – follicle cells form a complete layer
 Follicle cells form gap junctions with the oocyte and produce **Meiotic inhibitory factor**
 Follicle cells are called granulosa cells
 Granulosa cell layer enclosed by the membrana granulosa, a basement membrane that acts as a barrier to capillaries
 Zona pellucida secreted by oocyte and follicle cells – with microvillar connections between the two.
 Ovary cells form 2 more layers – theca interna, theca externa

Oogenesis

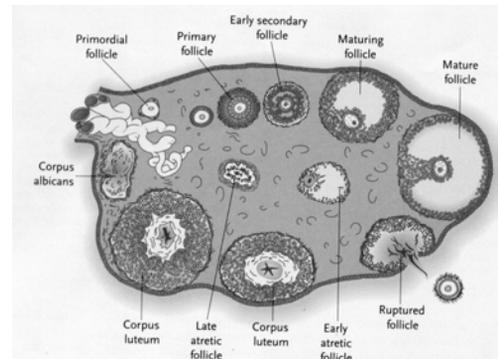


From BM Carlson, 1999

Follicle Development

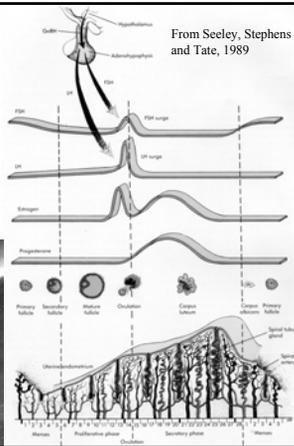
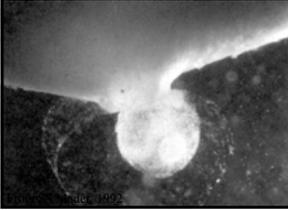
Secondary follicle – formation of the antrum (cavity) fluid filled, liquor folliculi
 Hormone production, androgens and estrogen
Tertiary or Graffian follicle – 12 hours prior to ovulation. cumulus oophorus = mound of cells that house the secondary oocyte
 Oogenesis controlled by cycles (Menstrual) of hormone release:
 Hypothalamus → **gonadotropin releasing hormone (GnRH)**
 Anterior pituitary → **Gonadotropins**, includes **luteinizing hormone (LH)** and **Follicle stimulating hormone (FSH)**
 Ovulation - tertiary follicle protrudes like a blister on the surface of the ovary – then bursts in response to LH and FSH
 Corpus Luteum – Follicle after ovulation – hormone producing Progesterone

Follicle Development



From BM Carlson, 1999

Hormonal Control of Menstrual Cycle



Menstrual Cycle

Menstrual Phase

Day 1-5 - Menstrual Phase

Progesterone-dependent (corpus luteum)

Uterus: Low progesterone – constriction of arteries veins

Sloughing of the endometrium

Ovaries: Folliculogenesis - 5-12 primordial follicles initiated

Primary follicles - squamous to cuboidal cell layer

Secretion of zona pellucida

Day 5-14 - Proliferative Phase

Day 13-14 - Ovulation

Day 14-28 - Secretory Phase

Menstrual Cycle

Proliferative Phase

Day 5-14 - Proliferative Phase

Estrogen-dependent (produced by granulosa cells)

Uterus: Endometrial stroma thickens (2-3-fold)

Uterine glands elongate

Spiral arteries grow

Epithelial cells become ciliated

Ovaries: Growing follicles - cell proliferation, multilayered

One follicle dominates – antrum formation, fluid uptake

Surrounding cells form theca interna and theca externa

Mature graafian follicle

Membrana granulosa - follicle cells lining antrum

Day 13-14 - Ovulation

Day 14-28 - Secretory Phase

Menstrual Cycle

Ovulation

Day 13-14 – Ovulation - Estrogen surge induces LH and FSH surge

Uterus: Proliferative phase continues

Ovaries: Oocyte resumes meiosis

Germinal vesicle breakdown

Metaphase in 20 hours

Unequal division – II^o oocyte and 1st polar body

2nd meiotic block

Cumulus oophorus - detaches and released into antrum

Ovulation: Day 14, follicle becomes vascularized

Bulges from the surface of ovary - stigma - small protrusion

Follicle wall thinning → cumulus-oocyte complex released

Ovulated ovum collected by the oviduct

Day 14-28 - Secretory Phase

Menstrual Cycle

Secretory Phase

Day 1-5 - Menstrual Phase

Day 5-14 - Proliferative Phase

Day 13-14 - Ovulation

Day 14-28 - Secretory Phase

Progesterone-dependent (corpus luteum)

Uterus: secretory phase - increase vasculature

Spiral arteries and spiral veins

Formation of glandular structures

Uterine epithelium becomes secretory

Ovaries: Corpus luteum forms from ruptured follicle

Produces Progesteron

Corpus luteum degenerates without implantation

Fertilization/Implantation

Day 15 – Fertilization

Unfertilized oocytes die **12-24 hours** after ovulation

Fertilization usually occurs in ampulla

Day 20 - Implantation

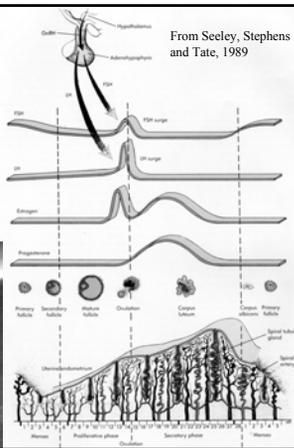
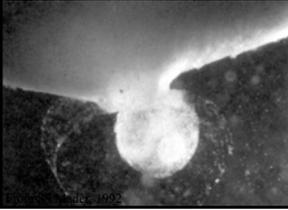
Implantation of the fertilized embryo occurs in the uterus

Uterine cells (trophoblast) produce Human Chorionic

Gonadotrophin (hCG)

hCG – maintains the corpus luteum (i.e. progesterone production)

Hormonal Control of Menstrual Cycle



Estrogen

17 β -estradiol, Steroid, from testosterone

Testosterone produced by thecal cells of the follicle – LH induced

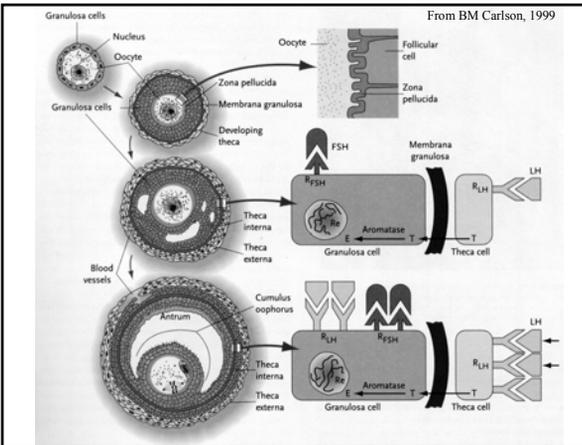
Testosterone passes to granulosa cell of the follicle

Granulosa cells express aromatase (enzyme) – FSH induced

Aromatase catalyzed reaction testosterone to 17 β -estradiol

17 β -estradiol released into the circulation, activates nuclear estrogen receptor – ligand-dependent transcription factor

Multiple Influences: Hypothalamus – GnRH (gonadotrophin releasing hormone – LH surge); Uterus - Proliferative phase; Breasts; Body fat; Bone growth



Progesterone

Steroid produced by granulosa lutein cells after ovulation – corpus luteum

Progesterone secretion by corpus luteum for 10 days – without implantation – it undergoes luteolysis – progesterone levels decrease – induces menstrual flow

Maintenance of Progesterone secretion by human chorionic gonadotropin (HCG) produced by the developing placenta

During pregnancy thecal lutein cells also produce progesterone

Progesterone released into the circulation, activates nuclear progesterone receptor – ligand-dependent transcription factor

FSH- Follicle Stimulating Hormone

Glycoprotein, 35 Kd, Released by Anterior Pituitary

(+) Hypothalamus, GnRH, gonadotropin releasing hormone

(-) Ovaries (granulosa cells), Inhibin (32 Kd), circulation

Females: → production of estrogen by follicle cells

Menstrual Cycle:

days 5-14 – proliferative phase, estrogen: follicle development

day 14 – ovulation – FSH surge

Males: → production of Androgen binding protein by Sertoli cells

LH – Luteinizing Hormone

Glycoprotein, 28 Kd, Released by Anterior Pituitary

(+) Hypothalamus, GnRH, gonadotropin releasing hormone

(-) Ovaries (granulosa cells), Inhibin (32 Kd), circulation

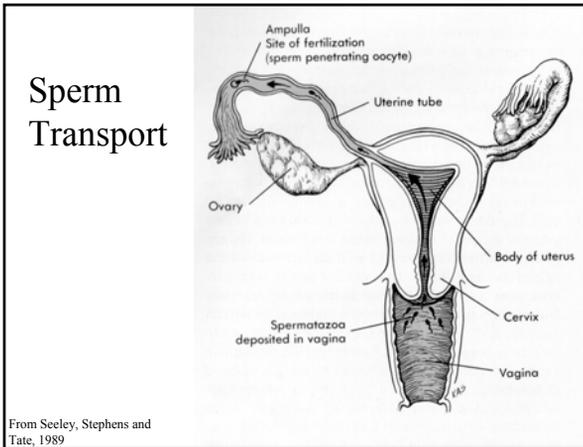
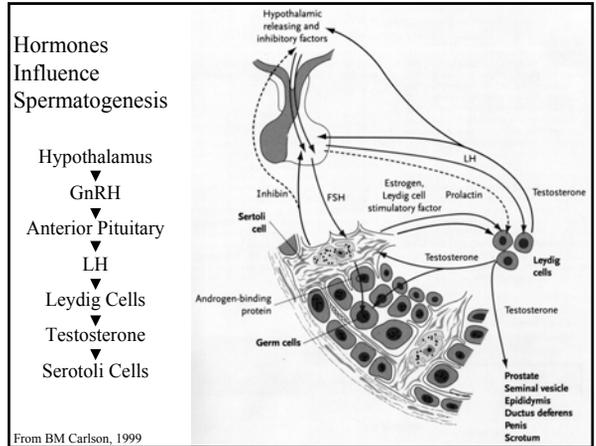
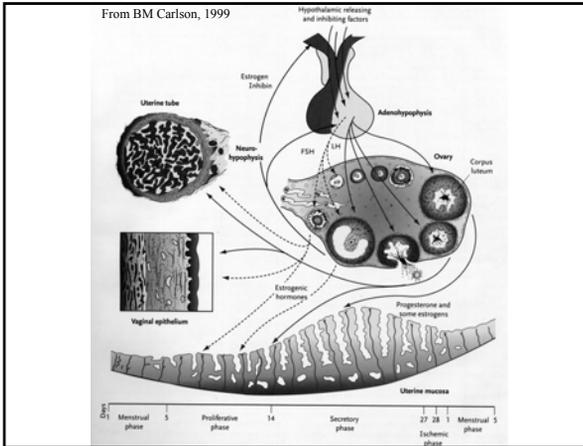
Females: → production of progesterone by follicle cells

Menstrual Cycle:

day 14 – LH surge induces ovulation and transforms the graafian follicle into the corpus luteum

days 14-28 – Secretory phase, LH required for progesterone production

Males: → Induces enzymes required for testosterone synthesis in Leydig cells



Birth Control Methods

Rhythm

Barriers – condoms, diaphragm, cervical cap

Pill (estrogen/progestin) – inhibits ovulation

IUD (intrauterine device) – mechanical interference

RU-486 – progesterone antagonist – induces menses

Sterilization – vasectomy / fallopian tube ligation

