

Chapter I: Gametogenesis

The **life cycle of a given species** is the set of processes that ensure the **continuation of the species from one generation to the next**.

In an adult individual, there are **two categories of cells**: one group includes **diploid cells** that do not undergo meiosis and constitute all **somatic cells (soma)**, and the other forms the **germ line (germen)**, which undergoes **chromosomal reduction during its differentiation**.

1. Definitions

Gametogenesis is the biological mechanism by which **gametes are formed in the organism**. It allows the production of **haploid cells from diploid cells**. In mammals, it is more specifically called **oogenesis in females** and **spermatogenesis in males**.

The **cell division** that occurs during gametogenesis and that changes the cell from the **diploid state to the haploid state** is called **meiosis**. Gametogenesis **begins in males at puberty** and can continue until an advanced age. In females, it **begins during embryonic life**, and the maturation cycle **is completed only if fertilization occurs**.

2. Gamete

A **gamete** is a **haploid reproductive cell** that has completed **meiosis and cytoplasmic differentiation**. In humans, as in most animals, the **female gametes are ova (eggs)** and the **male gametes are spermatozoa (sperm cells)**.

The organs that produce gametes are called **gonads**:

- **ovaries in females**
- **testes in males**

A gamete is a **mature male (spermatozoon) or female (ovum) sex cell** that, when combined with another gamete, forms an **egg or zygote**, from which a new organism develops. Gametes derived from **germ cells (gonial cells)** have **different structures**.

Female gametes are generally **large cells containing a large amount of cytoplasm and organelles**. Male gametes are **small cells with very little cytoplasm**. They are usually **motile and capable of active movement**.

1. Spermatogenesis

Spermatogenesis enables the production of specialized reproductive cells, **haploid male gametes called spermatozoa**, from **diploid stem cells called spermatogonia**. This process, which continues **throughout the life of the male**, takes place in the **male reproductive system**, specifically in the **seminiferous tubules of the testis**. The **male reproductive system** consists of (*Figure 1*):

- ✓ **Two testes**
- ✓ **Excretory ducts**
 - **Intra-testicular ducts:** straight tubules, rete testis
 - **Extra-testicular ducts:** efferent ducts, epididymis, vas deferens, urethra
- ✓ **Accessory glands:** seminal vesicles, prostate gland, Cowper's glands
- ✓ **A copulatory organ:** the penis

1.1. Site of occurrence and its evolution over time

Spermatogenesis begins at **puberty** and can continue until **advanced age**. Its duration is **fixed and characteristic for each species**. This duration is:

- **61 days in the bull**
- **49 days in the ram and the stallion**
- **74 days in humans**

This duration is always **constant regardless of external or internal factors**. Only the **intensity of spermatogenesis** (the number of spermatogonia that begin their development) may change depending on several factors such as **protein, lipid and vitamin intake (A, E), trace elements, temperature, pharmacological factors**, etc.

Spermatogenesis takes place in the **seminiferous tubules of the testes**. The **testis** is an **ovoid gland** located in an **external cutaneous sac called the scrotum**. In **sagittal section**, the testis has the following structure: It is surrounded by the **tunica albuginea**, a **fibrous connective capsule** that is inextensible. A thickened portion at the **upper pole forms the body of Highmore (mediastinum testis)**. From the **tunica albuginea**, **thin connective partitions (septa testis)** extend and divide the testis into **testicular lobules** (about **200 to 300 per testis**).

Each **lobule contains 2 to 3 seminiferous tubules**. The **seminiferous tubules** of each lobule converge into a **straight tubule**, which continues into the **rete testis** (a dense network of canaliculi with irregular diameters). The **rete testis** collects the straight tubules coming from the seminiferous tubules and gives rise to the **efferent ductules** that enter the **epididymis**. The **straight tubules and the rete testis** are embedded in the **body of Highmore** (*Figure 2*).

1.2. Continuous nature and origin of the cells producing male gametocytes

Spermatogenesis is a **continuous process** in most animals, but with **seasonal variations** in some species such as **cattle and goats**, and a **cessation during hibernation** in certain rodents (e.g., hamsters). The **daily production of spermatozoa per testis** is approximately:

- **12 billion in the bull**
- **3 billion in the ram**

The **testicular parenchyma** includes the **seminiferous tubules** and the **interstitial tissue**.

A. Seminiferous tubules

In **cross-section (Figure 3)**, the seminiferous tubules appear to consist of:

- **A thin external connective membrane** containing **contractile cells (myoid cells)** whose contraction facilitates the transport of spermatozoa.
- **The germinal epithelium**, a very specialized epithelium composed of **two types of cells**:
 - ✓ **Sertoli cells**

Through their numerous extensions, they are in **close contact with germ cells**. In addition to their **support and nutritional role**, Sertoli cells promote the **maturation and migration of spermatozoa toward the lumen** and form a **physiological barrier for germ cells** by ensuring the filtration of nutrients and hormones. They also: secrete an **androgen-binding protein (ABP)**, produce **MIS (Müllerian inhibiting substance / anti-Müllerian hormone)**, produce **inhibin**, a hormone that **controls the secretion of FSH**

- ✓ **Germ line cells**

Located between Sertoli cells and arranged in **more or less regular layers from the periphery toward the center of the seminiferous tubule**, they represent the **successive stages of spermatogenesis**, namely:

- **Spermatogonia**
- **Primary spermatocytes (I)**
- **Secondary spermatocytes (II)**
- **Spermatids**
- **Spermatozoa**

B. Interstitial tissue

The **interstitial tissue** is a very **thin connective tissue** that contains:

- ✓ **Vascular and nervous elements of the testis**

✓ **Clusters of interstitial cells (Leydig cells)**

These **endocrine glandular cells (Leydig cells)** may be isolated or grouped in clusters. **Leydig cells synthesize and release testosterone.**

1.3. Components of the Male Gametocyte (Spermatozoon)

The morphology of spermatozoa varies among species, but their general structure remains the same. They consist of a head, a neck, an intermediate piece, and a tail or flagellum (Figure 4).

- ✓ **The Head:** It is almost exclusively made up of the nucleus with n chromosomes and is capped by the acrosome. Its shape is elongated in stallions, ovoid in ruminants, and sickle-shaped in rats. The acrosome of the spermatozoon is rich in proteolytic enzymes, allowing it to penetrate the membranes surrounding the oocyte during fertilization.
- ✓ **The Neck:** The neck of the spermatozoon is a narrow area that contains the centriole, which is the starting point of the axial filament, the main structure of the intermediate piece and the tail.
- ✓ **The Intermediate Piece:** This section is rich in enzymes specific to the metabolism of the spermatozoon and is primarily composed of a mitochondrial sheath wrapped in a helix around the axial filament.
- ✓ **The Tail:** The tail is the longest part of the spermatozoon; it consists of contractile fibrils responsible for the motility of the cell.

The size of spermatozoa varies among species: 50 to 80 μm in mammals and 100 to 300 μm in birds. Their speed of movement ranges from 2 to 5 mm/min. The mode of movement corresponds to undulations of the flagellum due to the sliding of microtubules against each other.

I.4. Chronology of spermatozoa development

Spermatogenesis includes **four phases: multiplication, growth, maturation, and differentiation.** The succession of these phases constitutes the **spermatogenic cycle.** During these phases, the **germ line cells** pass through **five characteristic cellular stages** during spermatogenesis:

- ✓ **Spermatogonia**
- ✓ **Primary spermatocytes (I)**
- ✓ **Secondary spermatocytes (II)**
- ✓ **Spermatids**
- ✓ **Spermatozoa**

These **five stages** are found in this order in the **wall of the seminiferous tubule**, starting from the **membrane at the periphery of the tubule toward the central lumen (Figure 5).**

a) Multiplication phase

The **stem spermatogonium** (2n chromosomes), stored along the **basal membrane of the seminiferous tubules** and quiescent since the **6th week of intrauterine life**, begins to multiply by

mitosis. It gives rise to **two daughter spermatogonia** that will have different fates. One daughter cell replaces its “mother” cell and becomes a **stem spermatogonium for a subsequent cycle**. The other daughter cell **divides actively** to give rise to **primary spermatocytes (2n chromosomes)**. Thus, the **stock of germ cells is continuously renewed and rejuvenated**.

b) Growth phase

The **primary spermatocytes (spermatocytes I)** undergo a **cytoplasmic growth phase**, transforming into **large diploid cells (2n chromosomes)**.

c) Maturation phase

This phase corresponds to **meiosis**. **Primary spermatocytes (2n chromosomes)** undergo the **first meiotic division (reductional division)**, producing **two secondary spermatocytes (spermatocytes II) with n chromosomes**. **Secondary spermatocytes (n chromosomes)** undergo the **second meiotic division (equational division)**, producing **two spermatids (n chromosomes)**. Thus, **one primary spermatocyte produces four spermatids at the end of meiosis**.

d) Differentiation phase

Also called **spermiogenesis**, this phase does **not involve cell division** but rather the **differentiation of spermatids into spermatozoa**. Spermatids transform into spermatozoa **within the cytoplasmic folds of Sertoli cells**, near the **lumen of the seminiferous tubule**, following several **morphological changes (Figure 6)**:

✓ **Formation of the acrosome**

The **Golgi apparatus** produces numerous vesicles that fuse to form a **single vesicle called the pro-acrosomal vesicle**. This vesicle attaches to and spreads over the **anterior pole of the nucleus**, forming the **acrosome**, which is **very rich in enzymes necessary for the spermatozoon to reach the oocyte during fertilization**.

✓ **Formation of the flagellum and the middle piece**

The **microtubules of the distal centriole** elongate and organize into a **typical axoneme (9 peripheral doublets and 1 central doublet)**.

This axoneme elongates and emerges from the cell by pushing the **plasma membrane** outward, remaining covered by a **cytoplasmic sheath**. In the **proximal part of the flagellum**, the **mitochondria are arranged in a spiral**, forming the **middle piece**.

✓ **Modification of the cytoplasm**

The development of **microtubules behind the acrosome** moves the cytoplasm toward the **flagellum**, which becomes covered by it.

Unused cytoplasmic fragments (**residual bodies**) are **phagocytosed by Sertoli cells** at the time of **spermatozoon release**.

1.5. Site of Acquisition of Spermatozoon Functionality

Spermatozoa are produced and formed in the testes and then released into the epididymis. In the epididymis, under the action of testosterone secreted by the Leydig cells, spermatozoa acquire their motility (spermatozoa produced in the testes are very slightly mobile or not mobile at all). In the male genital tract, spermatozoa remain immobile; their motility and metabolism are activated at the moment of ejaculation when they come into contact with the secretions of the accessory glands (seminal vesicles and prostate). These secretions provide the energetic substrates and oxygen necessary for their motor activity.

In the absence of ejaculation, spermatozoa gradually lose their fertilizing ability and their motility and are eventually eliminated by phagocytosis. During their passage through the epididymis, a number of proteins secreted by the epididymal epithelium, under the influence of testosterone, bind to specific regions of the sperm head. Spermatozoa thus acquire the ability to bind to the zona pellucida of the oocyte, a necessary step for fertilization.

1.6. Origin and Chemical Composition of Seminal Fluid

Accessory glands are exocrine glands; they provide almost all of the seminal plasma (seminal fluid) necessary for the survival of spermatozoa in the excretory ducts and play a role in the physiology of sexual activity.

- ✓ **Seminal vesicles** are lobulated glands located near the bladder. They produce more than half of the seminal fluid with an acidic pH. This fluid is viscous and rich in proteins, potassium, and fructose. Seminal vesicles are absent in the cat and the dog.
- ✓ **Prostate** is present in all mammals. It is poorly developed in ruminants and completely surrounds the urethra in the bull. It produces a fluid that activates spermatozoa and is rich in enzymes and prostaglandins.
- ✓ Cowper's glands (bulbourethral glands) have the size and shape of a hazelnut in the bull. Their secretion often precedes the semen itself. Their most probable function is to clean the urethra and lubricate the vagina during sexual excitation.