Gametogenesis

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Objectives

At the end of this lecture, the medical student will be able to

• Identify the different stages of gametogenesis in males and females
• Name the functions of sertoli cells and granulosa cells
• Outline the stages of spermiogenesis
Gametogenesis

- Is the process of formation of gametes from germ cells in the testes and ovaries
- Many principles are the same in both male and female

- Is divided into 4 stages
  1. Extragonadal origin of primordial germ cells
  2. Proliferation of germ cells by mitosis
  3. Meiosis
  4. Structural and functional maturation of ova and spermatozoa
primordial germ cells

- Gametes are derived from **primordial germ cells (PGCs)** that are formed in the **epiblast** during the second week and that move to the **wall of the yolk sac**.
During the fourth week, these cells begin to migrate, by ameboid movement, from the yolk sac toward the developing gonad, where they arrive by the end of the fifth week.

Mitotic divisions increase their number during their migration and also when they arrive in the gonad.
Oropharyngeal teratoma

- These tumors may arise from pluripotent cells
  1. primordial germ cells or from
  2. epiblast cells
- Tissues within the tumors include derivatives of all three germ layers and may include gut, bone, skin, teeth,
Oogenesis

Is the process whereby oogonia differentiate into mature oocytes
Oogenesis
Maturation of Oocytes Begins before Birth

- Once primordial germ cells have arrived in the gonad of a genetic female, they differentiate into oogonia.
Oogonia

- undergo a number of mitotic divisions,
- by the end of the third month, they are arranged in clusters surrounded by a layer of flat epithelial cells (follicular cells), originate from surface epithelium covering the ovary.
- The majority of oogonia continue to divide by mitosis, but some of them give rise to primary oocytes that enter prophase of the first meiotic division.
• By the fifth month of prenatal development, the total number of germ cells in the ovary reaches its maximum (7 million). At this time, cell death begins, and many oogonia as well as primary oocytes become atretic.

• By the seventh month, the majority of oogonia have degenerated except for a few near the surface. All surviving primary oocytes have entered prophase of meiosis I, and most of them are individually surrounded by a layer of flat epithelial cells (primordial follicle).
Near the time of birth, **all primary oocytes** have started prophase of meiosis I, but instead of proceeding into metaphase, they enter **the diplotene stage**, a resting stage during prophase that is characterized by a lacy network of chromatin.

Primary oocytes remain arrested in prophase and do not finish their first meiotic division before puberty is reached. This arrested state is produced by **oocyte maturation inhibition (OMI)**, a small peptide secreted by follicular cells.

The total number of primary oocytes at birth is estimated to vary from **700,000 to two million**. During childhood, most oocytes become atretic; only approximately **400,000** are present by the beginning of puberty, and fewer than **500** will be ovulated.
The diplotene stage is the most suitable phase to protect the oocyte against environmental influences?

- Some oocytes that reach maturity late in life have been dormant in the diplotene stage of the first meiotic division for 40 years or more before ovulation.
- The fact that the risk of having children with chromosomal abnormalities increases with maternal age indicates that primary oocytes are vulnerable to damage as they age.
Ovarian Cycle

- At puberty, the female begins to undergo regular monthly cycles.
- Gonadotropin-releasing hormone (GnRH), produced by the hypothalamus, acts on cells of the anterior pituitary gland, which in turn secrete gonadotropins. These hormones, follicle-stimulating hormone (FSH) and luteinizing hormone (LH), stimulate and control cyclic changes in the ovary.
Each month, 15 to 20 follicles selected from the pool of primordial follicles begin to mature and passing through three stages:

1. primary,
2. secondary or antral, and
3. Tertiary or mature vesicular (Graafian) follicle.

The antral stage is the longest, whereas the mature vesicular stage encompasses approximately 37 hours before ovulation.

Under normal conditions, only one of these follicles reaches full maturity, and the others degenerate and become atretic.

corpus atreticum: When a follicle becomes atretic, the oocyte and surrounding follicular cells degenerate and are replaced by connective tissue
Unilaminar primary follicle

- Primary oocyte surrounded by a layer of cuboidal epithelium
- Beginning of zona pellucida
- **A** Primordial follicle
  - **B** Primary follicle
  - 1 Oocyte
  - 2 Follicular epithelium
Multilaminar primary follicle

- Follicular cells proliferate under the influence of FSH and produce a stratified epithelium of granulosa cells
- Zona pellucida a layer of glycoproteins on the surface of the oocytes secreted by the Granulosa cells and the oocytes.
- A basement membrane separating the granulosa cells from the theca folliculi
Secondary (vesicular, antral)

- Fluid-filled spaces appear between the granulosa cells. Coalescence of these spaces form the antrum which is crescent-shaped, but with time, it enlarges. Granulosa cells surrounding the oocyte remain intact and form the cumulus oophorus.
- The follicle is surrounded by the theca interna, which is composed of cells having characteristics of steroid secretion, rich in blood vessels, and the theca externa, which gradually merges with the ovarian connective tissue.
Tertiary follicle

- there is an abrupt increase in LH that causes the primary oocyte to complete meiosis I and the follicle to enter the preovulatory stage.
Maturation of the oocyte.

- Meiosis I is completed, resulting in formation of two daughter cells of unequal size, each with 23 double-structured chromosomes. One cell, the secondary oocyte, receives most of the cytoplasm; the other, the first polar body, receives practically none. The first polar body lies between the zona pellucida and the cell membrane of the secondary oocyte in the perivitelline space.
- The cell then enters meiosis II but arrests in metaphase approximately 3 hours before ovulation.
• Meiosis II is completed only if the oocyte is fertilized; otherwise, the cell degenerates approximately 24 hours after ovulation.
• The first polar body may undergo a second division
Ovulation

- The oocyte, in metaphase of meiosis II, is discharged from the ovary together with a large number of cumulus oophorus cells.
- Some of the cumulus oophorus cells then rearrange themselves around the zona pellucida to form the corona radiata.
- Follicular cells remaining inside the collapsed follicle differentiate into lutean cells.
Ovulation

- is generally accompanied by a rise in basal temperature &
- there is middle pain
Corpus Luteum

- After ovulation, **granulosa cells** remaining in the wall of the ruptured follicle, together with **cells from the theca interna**, are vascularized by surrounding vessels.
- **Under the influence of LH**, these cells develop a yellowish pigment and change into lutean cells, which form the corpus luteum and secrete the hormone progesterone.
- Progesterone, together with estrogenic hormones, causes the uterine mucosa to enter the progestational or secretory stage in preparation for implantation of the embryo.
Fate of the corpus luteum

• **If fertilization does not occur**, the corpus luteum reaches maximum development approximately 9 days after ovulation.

• Subsequently, the corpus luteum shrinks because of degeneration of lutean cells and forms a mass of fibrotic scar tissue, the **corpus albicans**.

• **If the oocyte is fertilized**, the corpus luteum continues to grow and forms the **corpus luteum of pregnancy** (corpus luteum graviditatis).
  - By the end of the third month, this structure may be one third to one half of the total size of the ovary.
  - Yellowish luteal cells continue to secrete progesterone until the end of the fourth month; thereafter, they regress slowly as secretion of progesterone by the trophoblastic component of the placenta becomes adequate for maintenance of pregnancy.
  - Removal of the corpus luteum of pregnancy before the fourth month usually leads to abortion.
Three moments in the life of a woman are apparent in which atresia takes place more rapidly.

- **The largest decrease** occurs in the 20th week after the maximum number of 7 million germ cells (per ovary) is reached, thus still in the **fetal period**.
- Immediately following **birth** a further, **short period of accelerated decline happens**.
- The third, **temporally longest period, of increased decline** takes place during **puberty**.
Spermatogenesis

Is a complex series of changes by which spermatogonia are transferred into spermatozoa.
In the male infant

- Germ cells can be recognized in the sex cords of the testis as large, pale cells surrounded by supporting cells.
- Supporting cells, which are derived from the surface epithelium of the gland in the same manner as follicular cells, become sustentacular cells, or Sertoli cells.
Shortly before puberty,

- the sex cords acquire a lumen and become the seminiferous tubules.
- Maturation of Sperm Begins at Puberty
- At about the same time, primordial germ cells give rise to spermatogonial stem cells.
Spermatogenesis can be divided into

- a. spermatocytosis
- b. meiosis
- C. spermiogenesis
spermatocytosis

- Spermatogonia proliferate by mitotic division to replace themselves and to produce primary spermatocytes
Meiosis

- 2 successive divisions
- Meiosis I produce secondary spermatocytes
- Meiosis II produce spermatids
The progeny of a single spermatogonium form a clone of germ cells that maintain contact throughout differentiation.

- Spermatogonia and spermatids remain embedded in deep recesses of Sertoli cells throughout their development.
The sertoli cells are supporting cells that have several functions.

- They form the blood-testes barrier: nutrients, and circulating substances do not directly reach the germ cells.
- They form invaginations surrounding the spermatocytes, spermatids and developing spermatozoa and are nutritive to them.
- They also produce antigen-binding proteins, which are necessary for spermiogenesis.
Spermiogenesis

- The series of changes resulting in the transformation of spermatids into spermatozoa include:
  (a) formation of the acrosome, which covers half of the nuclear surface and contains enzymes to assist in penetration of the egg and its surrounding layers during fertilization;
  (b) condensation of the nucleus;
  (c) formation of neck, middle piece, and tail; and
  (d) shedding of most of the cytoplasm.
• In humans, the time required for a spermatogonium to develop into a mature spermatozoon is approximately 74 days, and approximately 300 million sperm cells are produced daily.

• When fully formed, spermatozoa enter the lumen of seminiferous tubules. From there, they are pushed toward the epididymis by contractile elements in the wall of the seminiferous tubules.
• Although initially only slightly motile, spermatozoa obtain full motility in the epididymis.
Clinical Correlates
Abnormal Gametes

- A. Primordial follicle with two oocytes.
- B. Trinucleated oocyte.
- C. Various types of abnormal spermatozoa.
Thank you

Next Lecture:

Fertilization
Key words of Fertilization

- Capacitation
- acrosome reaction
- Fast block to polyspermy
- Slow block to poly spermy
- Contraceptive Methods
- Infertility
- In vitro Fertilization (IVF)
- Intracytoplasmic sperm injection