Lecture 1:
Overview Of Reproductive System, Fertilization & Sex Differentiation
Overview Of Reproductive System: Physiology

- Reproductive Organs
  - production of offspring
- Gonads: Under the control of Hypothalamo – Hypophysio – Gonadal Axis
  - Endocrine Function: production of Sex Hormones
    - Estrogens & Progesterone in Females
    - Androgens (Testosterone) in Males
  - Gametogenesis: production of Germ cells
    - Ovum in Females by Oogenesis
    - Spermatozoa in Males by Spermatogenesis
• GnRH is released into the hypothalamic Hypophyseal portal system, which is located in median eminence and provides a vascular link to the anterior pituitary. GnRH is released in anterior pituitary where it activates the synthesis of LH and FSH by Gonadotrophs. Gonadotropin stimulate gonadal endocrine and gametogenesis functions.
Steps in Sexual Development & Differentiation

- Sex & Gender: Male ♂ or Female ♂ is determined in 4 steps

  1- genotypic sex - sex chromosomes: Male genotype (44+XY), Female genotype (44+XX)
     - ovum - contains an “X”
     - male genetic sperm - contains an “Y”
     - female genetic sperm – contains an “X”

  2- Gonadal sex: having testis or ovaries

  3- Phenotypic sex - internal and external genitalia

  4- Mental sex-sexual identity - one’s identity as masculine (male), 'feminine(female) or neutral
Sex determination before Gonadal & Genital Differentiation

- Sex chromatin (Bar body)
  - dense X chromosome

  - Visible In 10-15% of polymorph nuclear Leukocytes in female fetus by light microscope as a “drumstick”.

- F-body
  - parts of Y chromosome stained by Fluorescent dyes

- Visible In all cells in male fetus by Fluorescent microscope.
Gonadal genesis & genotypic sex differentiation

Coelomic epithelium

Testis Determining Factor (TDF)

SRY Gene on the short arm of Y chromosome
Phenotypic sex differentiation based on Secretory Functions of fetal testes

HCG \rightarrow Fetal Testis

- Leydig cells via LH activity of HCG
- Sertoli cells via FSH-like activity of HCG

- Testosterone
- Dihydrotestosterone

- Development of Male internal genitalia from the Wolfian duct
- Development of Male external genitalia
- Suppresses development of Mullerian duct

MIS/AMH/MRF
Pathways of synthesis of steroid hormones in the gonads. Testosterone is the major product of the testis. Estradiol and progesterone are the major products of the ovary. The enzymes are:

1: 20,22-desmolase
2: 17α-hydroxylase/17,20 desmolase
3: 17β-hydroxysteroid dehydrogenase
4: 3β-01-dehydrogenase,
5: aromatase
6: 5α reductase
7: 3α-reductase.
**Sexual identity (Development of Sexual Brain)**

- **In Male:**
  - Testosterone secreted into the blood reaches the brain
  - Testosterone converted to estradiol and Dihydrotestosterone in the brain
  - Estradiol masculinizes the brain

- **In Female:**
  - Alpha-fetoprotein binds to estradiol
  - Prevents estradiol from entering the brain
  - Protects female brains from being masculinized by estradiol
Abnormalities in sex differentiation

I- Genetic abnormalities

- Chromosomal non-disjunction
  - Mitosis
    - Mosaicism
    - Euhermapherodism
  - Meiosis
    - 44XO-Turner’s synd.
      - Female – Infertile
    - 44XXX- Normal phenotype
    - 44YO-Lethal
    - 44XXY-Klinefelter’s synd.
      - Male phenotype-infertile
Genotype Vs phenotype

- Is it possible to have a normal phenotype with opposite genotype?
- E.g. 44XX male or 44XY female
Abnormalities in sex differentiation
II- Hormonal abnormalities

- **Female pseudohermaphroditism**
  - Congenital virilizing adrenal hyperplasia of fetus
  - Maternal androgen excess
    - Virilizing ovarian tumor
    - Treatment with androgens or certain synthetic progestational drugs

- **Male pseudohermaphroditism**
  - Androgen resistance
  - Defective testicular development
  - Congenital Desmolase deficiency
  - Congenital 17-α Hydroxylase deficiency
  - Congenital 5-α Redoctase deficiency
    - Testicular Feminizing Syndrome (blind vagina)
Lecture 2:
Puberty & Adult Male Reproduction
ADOLESCENCE & PUBERTY

- in the boys usually 10-14 years old
- in the girls usually 8-13 years old
- adolescence = endocrine, physical, and behavioral changes
- puberty = “awaking” Gonadal endocrine & gametogenesis functions
Suggested mechanisms involved in puberty

- Pineal Gland
- Melatonin
- Hypothalamic-pineal sympathetic pathway
- Light Impulses From eyes
- Leptin
- Lipocyte
- Adrenal Androgens
- Gonadotrophs
- Gonad
- LH
- FSH
- GnRH

Light Impulses from the eyes stimulate the pineal gland, which produces melatonin. Melatonin inhibits the hypothalamic-pineal sympathetic pathway. Leptin and hypothalamic hypophyseal portal system also play roles in this process.
Pubertal Stages in Females

- Hormonal changes during puberty in girls
  - Stage 1: prepubertal
  - Stage 2: Breast Buds (Thelarche)
  - Stage 3: Breast enlargement & increase in Adrenal Androgenic Stimulatory Hormone AASH (Adrenarche)
  - Stage 4: development of Areola and Auxiliary & Pubic hair (Pubarchea) - female escutcheon (triangle with base up)
  - Stage 5: adult Breast, Oogenesis activity & 1st Menstruation (Menarche)
Pubertal Stages in Males

- Hormonal changes during puberty in boys
- Stage 1: prepubertal
- Stage 2: Testes enlargement (Gonadarche)
- Stage 3: penile enlargement & increase in Adrenal Androgenic Stimulatory Hormone / AASH (Adrenarche)
- Stage 4: growth of Glans Penis & Auxiliary & Pubic hair (Pubarche) - male escutcheon (triangle with apex up)
- Stage 5: adult genitalia & spermatogenesis activity.
- Spermarchea = 1st Ejaculation
Adult Male Reproductive Physiology

- Structure & function of Male Gonad (Testis)
- Hypothalamic-Pituitary-Testicular Axis
- Functions of Luteinizing Hormone
- Functions of Follicle-Stimulating Hormone
- Functions of Leydig Cells
- Functions of Sertoli Cells
- Hormonal Production Rates
- Actions of Androgens
- Spermatogenesis
- Male reproductive activity
Pulsatile secretion of G\textsubscript{n}RH from Hypothalamic Arquate Neurons into the Hypothalamic-Pituitary portal system.

Pulsatile secretion of LH & FSH from Gonadotrophs into the circulation.
Plasma Testosterone Levels at various ages in males

- **LH** (LH like activity of HCG) induces a rise in cellular cAMP in **Leydig cells**, this increases cholesterol production and **testosterone** is released in response.
- **Fetal** rise in testosterone → development of genitalia
- Function of **neonatal** rise in testosterone unknown.

- **Leydig cells** in testis quiescent until **puberty**. Onset of puberty triggered by GnRH.
- **Testosterone at puberty** ⇒; 2° sexual characteristics & negative feedback control on Gonadotropins
Mechanism of testosterone and dihydrotestosterone action
**Fig. 52-16** The spectrum of testosterone (T) effects. Note that some effects result from the action of T itself, whereas others are mediated by dihydrotestosterone (DHT) and possibly estradiol (E2) after they are produced from testosterone. VLDL, LDL, HDL: Very-low-density, low-density, and high-density lipoproteins, respectively.
Testicular function: spermatogenesis

Figure 27.8b, c
Spermiogenesis: Spermatids to Sperm

Figure 27.9a
Hormonal regulation of Spermatogenesis

- **Sertoli cells** lining the seminiferous tubules stimulated by **Leydig-derived** testosterone.
- release of Mullerian Inhibiting Substance (in fetus).
- **ABP**, estradiol, activin and inhibin.
- Promote development of sperm
Male sexual activity

- Under neural control (sexual reflexes)

- Erection (Arousal): stiffness of penile shaft

- Emission: Propulsion of sperm and glandular fluids to the internal urethra

- Ejaculation: rhythmic Propulsion of Semen out of the urethra

- Resolution: the male sexual excitement disappears almost entirely within 1 to 2 minutes and erection ceases
The prostate, bulbourethral & urethral glands

- 1- Deferent duct
- 2- Ampulla of the deferent duct
- 3- Seminal vesicle
- 4- Ejaculatory duct
- 5- Prostate
- 6- Outflow canals of the prostate
- 7- Bulbourethral gland (Cowper's)
- 8- Urethral gland (Littre's)
- 9a- Prostatic part of the urethra
- 9b- Membranous part of the urethra
- 9c- Spongy part of the urethra
Erectile tissue of the penis

- Deep penile fascia
- Corpus cavernosum
- Central artery
- Urethra
- Corpus spongiosum
Reflex pathways for erection. Nitric oxide, a vasodilator, is the most important neurotransmitter to the arteries in this reflex.
Nitric oxide, a vasodilator, is the most important neurotransmitter to the arteries in Erection reflex.
Composition of human semen

Color: White, opalescent

Specific gravity: 1.028

pH: 7.35-7.50
Sperm count: Average about 100 million/mL, with fewer than 20% abnormal forms

Other components:
- Fructose (1.5-6.5 mg/mL)
- Phosphorylcholine
- Ergothioneine
- Ascorbic acid
- Flavins
- Prostaglandins
- Spermine
- Citric acid
- Cholesterol, phospholipids
- Fibrinolysin, fibrinogenase
- Zinc
- Acid phosphatase
- Phosphate
- Bicarbonate
- Hyaluronidase

From seminal vesicles (contribute 60% of total volume)

From prostate (contributes 20% of total volume)

Buffers