Free water clearance (C H2O)

- Free water clearance is the difference between the urine volume/min and clearance of osmoles (Cosm)
- CH2O = V – (Uosm .V / Posm)

Where: Uosm and Posm is the urine and plasma osmolality.

- It is used to determine gain or loss of water by the kidneys:

a) CH2O is -ve so the urine is hypertonic maximal antidiuresis.

b) CH2O is +ve so the urine is hypotonic maximal diuresis as in diabetes insipidus.

Remember that:

- Any substance that is neither reabsorbed nor secreted by the renal tubules, as inulin, must have a plasma clearance = glomerular filtration rate = 125 ml/min.
- Any substance that is partially reabsorbed must have a clearance less than CIN e.g., urea.
- Any substance that is partially secreted must have a clearance more than CIN e.g., creatinine.
- Any substance that is completely reabsorbed must have a zero clearance e.g., glucose.
- Any substance that is completely removed from the kidney (totally secreted) by single circulation must have a clearance similar to renal plasma flow.
- Any substance that have a clearance more than renal plasma flow this means that this substance is totally secreted and also is synthesized by kidney e.g., ammonia.

Name	Equation	Units	Comments
Clearance	$C_x = \frac{[U]_x \dot{V}}{[P]_x}$	mL/min	x is any substance
Clearance ratio	$\text{Clearance ratio} = \frac{C_x}{C_{inulin}}$	None	Also means fractional excretion of x
Renal plasma flow	$RPF = \frac{[U]_{PAH} \dot{V}}{[RA]_{PAH} - [RV]_{PAH}}$	mL/min	
Effective renal plasma flow	$\text{Effective RPF} = \frac{[U]_{PAH} \dot{V}}{[P]_{PAH}}$	mL/min	Underestimates RPF by 10%; equals C_{PAH}
Renal blood flow	$RBF = \frac{RPF}{1 - Hct}$	mL/min	1 minus Hct is fraction of blood volume that is plasma
Glomerular filtration rate	$GFR = \frac{[U]_{inulin} \dot{V}}{[P]_{inulin}}$	mL/min	Equals C_{inulin}
Filtration fraction	$FF = \frac{GFR}{RPF}$	None	
Filtered load	$\text{Filtered load} = GFR \times [P]_x$	mg/min	
Excretion rate	$\text{Excretion} = \dot{V} \times [U]_x$	mg/min	
Reabsorption or secretion rate	Reabsorption or secretion = Filtered load – Excretion	mg/min	If *positive*, net reabsorption If *negative*, net secretion
Free-water clearance	$C_{H_2O} = \dot{V} - C_{osm}$	mL/min	If *positive*, free water is excreted If *negative*, free water is reabsorbed

Male Reproductive System

The male germ cells (sperms) are produced in the primary sex organs (two testes).in addition to these primary sex organs, there are secondary sex organs that provide the necessary tract and environment for the sperms.

Structure of male reproductive system

(I)The primary sex organ (testis):

*The testis is a compound organ composed of:

sertoli cell function

A-The seminiferous tubules:

-These are long, tortuous, hallow tubules in which spermatogenesis takes place. The seminiferous tubules are lined with spermatogonia. The spermatogonia lie close to the basement membrane and mature into spermatozoa which moves to the center of the tubules.

- **Sertoli cells** which are glycogen containing cells from which the sperms obtain their nourishment.

*Blood-testis barrier:

Tight junction between adjacent Sertoli cells near the basal lamina form a blood- testis barrier, that protects the germ cells from blood-borne noxious agents, prevents antigenic products of germ cell division and maturation from entering the circulation and generating an autoimmune response.

1. Nourishment
2. Formation of Blood-testis barrier
3. Shaping of spermatocytes during spermatogenesis
4. Secretes following hormones: Mullerian inhibitory factor (MIF) , Estradiol, Inhibin, activin and Androgen – binding protein

B) The interstitial cells of Leydig:

They are located between the seminiferous tubules and produce testosterone.

Spermatogenesis

-The spermatogonia lie on the tubular membrane are non-motile stem cells, they divide by mitosis to form two cellular pools : a pool of additional stem cells, which undergo continual renewal by mitosis, and a pool of type A spermatogonia, which enter the maturation process called spermatogenesis.

-Spermatogenesis requires about 64 – 74 days in man.

spermatogenesis control

The role of the **Sertoli cells** in spermatogenesis

•They provide a special environment for germinal cells development.

•They secrete a fluid that provide nutrients for the developing sperm.

•Spermiation :the conversion of the spermatid to mature sperm. During this process, the spermatids are attached to the Sertoli cells, which secrete digestive enzymes that remove most of the cytoplasm from the spermatids.

•They play a physical role in shaping the head and tail of the sperm.

•They secrete some hormones:

(1)Mullerian inhibitory factor (MIF) during fetal development to inhibit the formation of fallopian tubes from the mullerian ducts in male fetus.

(2)Estradiol , as one of the stimulatory factors in spermatogenesis.

(3)Inhibin, has a feedback inhibitory effect on the anterior pituitary gland to prevent over secretion of FSH.

(4)Androgen – binding protein (ABP), that maintain a high, stable supply of androgen in the tubular fluid.

(5)Activin, follistatin, insulin- like growth factor-1, transferrin and cytokines.

***Factors affecting spermatogenesis:**

1-Central nervous system

*The hypothalamus contains dopaminergic and noradrenergic neurons, when stimulated → release of releasing factors → ant. Pit. → controlling gonadotropins secretions.

* Various psychic stimuli feeding into the hypothalamus → marked excitatory and inhibitory effect on gonadotropin secretion →altering the degree of fertility.

2- Hormonal factors

a)Pituitary gonadotropins

***-FSH:**

- needed for growth and maturation of the testes.

-needed for the normal functions of Sertoli cells.

- facilitate the last stages of spermatid maturation and promote the production of androgen binding protein (ABP).

***- LH:**

maintains testosterone secretion by the Leydig cells.

b)Testosterone:

-Responsible for the development and maintenance of the germinal epithelium.

- needed for complete meiosis.

- needed for spermiogenesis.

c)Estrogen:

- formed by the Sertoli cells under FSH stimulation.

- essential for spermiation.

- excessive estrogen inhibits FSH secretion→ depression of spermatogenesis.

d)Thyroxin:

Stimulates spermatogenesis via the stimulatory effect on cell metabolism.

e)Growth hormone(GH):

promotes early division of the spermatogonia, in its absence as in pituitary dwarfs, spermatogenesis is severely deficient or absent.

3- Temperature:

•spermatogenesis requires a temperature lower than that of the interior of the body. The testes are normally maintained at a temperature of about 32 ºC.

•when the testes are retained in the abdomen. Degeneration of the tubular wall and sterility result.

•Hot baths (45 ºC for 30 min / day) and insulated athletic supporters reduce the sperm count.

4- Diet:

Complete protein starvation causes arrest of spermatogenesis, probably due to failure of gonadotropin secretion.

Vitamin E deficiency in animals causes irreversible tubular degeneration. This is not proved in man.

The tubular germ cells require vit. B group as catalysts for metabolic processes.

Vit. A: it ,s deficiency causes keratinization and atrophy of the germinal epithelium.

Vit. C: it ,s deficiency inhibits spermatogenesis as it is needed in testosterone synthesis.

5- Irradiation:

The germinal epithelium can be destroyed by certain doses of radiations. These doses spare Sertoli cells and the endocrine cells of the testes.

6- Hypoxia & toxins :

(bacterial or chemical) depress spermatogenesis.

The Male Sexual Act

1-Erection:

• Erection is initiated by dilation of the arterioles of the penis. As the erectile tissue of the penis fills with blood, the veins are compressed blocking outflow and adding to the turgor of the organ.

• The integrating centers in the lumber segments of the spinal cord are activated by impulses through afferents from the genitalia and descending tracts that mediate erection in response to erotic psychic stimuli.

• The efferent parasympathetic fibers are in the pelvic nerve(nervi erigentes).

• The fibers presumably contain acetylcholine, and vasoactive intestinal peptide(VIP) as cotransmitter.

Endocrine function of the testicles

Testosterone hormone function

Testosterone (T):

•Mechanism of action of (T):

-Like other steroids, T binds to an intracellular receptors, and the receptor-steroid complex then binds to DNA in the nucleus, facilitating transcription of various genes.

•Actions of (T):

1)During fetal life

- (T) is responsible for the development of the male sex organs e.g. the formation of a penis and a scrotum.

- (T) is responsible for descend of the testis into the scrotum during the last 2 months of gestation.

2)At puberty:

A-On the primary sex organs (T) is essential for spermatogenesis

B-On the secondary sex organs: Seminal vesicles, prostate, bulbourethral glands and the external genitalia are dependent on (T) for their growth and maturation. (T) is responsible for the maintenance of their integrity and function.

C- On the secondary sex characteristics:

1)-The distribution of body hair:

Beard appears. Hairline on scalp recedes antrolaterally. Pubic hair grows with male pattern(triangle with apex up). General body hair increases.

2)-Baldness: decrease the growth of hair on the top of the head.

3)-Voice: (T) causes hypertrophy of the laryngeal mucosa and enlargement of the larynx ŝdeeper voice.

4)-Skin: (T) increases thickness of the skin. It also increases the rate of secretion of the sebaceous glands → acne formation.

5)-Broaden shoulder and increased muscle bulk.

D- General metabolic effects:

(T) increases proteins synthesis.

(T) increases the quantity of bone matrix, and causes Ca++ retention.

(T) increases basal metabolic rate. # (T) increases food intake.

(T) increases RBCs number, by stimulating erythropoietin synthesis.

(T) increases Na+ reabsorption in the distal convoluted tubules ššlight increase in the extracellular fluid.

E- Regulation of behavioral effects, including libido.

(II) Dihydrotestosterone (DHT):

-About 20 % of plasma DHT is synthesized by the testis, probably because of the action of 5-α -reductase from the Sertoli cells on testosterone secreted by the Leydig cells. The remainder is derived from the peripheral conversion of T to DHT by 5 α -reductase in some target cells.

-DHT circulates in blood, with a plasma level that is 10 % of the T level.

-T- receptor complexes are less stable than DHT-receptor complexes in the target cells. Thus DHT is more potent than T. Congenital 5 α -reductase deficiency, produces **male pseudo-hermaphroditism**.

(III) -Estrogens

estrogen

30 % of estrogens secreted by the testes, some from Leydig cells and some from Sertoli cells.

70 % of estrogens formed by aromatization of circulating T and androstenedione.

very small amount may be secreted by the adrenal cortex.

in men, the plasma estrogen level is 2 ng /dL.

the peripherally derived estrogens may be released into the blood and transported to other tissues, where they may exert some biological actions. This is particularly evident in certain endocrine disorders, in which plasma (T) levels are depressed causing an elevation in the ratio of plasma estrogens to androgens. Under these condition, some feminization of the male body may occur. Inappropriate breast development, or gynecomastia.

ovarian cycle

1- Follicular phase :

At the start of each cycle , several (6-12) primordial follicles enlarge and develop to primary (pre-antral) follicles under the effect of FSH which released from anterior pituitary gland in response to the presence of low basal level of estrogen .

Primary follicle : the size of primary oocyte is increased , the follicular cells become cuboidal and proliferate forming many layers of granulosa cells around the oocyte .

- The ovarian stromal cells form theca folliculi

-Theca cells synthesize LH recepters and form antrogen under the effect of LH hormone and granulosa cells synthesize FSH receptors , convert androgen to estrogen under the effect of FSH hormone .

-After **one week** , one of the follicle , in one ovary , enlarges and highly developed more than other and secrete more estrogen (antral follicle) = **dominant** = secondary follicle and others regress (competing) .

Antral follicle :

The spaces unite and give one large space, oocyte is located in a mass of granulosa cells that project into antrum, the first layer of granulosa cells that surround the oocyte and enclose contact with zona pellucida , becomes elongated and is called **corona radiate** .

The mechanism : (why **one follicle** enlarges and the **other regress**)

A- **The dominant follicle** secretes more estrogen, that causes :

1- decrease FSH by negative feedback mechanism with hypothalamus and anterior pituitary, decrease the degree of stimulation of competing follicles thus stop its growth and become atretic .

2- increases granulosa cells proliferation and increase FSH receptors on granulosa cells, response of granulosa cells to FSH → ↑estrogen secretion from dominant follicle (+ve feedback) → more growth of the dominant follicle becomes.

B- The dominant follicle secretes inhibitory peptides which impairs binding of LH to its receptors in the competing follicles.

In the presence of FSH and increasing quantities of estrogen , the outer layers of granulosa cells of large antral follicle now synthesize LH receptors, moreover LH can induces the formation of its own receptor in FSH primed granulosa cells . thus granulosa cells start to synthesize. Progesterone instead of estrogen.

At the mid-cycle when estrogen level in the circulation reaches a high critical level and this level is maintained for a critical time , it induces sudden rapid increase in LH (LH surge) ie estrogen → ↑ LH , moreover , presence of progesterone

a) Facilitate the +ve feedback mechanism of estrogen on LH . b) induces FSH surge .

FSH and LH surge induce ovulation .

Just before ovulation , the follicle become **mature grafian follicle** (reach 1- 2 cm in diameter and oocyte undergoes meiotic reduction division to produce secondary oocyte and first polar body .

The secondary oocyte enters the second meiotic division to arrest again in its metaphase until after ovulation and fertilization .

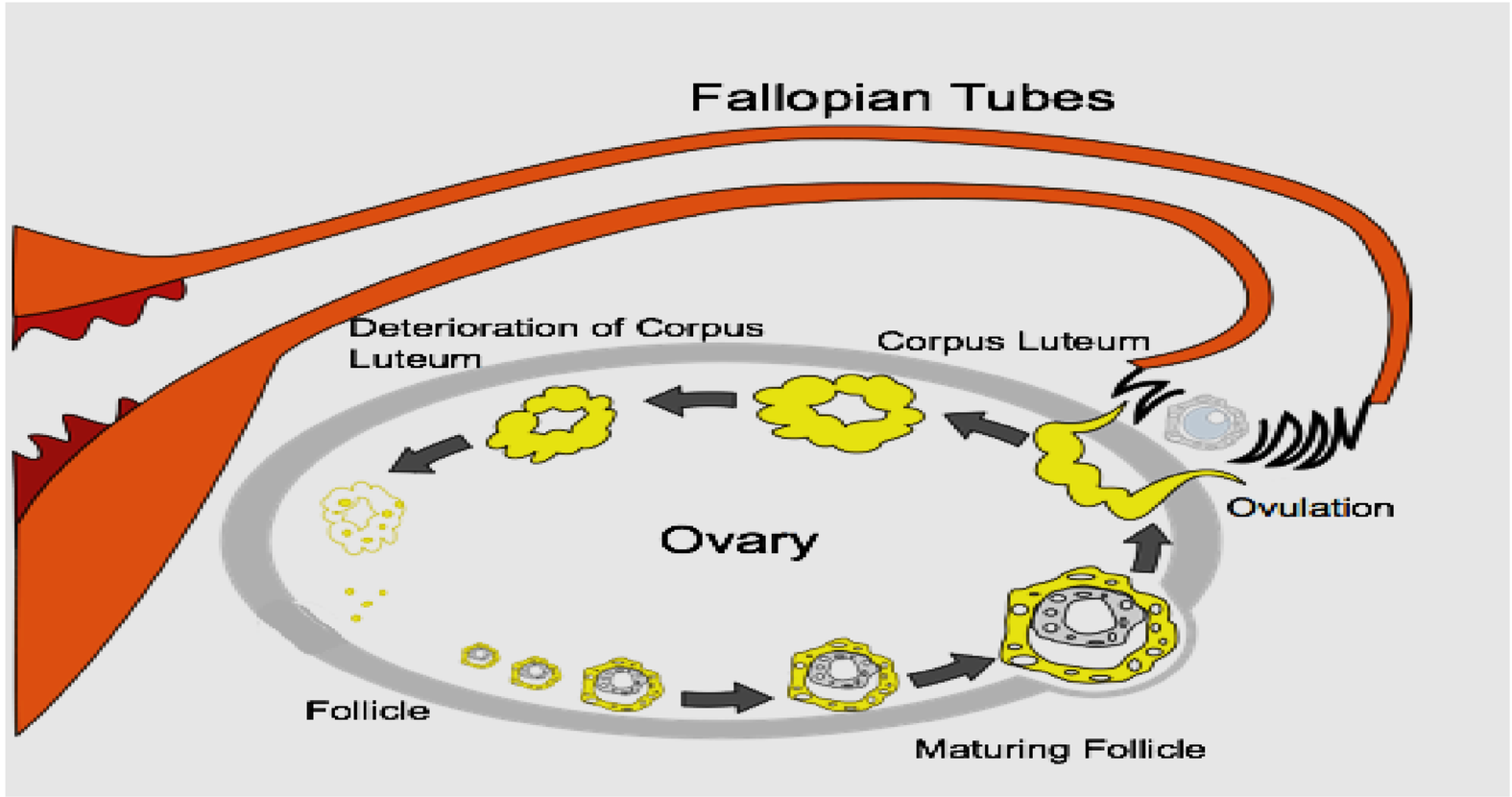
2- Ovulation

- It is the process of rupture of mature Graafian follicle and expulsion of ovum into the peritoneal cavity to be picked up by the fimbriated end of the fallopian tube .

- It takes place approximately in the day **14** of the cycle .

- The cause of ovulation is GnRH surge .

- If the ovum is not fertilized within 24 hours after ovulation , it degenerates .



3-Luteal phase

The follicle which rupture at the time of ovulation, fills with blood forming **corpus haemorrhagicum**, the clotted blood is removed by phagocytosis, the follicle is converted to **corpus luteum** under the effect of LH that accelerates the proliferation and hypertrophy of granulosa cells and incorporation of **theca interna cells** within the follicle .

Now granulosa cells and theca interna cells are called **lutein cells** which are lipid rich cells so corpus luteum is **yellow** in colour. Corpus luteum is a temporary endocrine gland, secretes **progesterone and estrogen** .

- Corpus luteum is maintained by **LH** .

- **Progesterone** reachs its peak level **8-9 days after ovulation** with a second peak of estrogen .

- The high levels of progesterone in presence of estrogen inhibit LH that lead to degeneration of corpus luteum , (luteolysis), and drop of estrogen level 9 days after ovulation. After 14 days of ovulation , it becomes **corpus albicans** .

- Corpus albicans persists for some time, then undergoes autolysis and is phagocytosed by macrophages leaving fibrous scar .

- N.B. if fertilization occurs corpus luteum is maintained by human chorionic gonadotrpin (HCGn) for 6 months then converted after **6 months** into corpus albicans.

Drop of estrogen level stimulates FSH secretion by its feedback action on hypothalamus and anterior pituitary gland to start another cycle .

FUNCTIONS OF THE PLACENTA

The Feto-placental unit :

The placenta is the site where fetal and maternal circulations are closely associated . Most of the gaseous and metabolic exchanges between fetus and mother take in this region of close proximity , although the place also functions as a barrier to the transfer of large molecules and cells .

A- The placenta is a site of selective exchange :

- Site of transport of nutrient materials for the fetus .
- Site of exchange of respiratory gases .
- It acts as a kidney for the excretion of waste products .
- It prevents the passage of harmful materials to fetus .

placenta (hormones)

B- The placenta as an Endocrine organ for maintaining pregnancy and preparing the mother for labor and lactation : It secretes 5 main hormones :

1- Estrogens :

- Cause enlargement of the breast tissue .
- Cause enlargement of the female external genitalia as a preparation for labor .
- Relax the sacroiliac joint and symphysis pubis ligaments to make easy passage of the fetus through the birth canal .

2- Progesterone :

- Increases decidual reaction development .

- Inhibits uterine contraction and prevents spontaneous abortion .

- Prepares the breast for lactation

3- Chorionic Gonadotrophin :

- It is a glycoprotein having the same function of LH.It replaces the anterior pituitary LH which by the 24th day of the menstrual cycle is only being secreted in small basal quantities because of the steroid feedback inhibition.

- It stimulates the growth of the corpus luteum to be the C.L of pregnancy to increase its secretion of estrogen and progesterone .

- It stimulates the interstitial cells of leyding in the testes of the male fetus to secrete testosterone hormone which causes descend of the testes into the scrotum and stimulates the development of the male sex organs .

- Its detection is the bases of pegnancy tests as it can be detected in maternal blood 6 – 8 days after fertilization .

4- Placental Lactogen (Somato-mammo-trophin)

Recently discovered and secreted about the 5th week of pregnancy .

- It has a luteotrophic function stimulating the corpus luteum to secrete oestrogen and progesterone (previously ascribed to be the function of chorionic gonadorophin) .

- It stimulates breast development (mammotrophic).

- It stimulates cellular growth (growth-promoting effect) and it inhibits glucose transport (inhibits insulin effect) i.e. it is similar to growth hormone .

5- Relaxin hormone (Relaxing Factor) :

It is secreted from the placenta and corpus luteum . It softens and relaxes the pelvice ligaments to help in the process of delivery (there are at least . 3 closely related polypeptides with molecular weight of about 9000 have relaxin activity)

27- All the following are signs of ovulation EXCEPT?
a. Appearance of human chorionic gonadotrophin in the urine
b. Increased body temperature at the proliferative face of the cycle
c. Proliferation of the vaginal epithelia and infiltration with leukocytes
d. Thick & tenacious cervical secretion
e. Increased level of progesterone at the second half of the cycle
ANS:A

24-Mechanism of menses is triggered by?
a. Decreased estrogen
b. Vasoconstriction oi the spiral arteries
c. Ischemic changes and necrosis of functional endometrium

d. increased progesterone level
e. Decreased progesterone level
ANS:A

20-Spermatogenesis begins in the ? Select one:
a. Uterine horn.
b. Rete testes.
c. Seminiferous tubules.
d. Seminal vesicles.
e. Prostate
ans:c

13-Progesterone hormone? Select one:
a. Stimulates LH secretion.
b. Has thermogenic effect.
c. Stimulates uterine contraction during pregnancy.
d. Makes the cervical mucus thin and alkaline.
e. Decrease blood glucose level
ans:b

14-Ovulation is associated with sudden rise in? Select one:
a. prolactin
b. estrogen
c. LH
d. Oxytocin
e. Growth hormone
ans:c

11-Progesterone produces the following functions, except? Select one:
a. It helps implantation of fertilized ovum.
b. Helps formation of early placenta.
c. Inhibits uterine contraction during pregnancy.
d. Responsible for growth of nipples.
e. Thermogenic.
Ans:d

3- which of these is incorrect ?
- capacitation in seminiferous tubule

58) Choose the INCORRECT match among the followings? Select one:
a. Sertoli cells ///// secrete testicular fluid
b. Spermatids ///// undergo second meiotic division
c. Epididymis ///// storage and maturation of sperms
d. Leydig cells ///// secrete testosterone
e. COWper's glands ///// mucus secreting glands

8) Testosterone should not be given to the pregnant woman because of the following reason?
a. Masculinization.
b. Acne.
c. Possible Virilization of the female fetus.
d. Deepening of voice.
e. Facial growth of hair.

145) Spermatogenesis begins in the ? Select one:
a. Uterine horn. b. Rete testes. c. Seminiferous tubules. d. Seminal vesicles. e. Prostate

50) All the following statements about testosterone are true EXCEPT?
a. Activation of testosterone may occurs at the skin
b. The prostate may help in activation of the testosterone
c. Androgen bind Protein (ABP) inhibit the function of testosterone
d. The site of action of testosterone is the nucleus
e. Free testosterone is less than 5 percent of the total serum testosterone

28) Substance commonly used to measure RBF ? Select one:
a. Inuline
b. Creatinine
c. Glucose
d. Para-amino- hippuric acid
e. Amino acids

29) About urea; all the following statements are true EXCEPT:
a. Blood urea is increased when the renal function is less than 40 percent.
b. Urea is actively secreted by the renal tubular cells
c. Urea concentration in the blood rises slightly after a high protein diet
d. Urea causes osmotic diuresis when blood urea concentration is increased
e. Urea clearance is less than 125 ml/ minute.

78) Progesterone hormone? Select one:
a. Stimulates LH secretion.
b. Has thermogenic effect.
c. Stimulates uterine contraction during pregnancy.
d. Makes the cervical mucus thin and alkaline.
e. Decrease blood glucose level

81) Ovulation is associated with sudden rise in? Select one:
a. prolactin b. estrogen c. LH
d. Oxytocin e. Growth hormone

56) Estrogen produces the following effects on breast, except? Select one:
a. Growth of nipples. b. Growth of acini. c. Growth of ducts.
d. Increase vascularity. e. Darkens areola .

80) Which of the followings statements regarding the female reproduction is CORRECT? Select one:
a. The maternal part of the placenta is called decidua capsularis
b. The mucosa of the vagina contains mucous secreting glands
c. The spiral arteries supply the basal layer of the endometrium
d. The first meiotic division is completed just before ovulation
e. Primordial follicles contain primary oocytes with haploid number of chromosomes

72) Large dose of progesterone? Select one:
a. Inhibits uterine contraction.
b. Inhibits ovarian cycle.
c. Inhibits both uterine contraction and ovarian cycle.
d. Does not inhibit both uterine contraction and ovarian cycle.
e. Decrease body temperature.