Female Reproductive System

PART 1

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Female Reproductive System

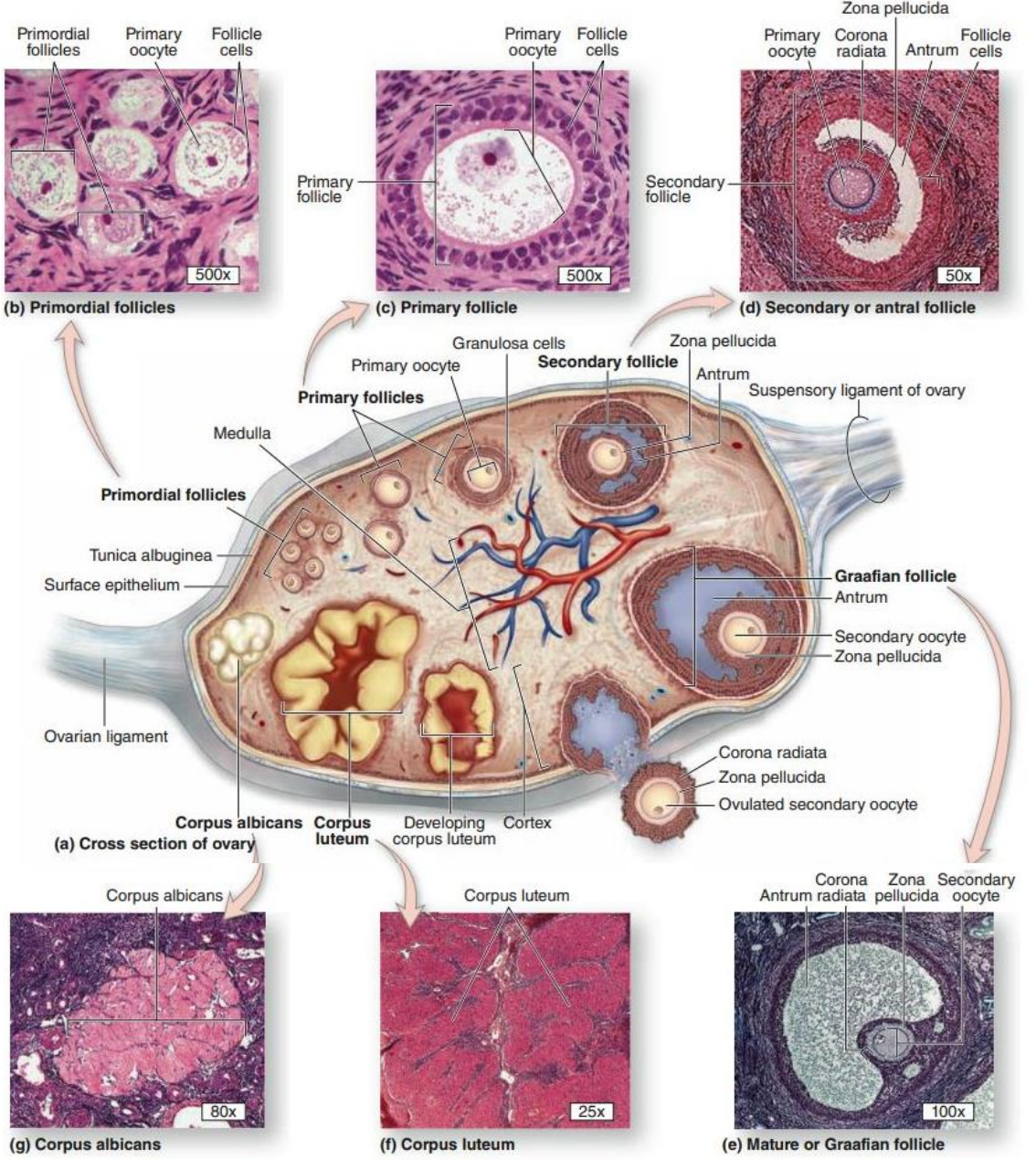
The female reproductive system includes (Fig. 20.1)

- A pair of ovaries
- A pair of uterine tubes
- Uterus
- Vagina
- External genitalia
- Mammary glands

THE OVARIES

The ovaries are the female gonads, responsible for the formation of ova. They also produce hormones (oestrogen and progesterone) that are responsible for the development of the female secondary sex characters, and produce marked cyclical changes in the uterine endometrium. Each ovary is an oval structure about 3 cm in long diameter.

Follicle development and changes within the ovary.



The ovary produces both oocytes and sex hormones. A diagram of a sectioned ovary **(a)** shows the **different stages of follicle maturation**, **ovulation**, and **corpus luteum formation and degeneration**. All of the stages and structures shown in this diagram actually would appear at different times during the ovarian cycle and do not occur simultaneously. Follicles are arranged here for easy comparisons. The **primordial follicles** shown are greatly enlarged. The histologic sections identify primordial follicles **(b)**, a primary follicle **(c)**, a secondary follicle **(d)**, and a large vesicular follicle **(e)**. After ovulation, the portion of the follicle left behind forms the corpus luteum **(f)**, which then degenerates into the corpus albicans **(g)**. (All H&E)

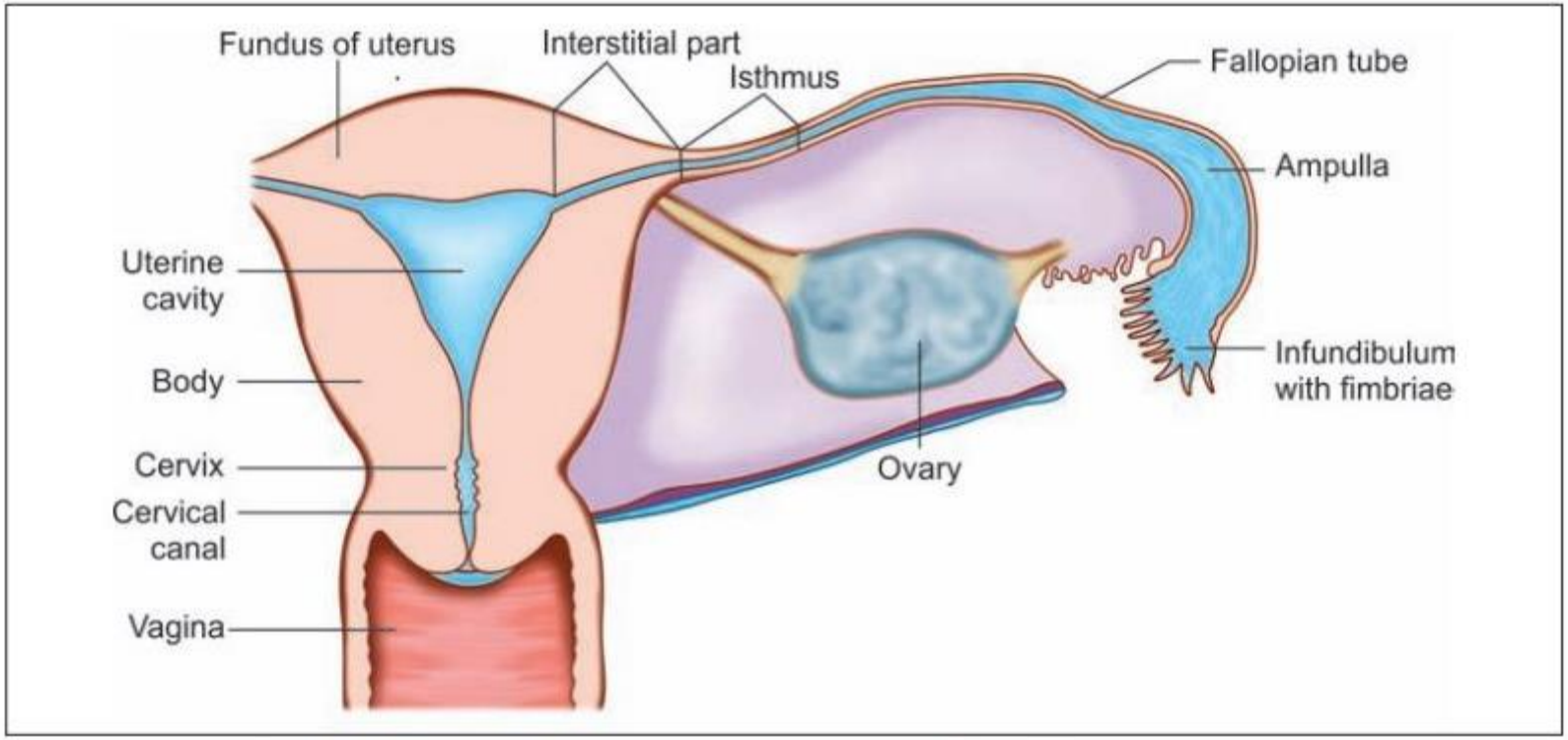


Fig. 20.1: Parts of female reproductive system (Schematic representation)

General Structure

Each ovary consists of the following parts

- ***Germinal epithelium:*** The free surface of ovary is covered by a single layer of cubical cells that constitute the ***germinal epithelium***. This epithelium is continuous with the mesothelium lining the peritoneum, and represents a modification of the latter.

Note: The term germinal epithelium is a misnomer. The epithelium does not produce germ cells. The cells of this epithelium bear microvilli, and contain numerous mitochondria. They become larger in pregnancy.

- ***Tunica albuginea:*** The germinal epithelium rests on a connective tissue layer called the ***tunica albuginea***. The tunica albuginea of the ovary is much thinner, and less dense, than that of the testis
- ***Cortex:*** Deep to the tunica albuginea the cortex has a stroma made up of reticular fibres and numerous fusiform cells that resemble mesenchymal cells. Scattered in this stroma there are ***ovarian follicles*** at various stages of development. Each follicle contains a developing ovum
- ***Medulla:*** The ***medulla*** consists of connective tissue in which numerous blood vessels (mostly veins) are seen. Elastic fibres and smooth muscle are also present. The hilum of the ovary is the site for entry of blood vessels and lymphatics. It is continuous with the medulla. The hilum also contains some remnants of the mesonephric ducts; and ***hilus cells*** that are similar to interstitial cells of the testis.

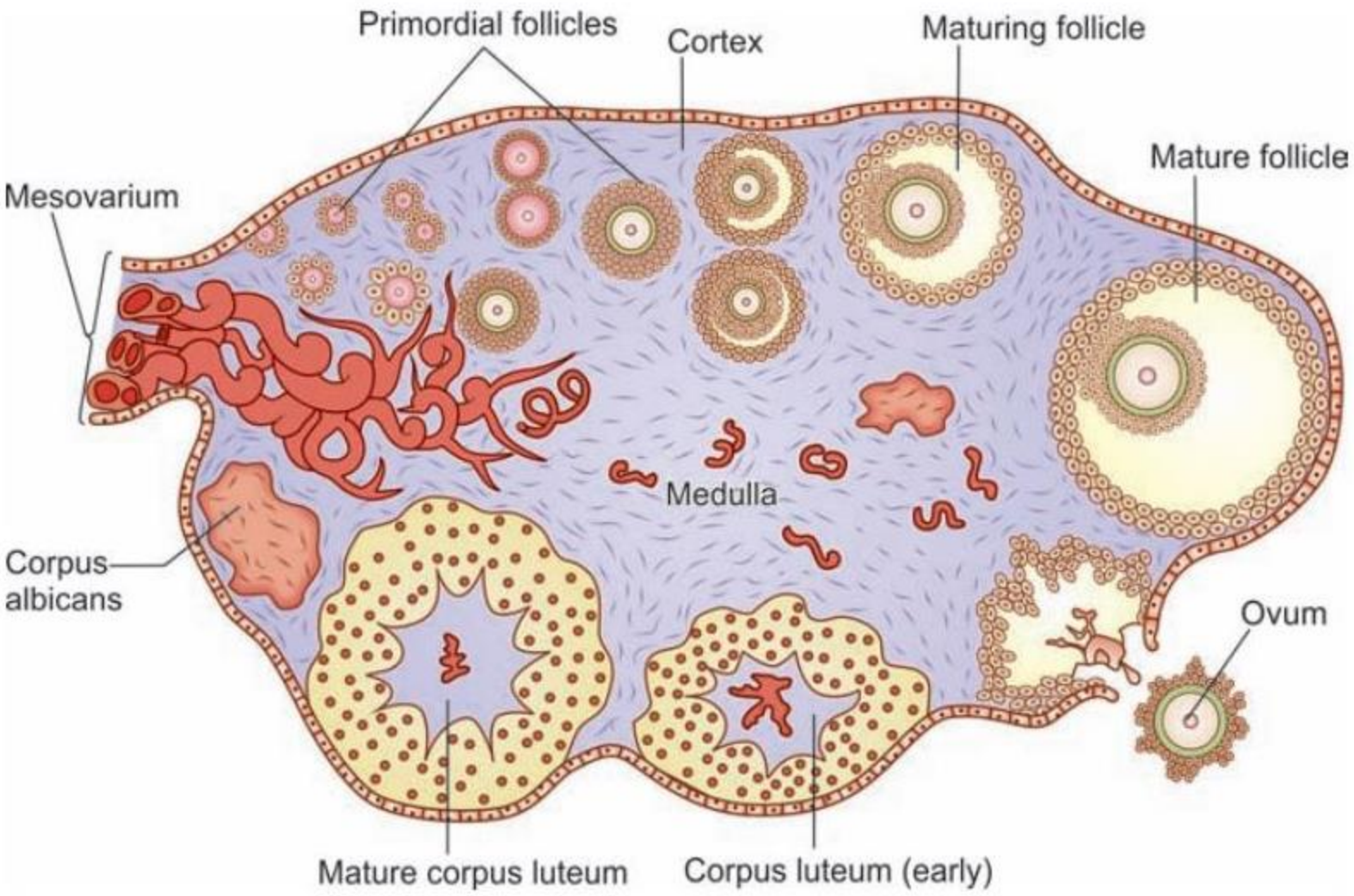
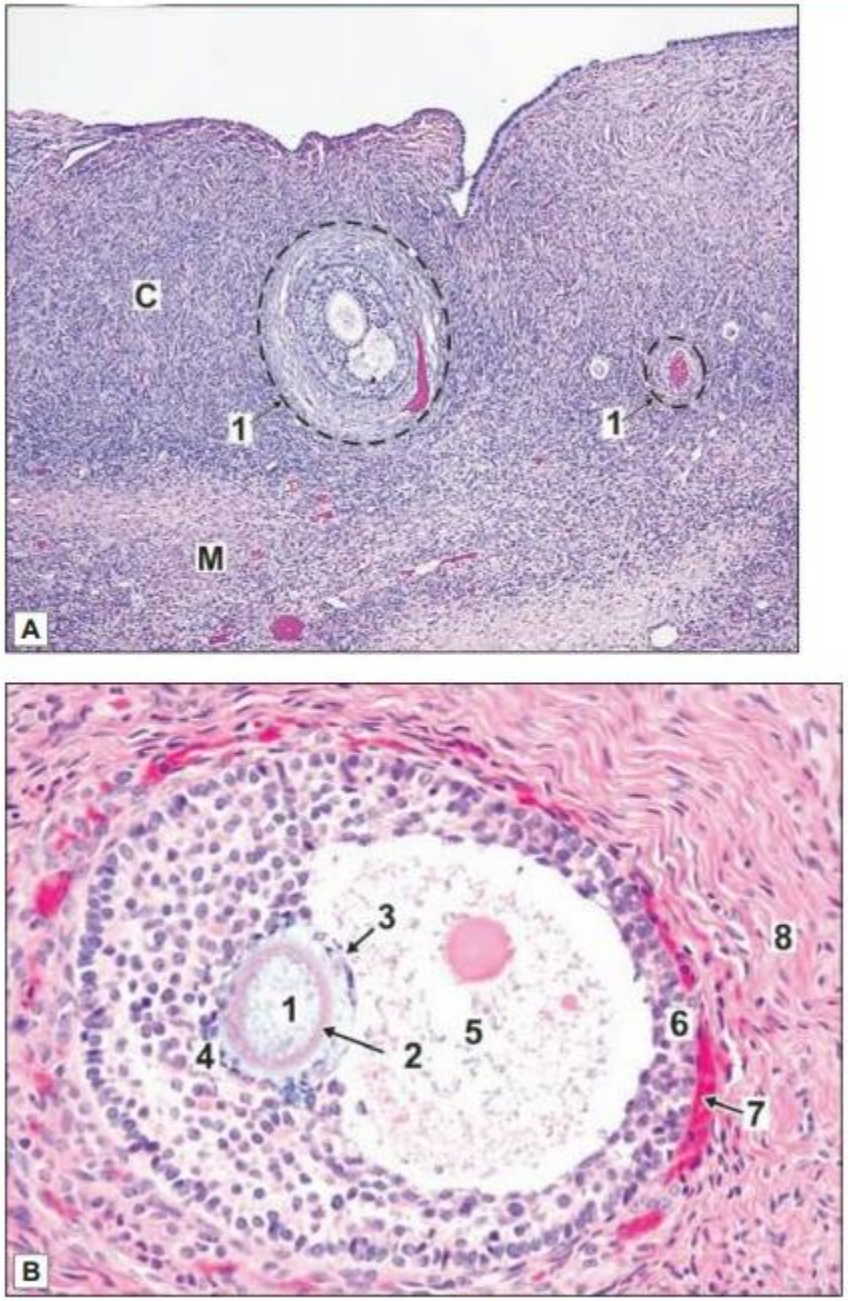


Fig. : Histological structure of ovary showing follicles at various stages of development (Schematic representation)

Ovary



A. Ovary (photomicrograph); B. Graafian follicle (photomicrograph)

- The surface is covered by a cuboidal epithelium. Deep to the epithelium there is a layer of connective tissue that constitutes the tunica albuginea
- The substance of the ovary has an outer cortex in which follicles of various sizes are present; and an inner medulla consisting of connective tissue containing numerous blood vessels
- Just deep to the tunica albuginea many primordial follicles each of which contains a developing ovum surrounded by flattened follicular cells are present.
- Large follicles have a follicular cavity surrounded by several layers of follicular cells
- The cells surrounding the ovum constitute the cumulus oophoricus
- The follicle is surrounded by a condensation of connective tissue which forms a capsule for it
- The capsule consists of an inner cellular part (the theca interna), and an outer fibrous part (the theca externa) collectively called as Theca folliculi. The follicle is surrounded by a stroma made up of reticular fibres and fusiform cells.

Key

C. Cortex
M. Medulla
1. Ovarian follicle
2. Zona pellucida
3. Cumulus oophoricus
4. Discus proligerus
5. Antrum folliculi
6. Membrana granulosa
7. Capsule of follicle
8. Stroma

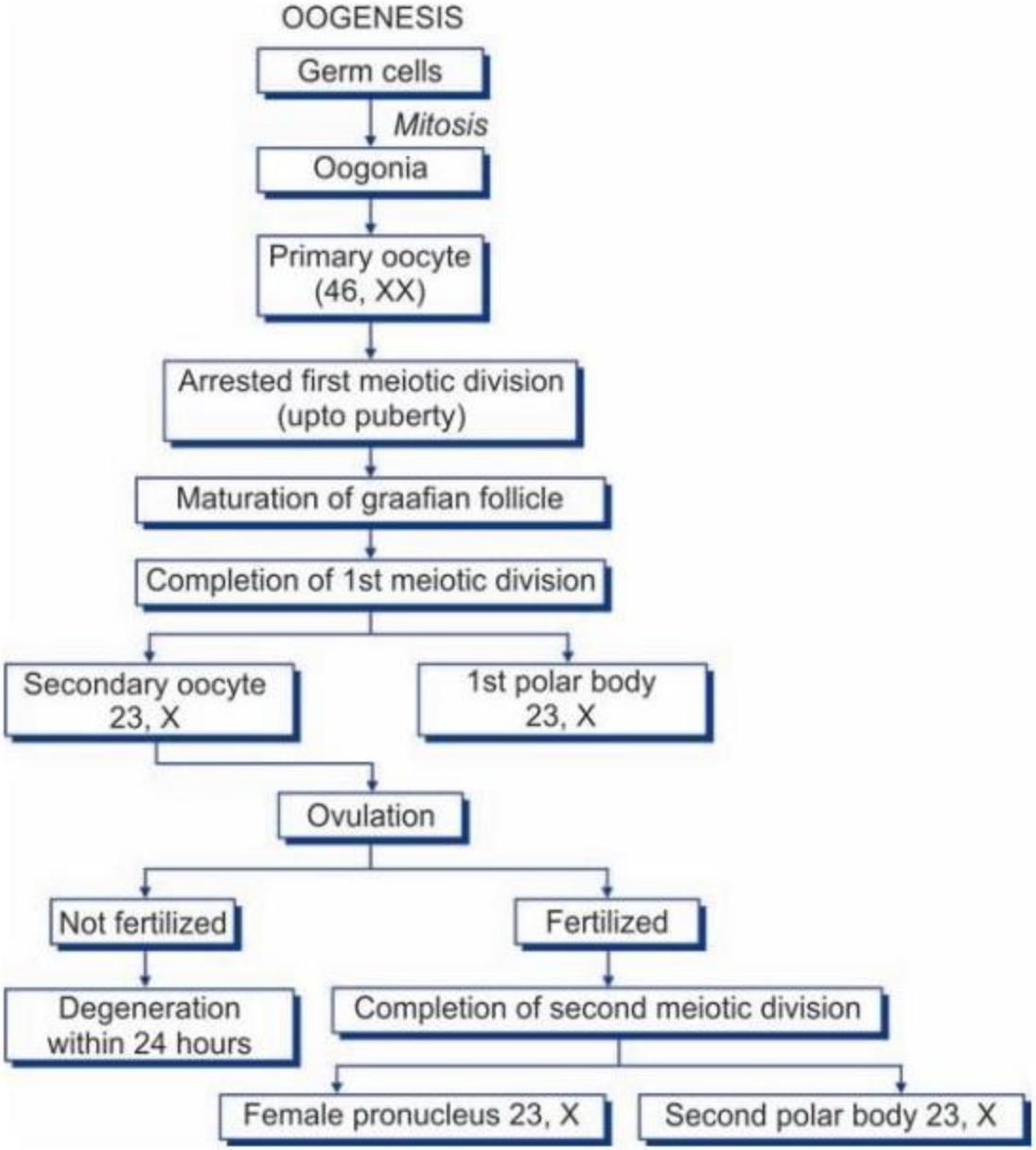
OOGENESIS

The process of formation of ovum from the stem cells is called oogenesis (Flowchart). The process of oogenesis consists of following stages:

- ***Oogonia:*** The stem cells from which ova are derived are called ***oogonia***. These are large round cells present in the cortex of the ovary. Oogonia are derived (in fetal life) from ***primordial germ cells*** that are formed in the region of the yolk sac, and migrate into the developing ovary. They increase in number by mitosis.

  All oogonia to be used throughout the life of a woman are produced at a very early stage (before birth) and do not multiply thereafter. At birth the number of oogonia in an ovary is about one million. Many oogonia formed in this way degenerate, the process starting before birth and progressing throughout life, so that the number of oogonia becomes less and less with increasing age.
- ***Primary oocyte:*** An oogonium enlarges to form a ***primary oocyte***. The primary oocyte contains the diploid number of chromosomes i.e., 46. It undergoes the first meiotic division to form two daughter cells each of which has 23 chromosomes.
- ***Secondary oocyte:*** The cytoplasm of the primary oocyte is not equally divided. Most of it goes to one daughter cell that is large and is called the ***secondary oocyte***. The second daughter cell has hardly any cytoplasm, and forms the ***first polar body***.

Flow chart : Stages of oogenesis.



Embryological Considerations

- At the time of birth all primary oocytes are in the prophase of first meiotic division. Their number is about 40,000.
- The primary oocytes remain in prophase and do not complete their first meiotic division until they begin to mature and are ready to ovulate.
- The reproductive period of a female is between 12 and 50 years of age. With each menstrual cycle, a few primary oocytes (about 5 to 30) begin to mature and complete the first meiotic division shortly before ovulation.
- The secondary oocyte immediately enters the second meiotic cell division. Ovulation takes place while the oocyte is in metaphase. The secondary oocyte remains arrested in metaphase till fertilization occurs.
- The second meiotic division is completed only if fertilization occurs.
- If fertilization does not occur, the secondary oocyte fails to complete the second meiotic division and degenerates about 24 hours after ovulation.
- In each menstrual cycle, 5 to 30 primary oocytes start maturing, but only one of them reaches maturity and is ovulated. The remaining degenerate.
- During the entire reproductive life of a female, only around 400 ova are discharged (out of 40,000 primary oocytes available).

- ***Ovum:*** The secondary oocyte now undergoes the second meiotic division, the daughter cells being again unequal in size. The larger daughter cell produced as a result of this division is the ***mature ovum***. The smaller daughter cell (which has hardly any cytoplasm) is the ***second polar body***. Thus, one primary oocyte ultimately gives rise to only one ovum.

Formation of Ovarian Follicles

Ovarian follicles (or ***Graafian follicles***) consists of a developing ova surrounded by follicular (granulosa) cells. The development and maturation of an ovarian follicle passes through four stages—the process is called folliculogenesis

- ***Primordial follicle:*** Some cells of the stroma become flattened and surround an oocyte . These stromal cells are now called ***follicular cells***. The oocyte (20–25 μm) and the flat surrounding cells form a ***primordial follicle***. Primordial follicles are the smallest and simplest in structure located at the periphery of the cortex. Numerous primordial follicles are present in the ovary at birth. They undergo further development only at puberty.
- ***Primary follicle:*** The first indication that a primordial follicle is beginning to undergo further development is that the flattened follicular cells become columnar

  Follicles at this stage of development are called ***primary follicles***. The outermost layer of the follicular cells rest on a well defined basement membrane which separates it from the ovarian stroma. A homogeneous membrane, the ***zona pellucida***, appears between the follicular cells and the oocyte (which enlarges in size 50–80 μm in diameter. With the appearance of the zona pellucida the follicle is now referred to as a ***multilaminar primary follicle***.

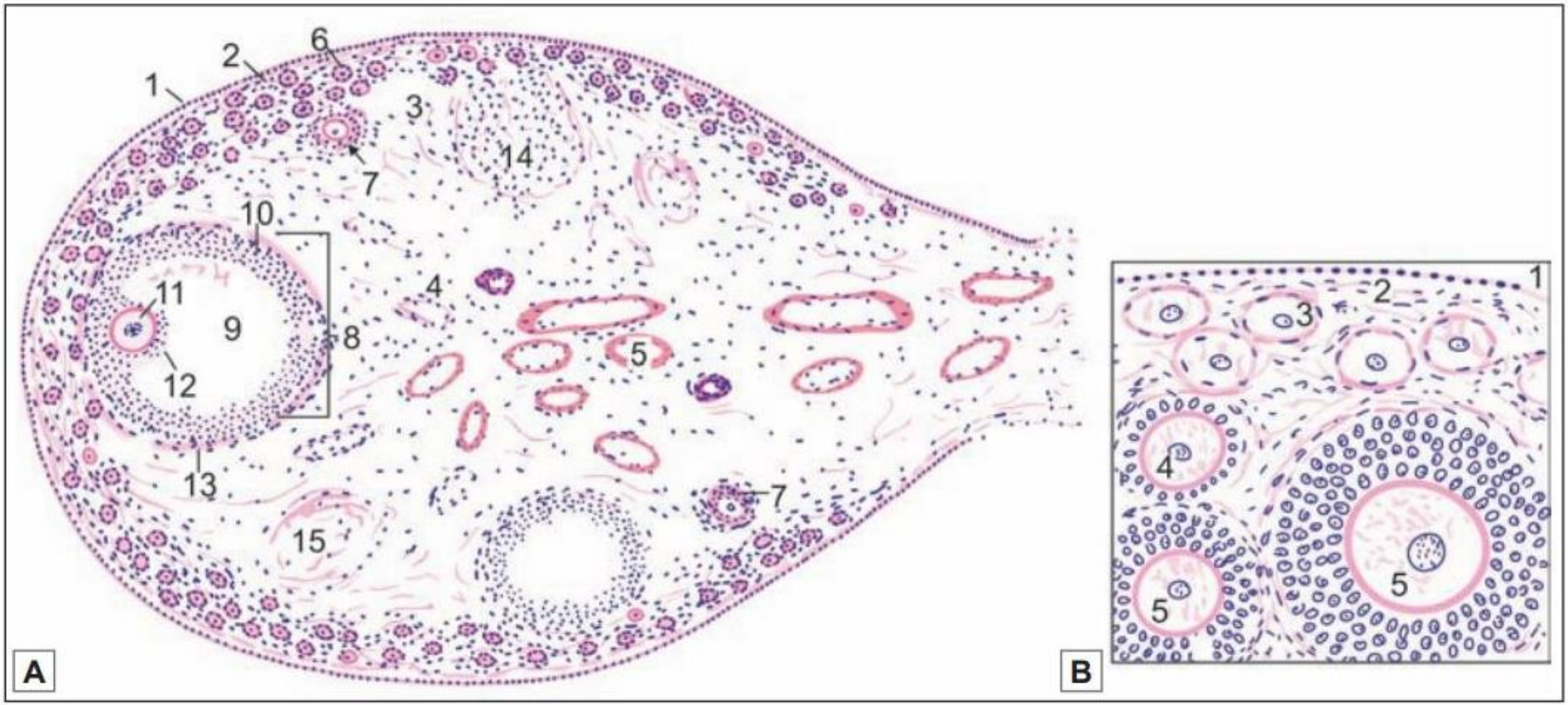


Fig. : Ovary, **A.** Panoramic view (Schematic representation). 1–cuboidal epithelium over surface; 2–tunica albuginea; 3–cortex; 4–medulla; 5–blood vessels; 6–primordial follicle; 7–secondary follicle; 8–graffian follicle; 9–follicular cavity; 10–granulosa cells; 11–ovum; 12-cumulus oophoricus; 13–capsule of follicle; 14–corpus luteum; 15-atretic follicle. **B.** Ovary (high magnification drawing) showing early stages in formation of follicles. 1–germinal epithelium; 2–tunica albuginea; 3–primordial follicle; 4–primary follicle; 5–secondary follicles (Schematic representation)

- ***Secondary follicle:*** The follicular cells proliferate to form several layers of cells that constitute the ***membrana granulosa***. The cells are now called ***granulosa cells***. The oocyte enlarges and reaches its maximum size (125 μm). This is a ***secondary follicle*** (Fig.).

  So far the granulosa cells are in the form of a compact mass. However, the cells to one side of the ovum soon partially separate from one another so that a ***follicular cavity*** (or ***antrum folliculi***) appears between them. It is with the appearance of this cavity that a true follicle (= small sac) can be said to have been formed. The follicular cavity is filled by a fluid, the ***liquor folliculi***. With the formation of follicular cavity the size of the follicle increases.

- ***Graafian follicle:*** With the further development, the follicular cavity rapidly increases in size. As a result, the wall of the follicle (formed by the granulosa cells) becomes relatively thin. The graffian follicle now measures about 10 mm or more in

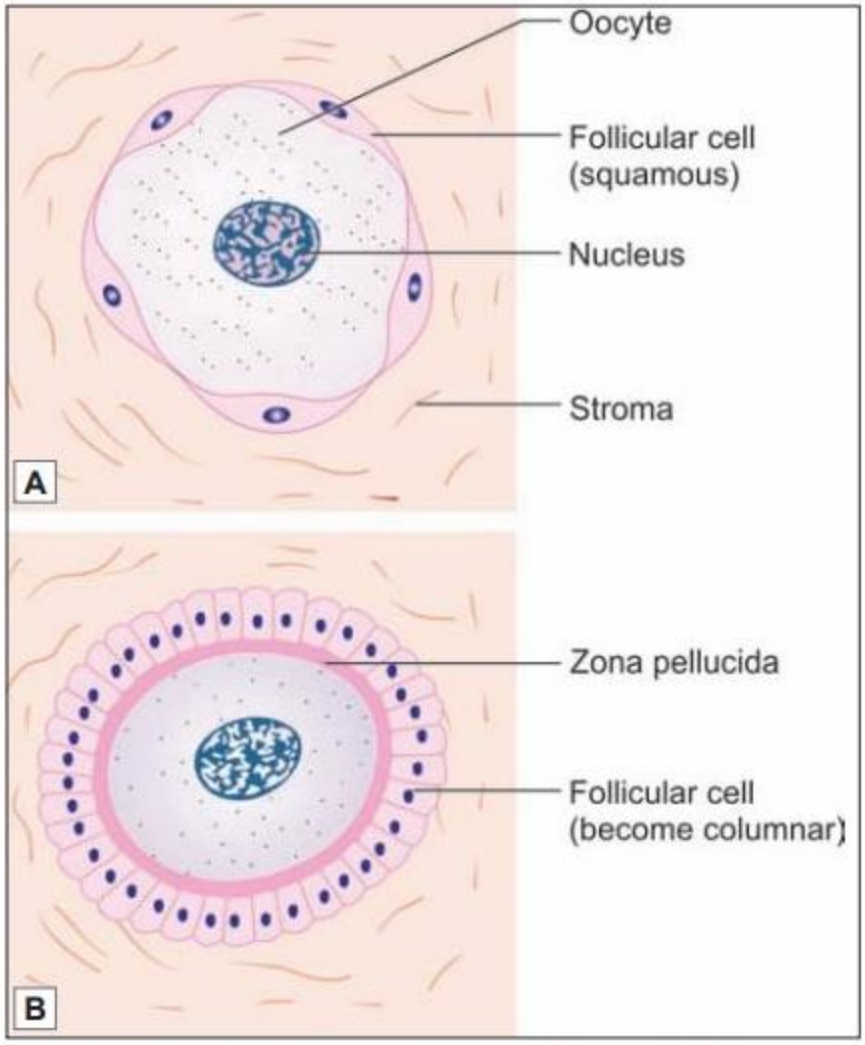


Fig. **A.** Primordial follicle; **B.** Primary follicle (Schematic repesentation)

diameter and is seen bulging out of the cortex (Fig.). The oocyte now lies eccentrically in the follicle surrounded by some granulosa cells that are given the name of ***cumulus oophoricus*** (or ***cumulus oophorus***, or ***cumulus ovaricus***). The inner most layer of cumulus oophorus that lies directly adjacent to the zona pellucida is called ***corona radiata***. The granulosa cells that attach the oocyte to the wall of the follicle constitute the ***discus proligerus*** (Fig.).

As the follicle expands the stromal cells surrounding the membrana granulosa become condensed to form a covering called the ***theca interna*** (theca = cover). The cells of the theca interna later secrete a hormone called ***oestrogen***, and they are then called the cells of the ***thecal gland***.

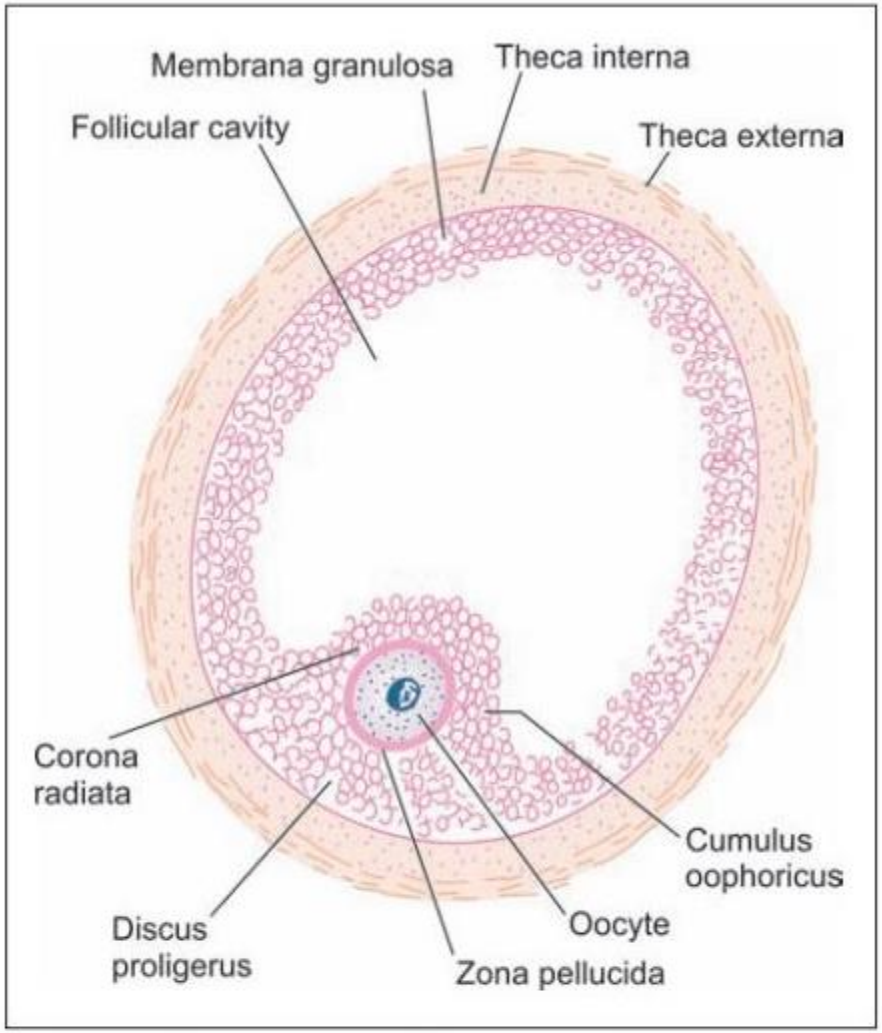


Fig. Mature ovarian follicle (Schematic representation)

Outside the theca interna some fibrous tissues become condensed to form another covering for the follicle. This is the ***theca externa***. The theca interna and externa are collectively called the ***theca folliculi***.

Ovulation

The ovarian follicle is at first very small compared to the thickness of the ovarian cortex. As the follicle enlarges it becomes so big that it not only reaches the surface of the ovary, but forms a bulging in this situation. As a result the stroma and the theca on this side of the follicle are stretched and become very thin .

An avascular area (***stigma***) appears over the most convex point of the follicle. At the same time the cells of the cumulus oophoricus become loosened by accumulation of fluid between

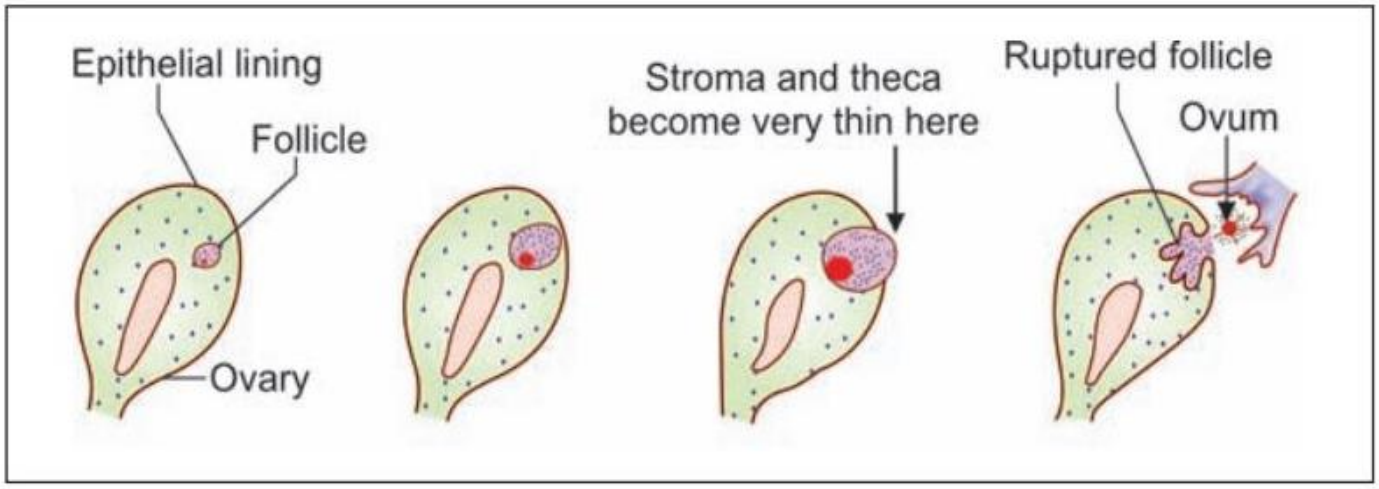


Fig. : Relationship of a growing ovarian follicle to the ovary (Schematic representation)

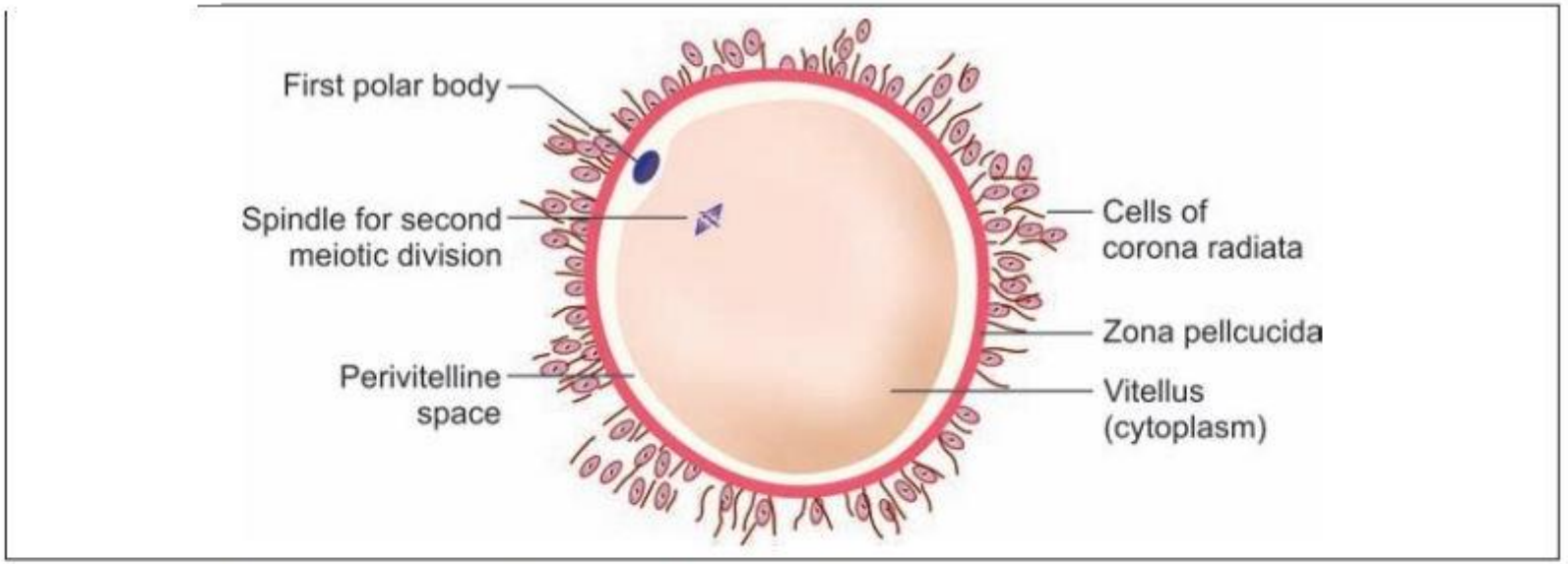


Fig. Structure of ovum at the time of ovulation (Schematic representation)

them. The follicle ultimately ruptures and the ovum is shed from the ovary. The shedding of the ovum is called ***ovulation. The 'ovum' that is shed from the ovary is not fully mature. It is really a secondary oocyte surrounded by zona pellucida and corona radiata*** (Fig.).

Fate of the Ovum

The ovary is closely embraced by the fimbriated end of the uterine tube. Therefore, the ovum is easily carried into the tube partly by the follicular fluid discharged from the follicle and partly by the activity of ciliated cells lining the tube. The ovum slowly travels through the tube towards the uterus, taking three to four days to do so. If sexual intercourse takes place at about this time, the spermatozoa deposited in the vagina swim into the uterus and into the uterine tube. One of these spermatozoa may fertilize the ovum. If this happens, the fertilized ovum begins to develop into an embryo. It travels to the uterus and gets implanted in its wall. On the other hand, if the ovum (secondary oocyte) is not fertilized it dies in 12 to 24 hours. It passes through the uterus into the vagina and is discharged.

Corpus Luteum

The corpus luteum is an important structure. It secretes a hormone, ***progesterone***. The corpus luteum is derived from the ovarian follicle, after the latter has ruptured to shed the ovum, as follows

- ***Corpus haemorrhagicum:*** When the follicle ruptures its wall collapses and becomes folded. Sudden reduction in pressure caused by rupture of the follicle results in bleeding into the follicle. The follicle filled with blood is called the ***corpus haemorrhagicum***. At this stage, the follicular cells are small and rounded.
- ***Corpus luteum:*** The cells now enlarge rapidly. As they increase in size their walls press against those of neighbouring cells so that the cells acquire a polyhedral shape

Their cytoplasm becomes filled with a yellow pigment called ***lutein***. They are now called ***luteal cells***. The presence of this yellow pigment gives the structure a yellow colour, and that is why it is called the corpus luteum (= yellow body).

Some cells of the theca interna also enlarge and contribute to the corpus luteum. The cells of the corpus luteum contain abundant smooth ER and considerable amount of lipids.

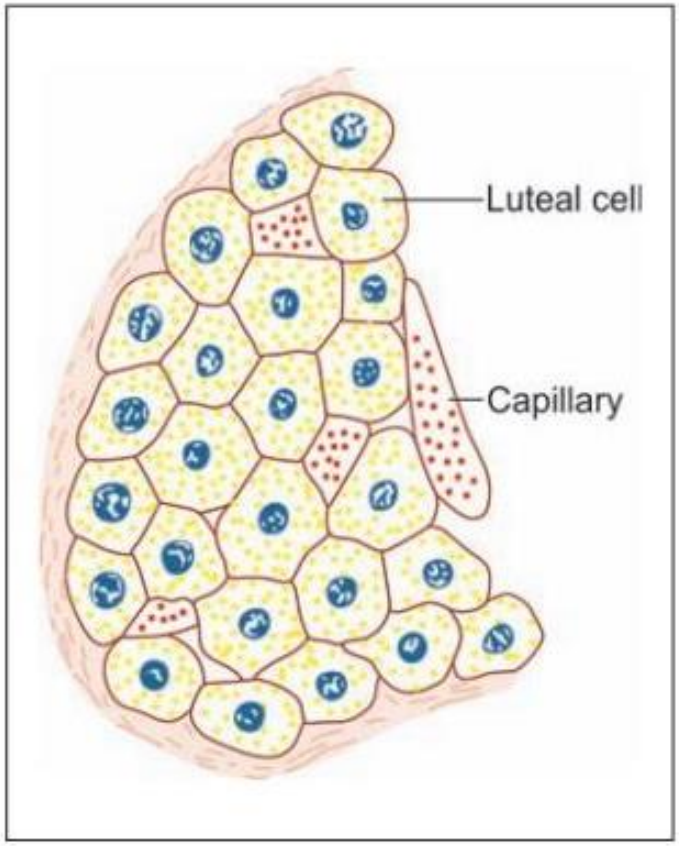


Fig. Corpus luteum. Note the large hexagonal cells filled with yellow granules (Schematic representation)

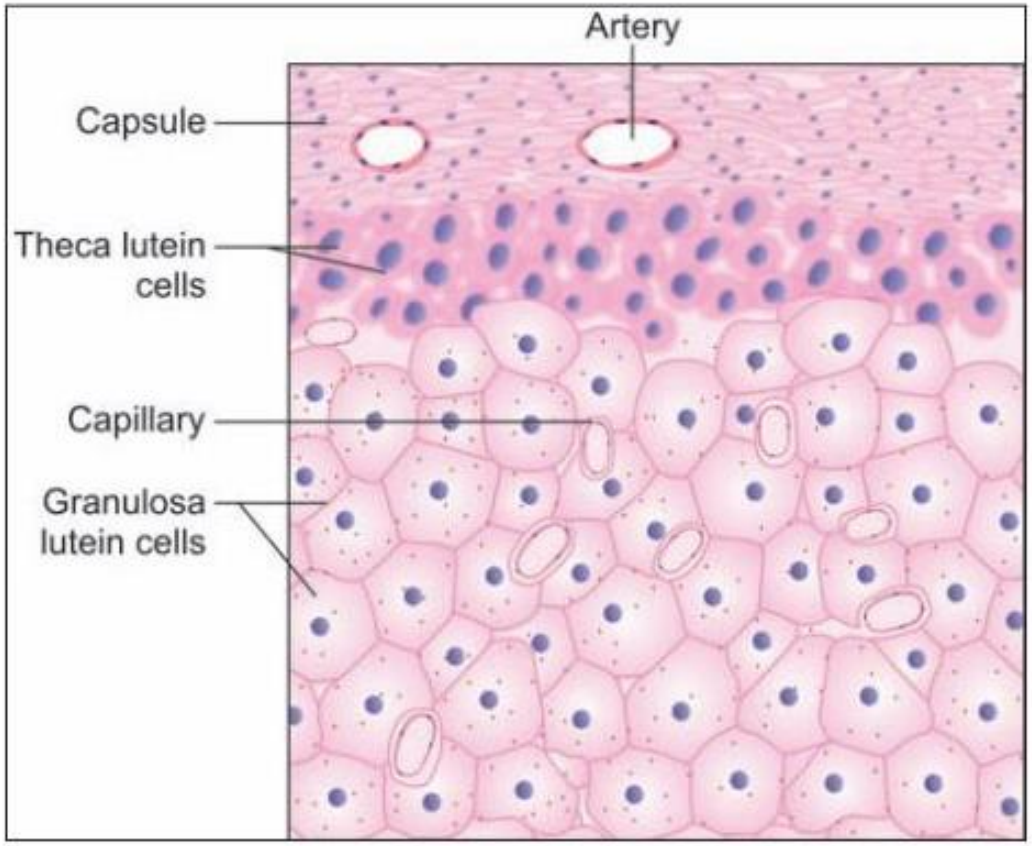


Fig. Corpus luteum (high magnification) (Schematic representation)

The corpus luteum secretes progesterone. This secretion has to be poured into blood like secretions of endocrine glands. All endocrine glands are richly supplied with blood vessels for this purpose. ***The ovarian follicle itself has no blood vessels, but the surrounding theca interna is full of them. When the corpus luteum is forming, blood vessels from the theca interna invade it and provide it with a rich blood supply.***

The subsequent fate of the corpus luteum depends on whether the ovum is fertilised or not.

- If the ovum is not fertilised, the corpus luteum persists for about 14 days. During this period it secretes progesterone. It remains relatively small and is called the ***corpus luteum of menstruation***. At the end of its functional life, it degenerates and becomes converted into a mass of fibrous tissue called the ***corpus albicans*** (= white body)
- If the ovum is fertilised and pregnancy results, the corpus luteum persists for three to four months. It is larger than the corpus luteum of menstruation, and is called the ***corpus luteum of pregnancy***. The progesterone secreted by it is essential for the maintenance of pregnancy in the first few months. After the fourth month, the corpus luteum is no longer needed, as the placenta begins to secrete progesterone.

Fate of Ovarian Follicles

The series of changes that begin with the formation of an ovarian follicle, and end with the degeneration of the corpus luteum constitute what is called an ***ovarian cycle***.

In each ovarian cycle one follicle reaches maturity, sheds an ovum, and becomes a corpus luteum. At the same time, several other follicles also begin to develop, but do not reach maturity. It is interesting to note that, contrary to what one might expect, these follicles do not persist into the next ovarian cycle, but undergo degeneration. The ovum and granulosa cells of each follicle disappear. The cells of the theca interna, however, proliferate to form the ***interstitial glands***, also called the ***corpora atretica***. These glands are believed to secrete oestrogens.

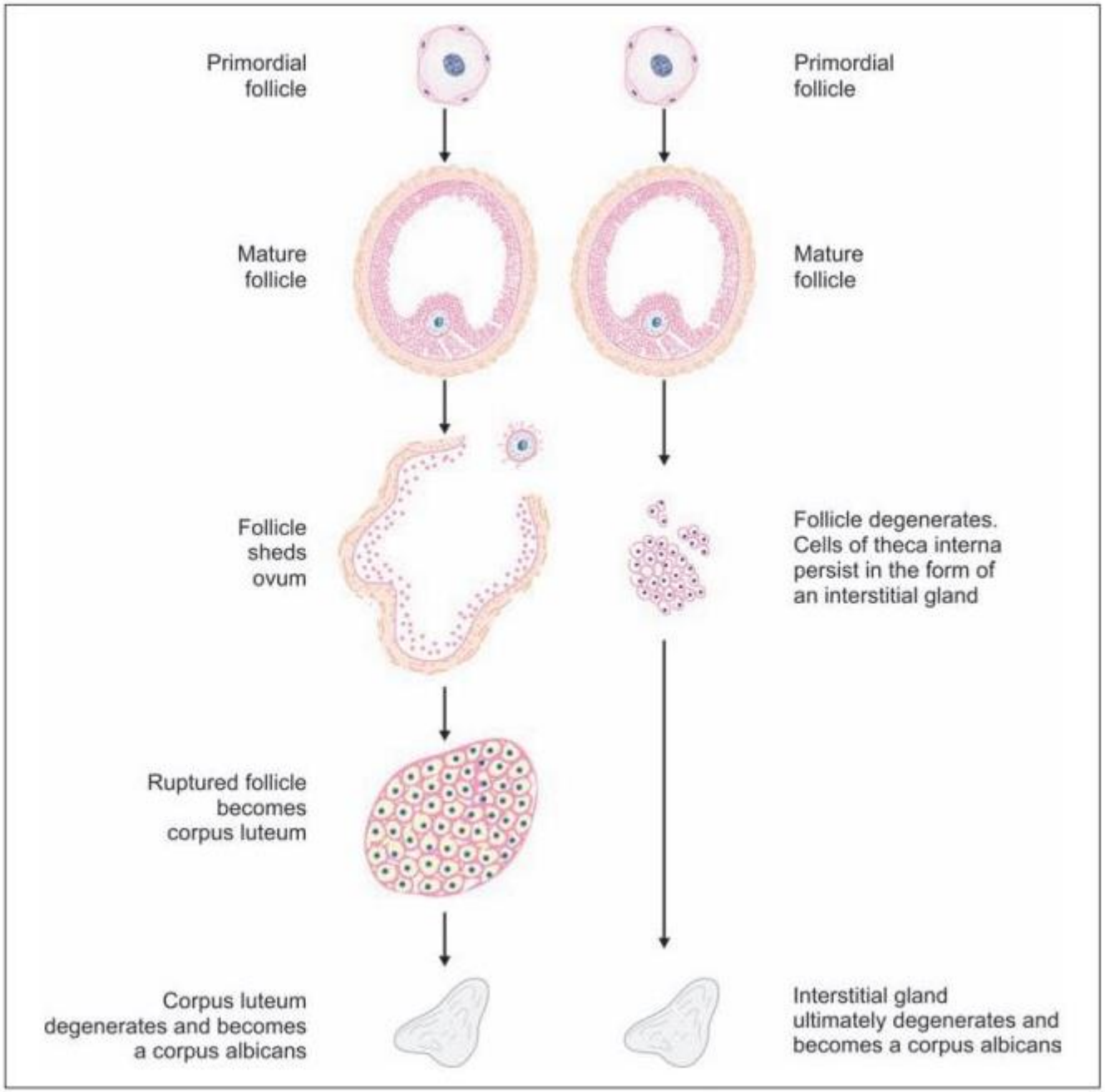


Fig. : Comparison of fate of ovarian follicles that shed an ovum and of those that do not (Schematic representation)

After a period of activity, each gland becomes a mass of scar tissue indistinguishable from the corpus albicans formed from the corpus luteum.

The cortex of an ovary (taken from a woman in the reproductive period) can show ovarian follicles (at various stages of maturation), corpora lutea, corpora albicantes, and corpora atretica.

The changes taking place during the ovarian cycle are greatly influenced by certain hormones produced by the hypophysis cerebri. The hormones produced by the theca interna and by the corpus luteum in turn influence other parts of the female reproductive system, notably the uterus, resulting in a cycle of changes referred to as the ***uterine cycle*** or ***menstrual cycle***.

UTERINE TUBES

Uterine tubes are paired muscular tubes and are also called ***fallopian tubes***. Each uterine tube has a medial or uterine end, attached to (and opening into) the uterus, and a lateral end that opens into the peritoneal cavity near the ovary. The tube has (from medial to lateral side),

- A ***uterine part*** that passes through the thick uterine wall
- A relatively narrow, thick walled part called the ***isthmus***
- A thin walled dilated part called the ***ampulla***
- Funnel shaped infundibulum. It is prolonged into a number of finger like processes or ***fimbriae***.

The wall of the uterine tube consists of following layers from within outwards.

Mucous Membrane

The mucous membrane shows numerous branching folds that almost fill the lumen of the tube (Plate). These folds are most conspicuous in the ampulla. Each fold has a highly cellular core of connective tissue. It is lined by columnar epithelium that rests on a basement membrane. Some of the lining cells are ciliated: ciliary action helps to move ova towards the uterus.

Other cells are secretory in nature and are also called as ***peg cells***. They contain secretory granules and are not ciliated. Their surface shows microvilli. A third variety of ***intercalary cells*** is also described.

Muscle Coat

The muscle coat has an inner circular layer and an outer longitudinal layer of smooth muscle. An additional inner longitudinal layer may also be present. The circular layer is thickest in the uterine part of the tube. The circular muscle is thickest in the isthmus. The pattern of mucosal folds is also different in this region. There is some evidence that the isthmus may have some control on the passage of a fertilised ovum through it.

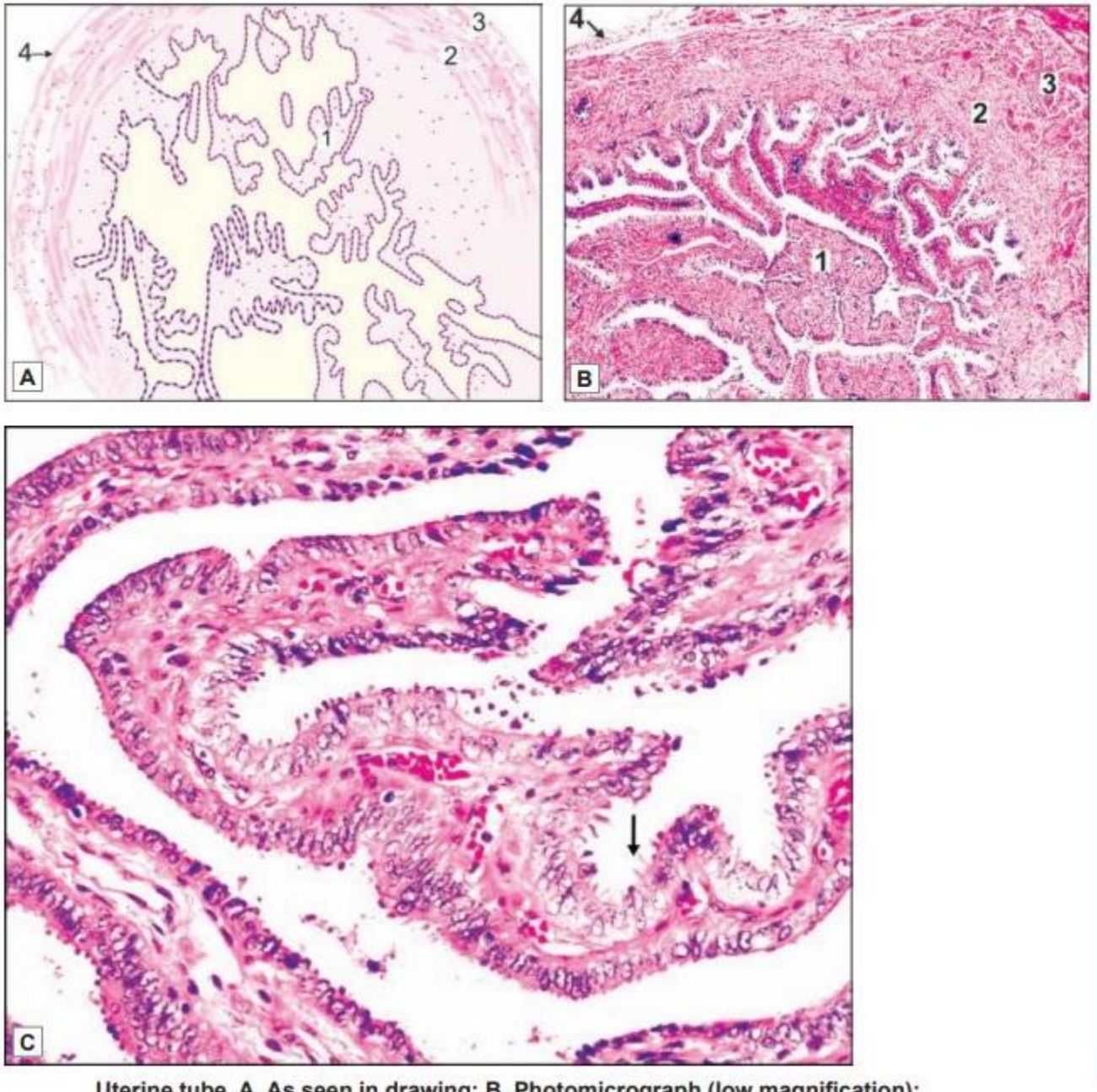
Serosa

It consists of mesothelium supported by connective tissue.

Functions

The uterine tube conveys ova, shed by the ovary, to the uterus. Ova enter the tube at its fimbriated end. Spermatozoa enter the uterine tube through the vagina and uterus. Fertilisation normally takes place in the ampulla. When fertilisation occurs, the fertilised ovum travels towards the uterus through the tube. Secretions present in the tubes provide nutrition, oxygen and other requirements for ova and spermatozoa passing through the tube.

Uterine Tube



Uterine tube. A. As seen in drawing; B. Photomicrograph (low magnification); C. Photomicrograph (high magnification)