MALE FERTILITY & INFERTILITY

BY

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TOPICS CONSIDERED

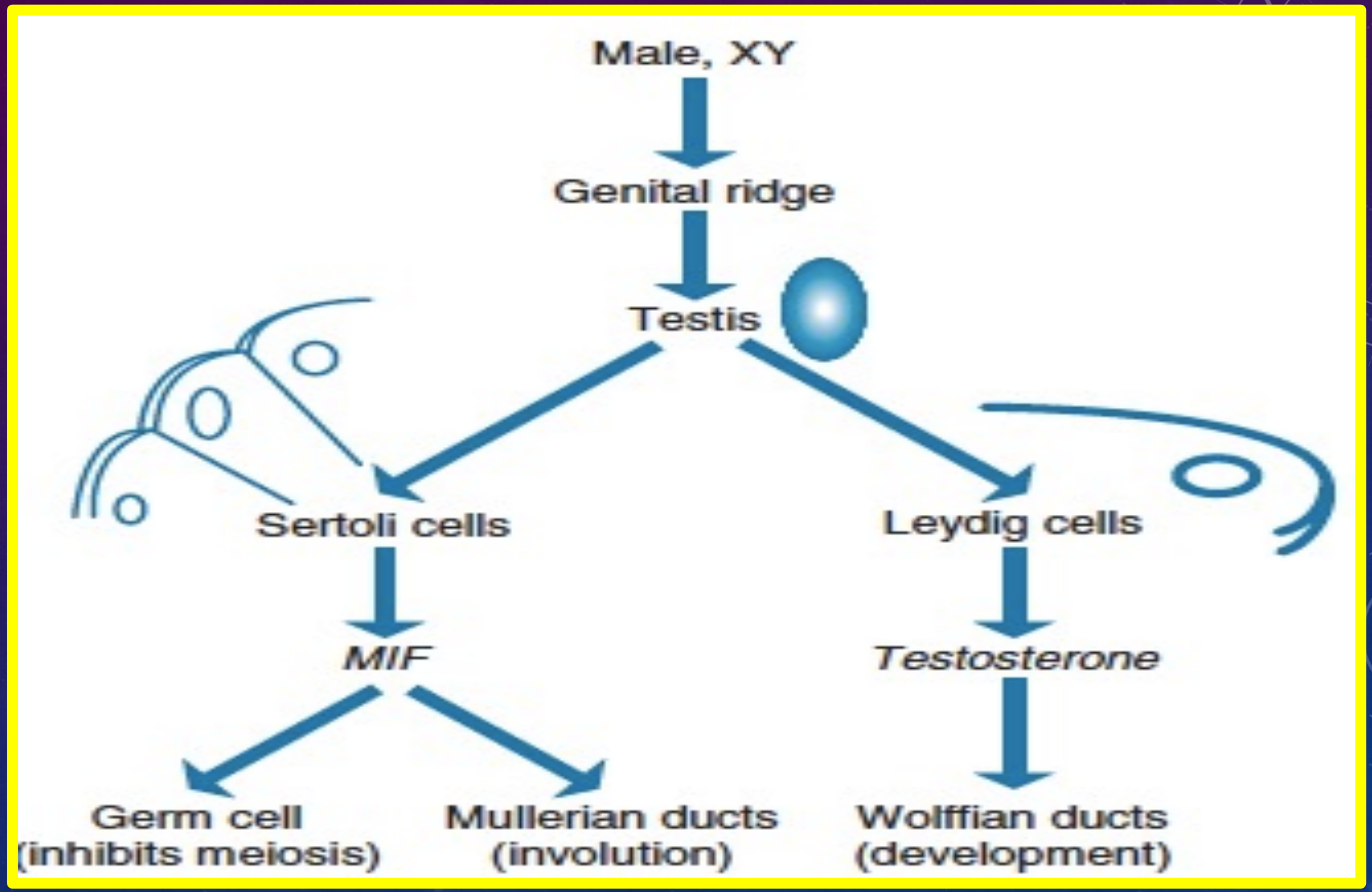
1. Reproductive anatomy and physiology
2. Evaluation of infertile male
3. Classification of male infertility problems
4. Treatment modalities

REPRODUCTIVE ANATOMY & PHYSIOLOGY

A. Emberiology
B. Gross anatomy
C. Reproductive hormonal axis
D. Extrahypothalamic central nervous system
E. Hypothalamic-Gonadotropin releasing hormone (GnRH)
F. Pituitary-Luteinizing hormone (LH) & Follicle-Stimulating hormone (FSH)
G. The testes
H. Feedback mechanisms
I. Testicular transport
J. Epididymal functions
K. Semen composition

A. EMBERIOLOGY

1. Genital organs include indifferent gonades, mesonephric duct and mullerian ducts at 5th week of gestation.
2. Migration of germ cells from the yolk sac (primordial germ cells) causing thickning of the urogenital ridge forms the indifferent gonad.
3. The presence or absence of testis determining factor (TDF) located in Y chromosome is responsible for sexual differentiation which determines gonadal sex (formation of testis)
4. During 8th week of gestation, testosterone is made by differentiating **leydig cells**
5. The mesonephric duct forms the ureters in both sexes and forms the vas deferens & epididymis in male
6. The mullerian duct forms the fallopian tubes, uterus and upper vagina in female. In male this development inhibited by mullerian inhibiting substance produced from primitive testis (appendix testis & prostatic uetricle)
7. Late in gestation,testicular descent into scrotum to be completed by birth.


Male, XY
Genital ridge
Testis
Sertoli cells
Leydig cells
MIF
Testosterone
Germ cell
(inhibits meiosis)
Mullerian ducts
(involution)
Wolffian ducts
(development)

B. GROSS ANATOMY

- The male reproductive system includes the following components: the testes and seminiferous tubules, efferent ductules and rete testis, epididymides, vasa deferentia, ejaculatory ducts, seminal vesicles, prostate, penis, and urethra.

C. REPRODUCTIVE HORMONAL AXIS

1. Components

a) Extrahypothalamic central nervous system

b) Hypothalamus

c) Pituitary

d) Testes

e) Steroid sensitive organs

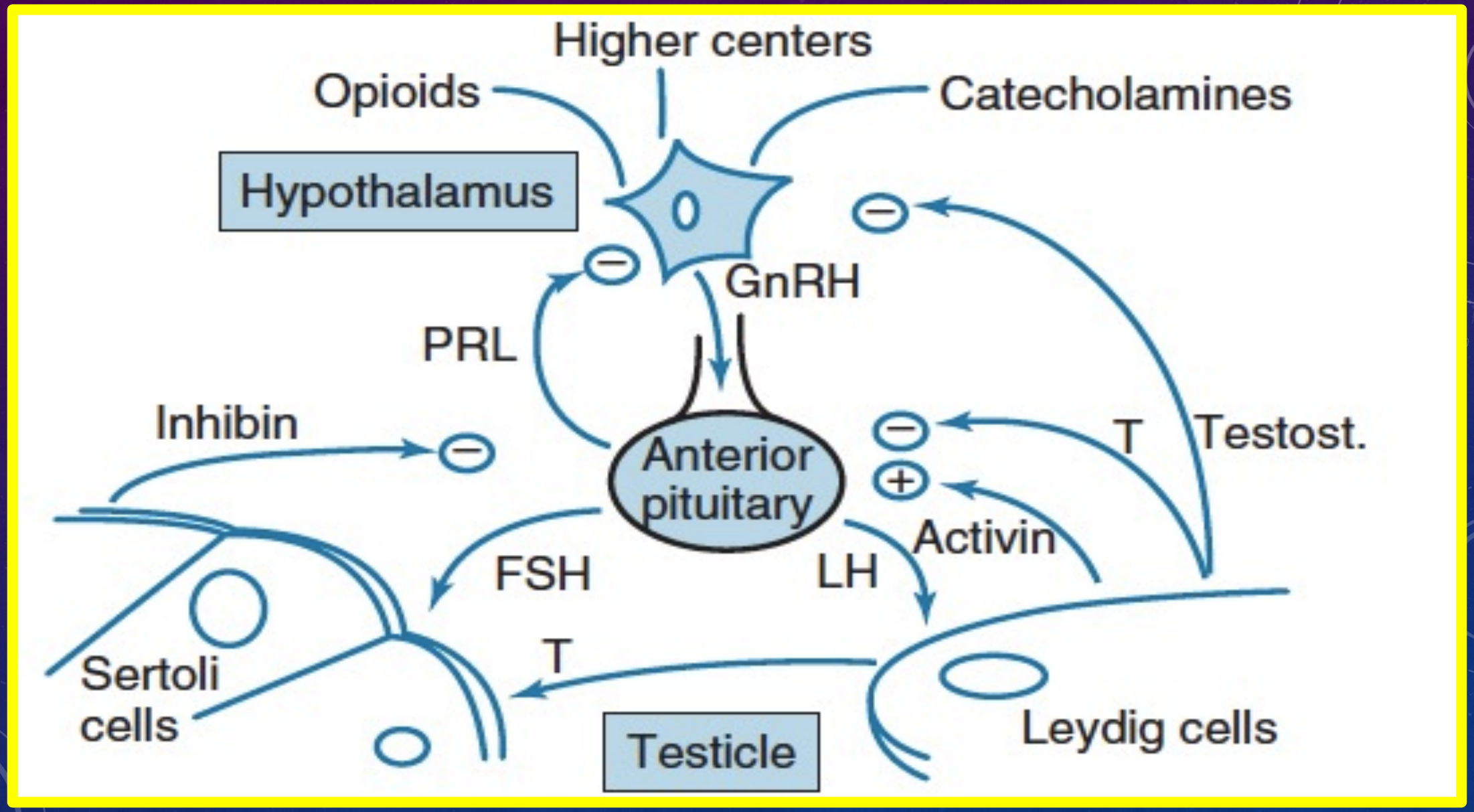
2. Functions

a) Normal male sexual development

b) Maintenance of secondary sexual characteristics

c) Male sexual behavior

d) Sperm production and maturation


Higher centers
Opioids
Catecholamines
Hypothalamus
GnRH
PRL
Inhibin
Anterior pituitary
T
Testost.
Activin
FSH
LH
T
Sertoli cells
Leydig cells
Testicle

D. EXTRAHYPOTHALAMIC CENTRAL NERVOUS SYSTEM

1. The extrahypothalamic central nervous system is responsible for a variety of stimulatory and inhibitory influences on fertility.

2. In humans, the effects of stress of both a physical and/or emotional nature are probably mediated through this system, but the mechanisms are unknown.

E. HYPOTHALAMIC-GONADOTROPIN RELEASING HORMONE (GNRH)

1. The anterior and ventromedial nuclei are most important for male fertility.
2. The hypothalamus is responsible for production of GnRH, which is the primary releasing substance involved in male sexual function.

F. PITUITARY-LUTEINIZING HORMONE (LH) & FOLLICLE-STIMULATING HORMONE (FSH)

1. The effect of GnRH is the production and release of LH and FSH from the anterior pituitary gland.
2. LH and FSH are both secreted episodically. LH is rapidly metabolized, causing wide swings in its concentration within the bloodstream when determined by radioimmunoassay techniques. Occasionally, more accurate LH levels are needed. FSH is more slowly metabolized, resulting in a more constant level within the bloodstream.

G. THE TESTES

1-Microscopic Anatomy:

a) Seminiferous tubules comprise the bulk (80%) of the testis and are responsible for sperm production. Thus, testis atrophy generally suggests a low sperm count.

b) The interstitium between the seminiferous tubules contains blood vessels, lymphatics, and Leydig cells.

2-Seminiferous Tubule Structural Organization

a) The tubules consist of long ducts lined by Sertoli cells.

b) Sertoli cells contain membrane receptors that bind FSH.

c) The Sertoli cells produce mullerian inhibiting substance in the fetus. Androgen binding protein (ABP), transferrin, and inhibin in the adult.

d) Sertoli cells appear responsible for regulation of the tubule microenvironment and sperm production.

e) Sertoli cells are also mainly responsible for the ‘‘blood-testis barrier.’’ This complex ‘‘blood-testis barrier’’ provides an immunologically privileged site for mature spermatozoa, as these haploid cells harbor unique and specific antigens that are not otherwise recognized as ‘‘self ’’ by the body’s immune system.

3. Seminiferous Tubules—Spermatogenesis

a) LH, FSH, and testosterone are all required for normal spermatogenesis.

b) Sertoli cells, lining 250 m of seminiferous tubules in the average testis, regulate the complex process of spermatogenesis.

d) The process of spermatogenesis takes about 60 days to complete. The average daily output is 125 million spermatozoa, which declines with age. A normal man makes 1200 sperm for every heartbeat.

e) Spermiogenesis is the maturation process of a spermatid to a spermatozoan.

4. Interstitium—Leydig Cells

a) Leydig cells contain membrane receptors that bind LH.

b) LH stimulation results in the conversion of cholesterol to testosterone.

c) Testosterone diffuses into the plasma (endocrine function) or into the seminiferous tubule lumen (paracrine function).

d) Testosterone may be active itself or may be reduced to dihydrotestosterone (DHT) by the enzyme 5-alpha reductase.

e) Testosterone is responsible in part for sexual differentiation, spermatogenesis, gonadotropin regulation, sexual maturation, and behavior.

H. FEEDBACK MECHANISMS

1.LH regulation.

a) Testosterone and estradiol are the major negative feedback substances that control the formation and release of LH.

b) Testosterone therefore regulates its own production and release by acting on the pituitary and in the hypothalamus. This has implications for clinical care: Exogenous testosterone supplements will suppress both endogenous testosterone (through decreased LH) and sperm production (through decreased FSH).

2. FSH regulation.

a) Testosterone and estradiol are the major modulators of pituitary FSH secretion. This is why exogenous testosterone supplements suppress spermatogenesis.

b) Sertoli cells produce inhibin which has an inhibitory effect on pituitary FSH output.

I. TESTICULAR TRANSPORT

1-The stages of spermatogenesis occur in a patchwork pattern and not in a wave-like manner within the seminiferous tubules.

2-The movement of the spermatozoa from the testis to the epididymis is controlled by four factors:

a) Fluid pressure generated within the seminiferous tubule.

b) Myoepithelial contractions of the seminiferous tubules.

c) Contraction of the tunica albuginea of the testis.

d) Cilia within and contraction of the wall of the efferent ductules.

3-The spermatozoa enter the epididymis in an immature state.

J. EPIDIDYMAL FUNCTIONS

1. Transport and Storage

a)The spermatozoa traverse the length of the epididymis in approximately 12 days.

b) Approximately 700 million sperm are stored within the epididymides and vasa deferentia. Approximately 60% of these are stored within the tail (cauda) of the epididymides. Sperm become progressively more motile as they traverse the epididymal tubules, knowledge of which is important in harvesting sperm from the epididymis for in vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI).

c) At the time of emission, regular coordinated contractions of the tails of the epididymides and the vasa deferentia occur, mediated by the sympathetic nervous system, propelling sperm into the prostatic urethra. During ejaculation, somatic nervous system stimulated rhythmic contractions of periurethral and pelvic floor muscles propel the sperm through the urethra.

2. Sperm Maturation

a) The chemical composition of the intraluminal fluid and spermatozoa changes significantly as one traverses the epididymis.

c) Motility and fertilizing capacity are gained during transport through the epididymis..

K. SEMEN COMPOSITION

1. the spermatozoa adding a small (<10%) amount to the total volume.

2. Prostatic fluid.

a) The prostatic fluid is usually found in the first part of the ejaculate and contributes approximately one quarter of the total volume. This fluid is acidic (pH <6.5).

b) Specific prostate products include liquefaction factors such as prostate-specific antigen (PSA), zinc, citric acid, acid, phosphatase, and spermine. The latter substance, when oxidized to aldehydes, produces the characteristic odor of semen.

c) PSA, serves to liquefy the coagulum of human semen after 5–20 minutes following ejaculation.

3. Seminal vesicle fluid.

a) The seminal vesicle fluid is usually found in the second part of the ejaculate and contributes approximately two-thirds of the total volume. This fluid is basic (pH >7.0).

b) Specific substances secreted by the seminal vesicles include coagulation factors, prostaglandins, and fructose. Fructose is measured on a semen analysis to investigate the diagnosis of ejaculatory duct obstruction.