

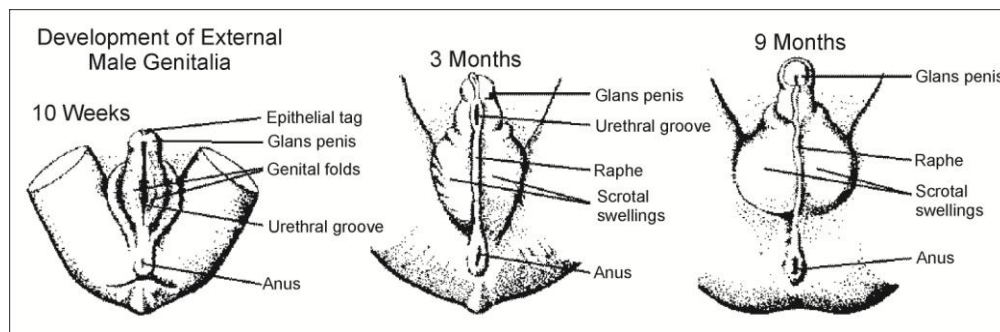


## Formation of the Male Sex Cells: Male Anatomy and Spermatogenesis

### Introduction

The male genitalia is designed to produce sperm and deliver them to the proper site to ensure fertilization for the continuation of the species. From our point of view, we simply want to understand the basic organization of the male sexual anatomy as a prelude to understanding the events that occur during fertilization. In the male genital tract, the sperm are not only formed but are also subjected to certain modifications and environmental conditions that are an essential prelude to successful fertilization.

### Development of External Male Genitalia



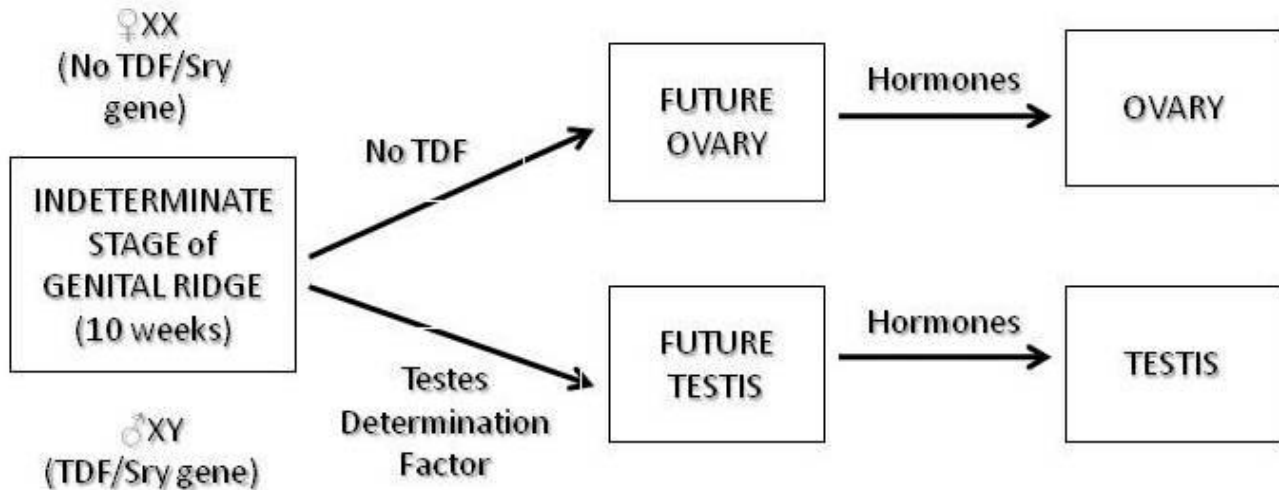
### Foreskin & HIV Receptors

Throughout the course, some interesting topics that are related to our areas of discussion--but not always central to them--will be brought up to add to our understanding of our lives. This is one example. There has been a lot of discussion about the topic of circumcision (removal of the foreskin--usually in newborns or young babies) in males. Recent scientific evidence indicates that the foreskin contains receptors for the HIV virus, thus making uncircumcised males more susceptible to contracting the virus (and thus developing AIDS). In 2006, WHO issued statement advising that circumcision could save millions of lives in Africa. As with any such situation, cultural issues make the implementation of circumcision difficult. Another point of interest is that the cells from the foreskin have proven to be very valuable for study on cell function in humans. Clearly the use of these cells will have even greater potential with this discovery.

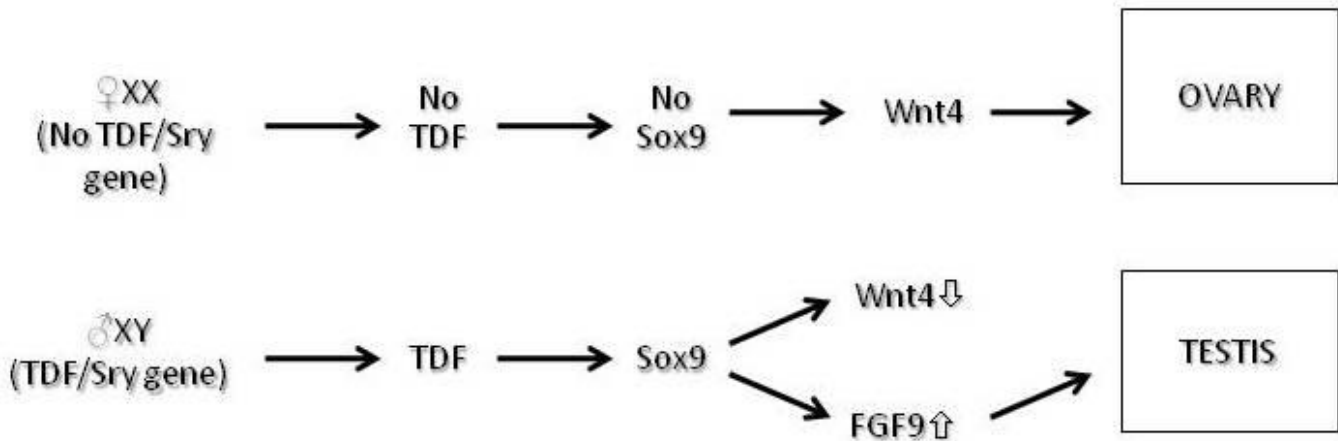
### TDF & Sexual Determination

The determination of sex begins at fertilization (Males XY, females XX). At the "Indeterminate Stage" of sexual development (~10 Weeks in above figure) the genital ridge is bipotential. It can develop either into male or female genitalia. A gene on the Y chromosome that is not present on the X chromosome leads to the production of testis determining factor (TDF). As its name implies TDF causes each genital ridge to develop into a testis. In the absence of TDF, the genital ridge develops into an ovary. TDF is also known as Sry (Sex determining Region of the Y chromosome).

## Male Anatomy and Spermatogenesis



As summarized in the following figure, the presence of TDF, a DNA-binding protein and possibly a transcription factor itself, induces the expression of the transcription factor Sox9 which in turn leads to an increased expression of fibroblast growth factor 9 (FGF9) and the down regulation of Wnt4 expression. Wnt (Wingless + segment gene *Int* in *Drosophila*) is a secreted protein that functions during development and various cancers. These events are part of the signaling pathways that underlie the development of the testis. In contrast, the lack of Sox9 expression in female embryos allows expression of the secreted protein Wnt4 leading to ovary development. Of course there are more genes involved in the final development of the ovaries and testes but Wnt, Sox9 and FGF9 are central.



Development of the male and female genital organs also involves many other events that are under the control of testosterone and other hormones.

### Male genital tract is designed to:

- Produce sperm
- Store sperm
- Release sperm as required
- Add regulatory components to sperm
- Add fluid

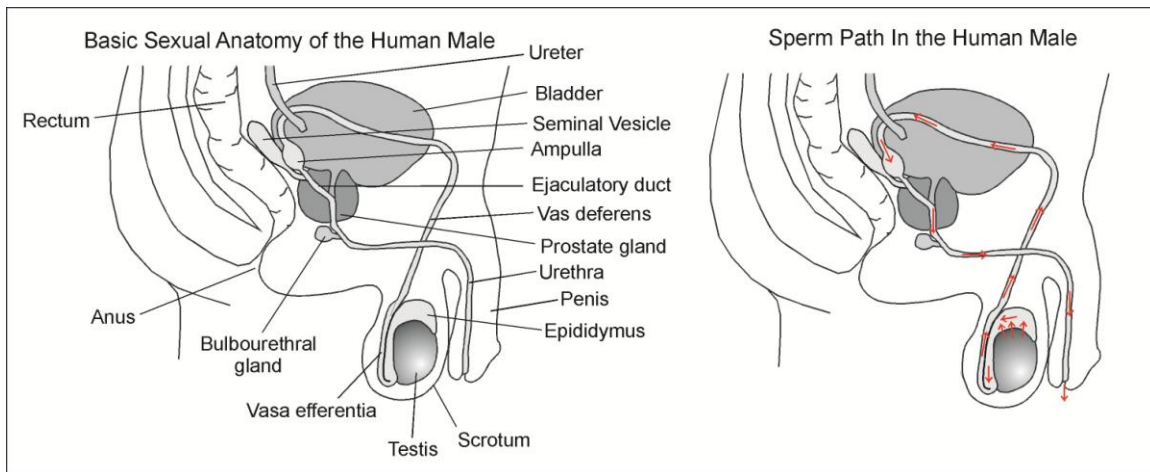
## Male Anatomy and Spermatogenesis

### The Urogenital System of the Human Male

- Sperm are produced in the testes
- The scrotum holds the testes outside of the body
- Together they lower the temperature for spermatogenesis
- Why does spermatogenesis need lower temperatures? No other developmental event requires this

### From the Testes to Ejaculation: The Fate of Sperm Cells

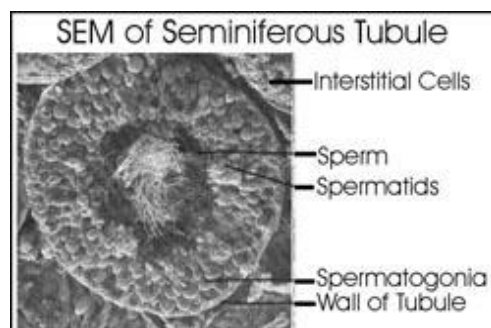
Sperm spend their life in the male body in a continuous series of tubes much like the plumbing (water pipes) in a house. As seen in the right-hand panel of the above figure, spermatogenesis occurs in the testes after which the full formed sperm leave the seminiferous tubules to enter the epididymus (blue arrow) where they remain stored until the appropriate moment.



Certain secretions are released in the epididymus that alter the sperm's environment and its surface characteristics, among other things. In preparation for ejaculation, the sperm follow the route demonstrated by the red arrows first leaving the epididymus to enter the vasa efferentia. The sperm move along each vas efferens and enter the vas deferens. As the sperm move along the vas deferens materials are added to the sperm and to the extracellular fluid (forming semen) that surrounds them. The prostate gland and seminal vesicles add fluid and nutrients at the time of sperm ejaculation providing most of the volume of the ejaculate. This complex of fluid and sperm cells travels up the urethra to be released externally.

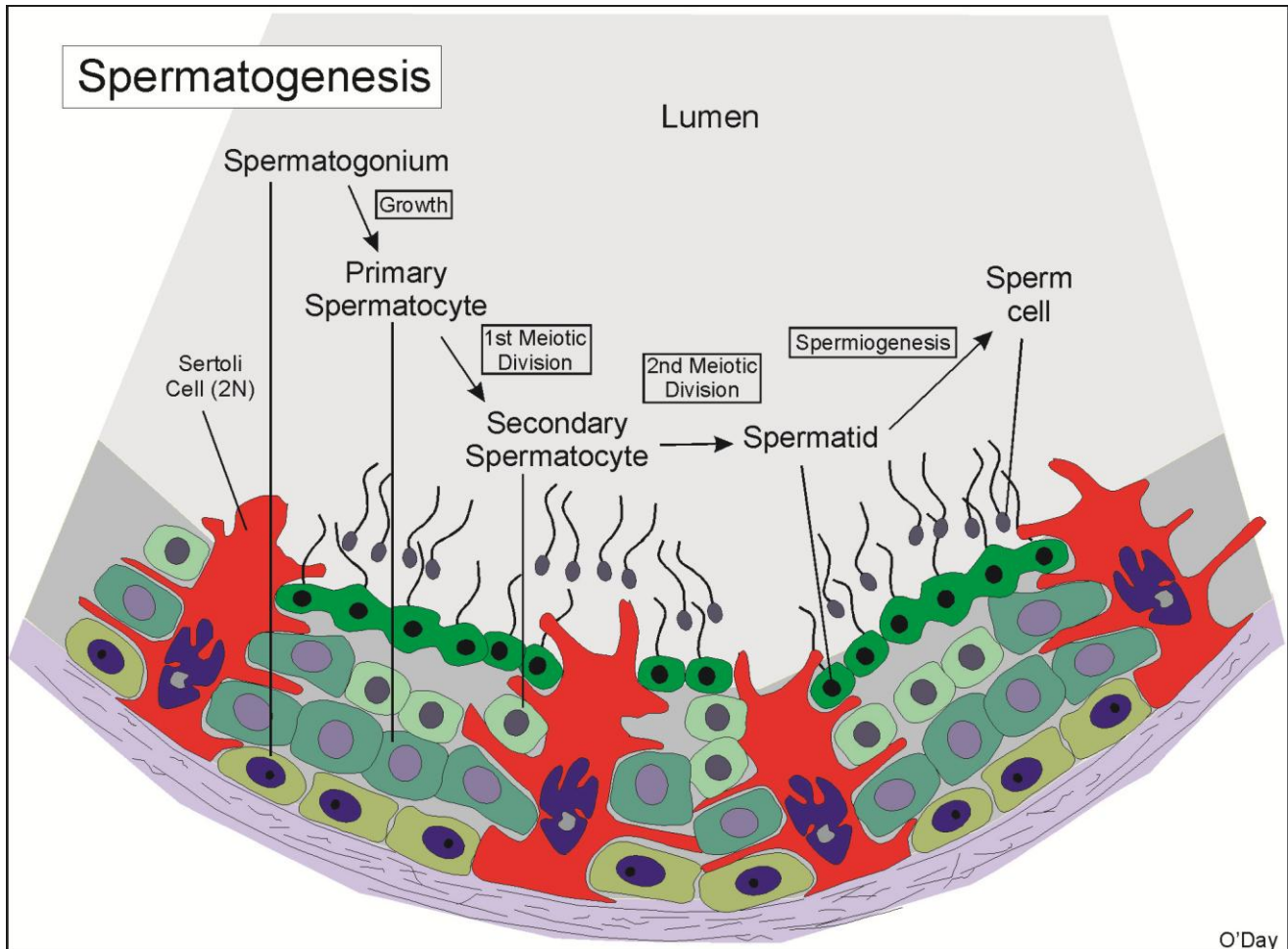
### The Organization of the Testes

- The testes is made of: seminiferous tubules, interstitial cells, blood vessels and extracellular material
- Spermatogenesis occurs in seminiferous tubules
- Spermatogenesis occurs from basement membrane towards the lumen of tubules



### The Testis & Spermatogenesis

The following diagram shows the organization of the events of spermatogenesis within the testis. The earliest stages are closest to the outer wall of the seminiferous tubule while the most mature stages are near its lumen.



### The Sequence of Events in Spermatogenesis

In the next lecture we will deal with the details of spermatogenesis. Here we simply want to introduce the subject and indicate how it is organized in a general way. Since the seminiferous tubules are, as their name specifies, small tubes, they appear like the cross-section of a pipe or hose. Instead of the wall being made up of copper (pipe) or rubber (hose), the wall is made up of cells and extracellular material or basement membrane as indicated above. The interstitial cells and extracellular matrix lies on the outside of the seminiferous tubule wall where it is in contact with non-reproductive supportive tissues, blood vessels and nerves. Spermatogenesis occurs on the inside of the wall where the stages of spermatogenesis are lined up with the earliest stages adjacent the basement membrane. Thus the spermatogonia (originally derived from the PGCs) that have now increased in number lie closest to the basement membrane. Spermatogenesis occurs in contact with special non-sexual, Sertoli Cells that also adhere to the basement membrane. Successive stages lie further and further away from the basement membrane in the following order: Primary spermatocytes, secondary spermatocytes, spermatids and spermatozoa. Some of these stages can also sub-divided into other sub-categories of cell types that don't concern us in this course.

## Male Anatomy and Spermatogenesis

### Sertoli Cell Functions

Sertoli cells are large somatic (diploid) cells attached to the basement membrane and extending to the lumen. As summarized below they regulate the formation and release of spermatozoa. They also maintain the blood/testis barrier because adjacent Sertoli cells are connected via tight junctions. This protects the developing sperm from the immune system. In addition to some special cytoplasmic attributes (e.g., elongated mitochondria, lipid droplets), they each have a large, irregular-shaped, indented nucleus containing a large distinct nucleolus.

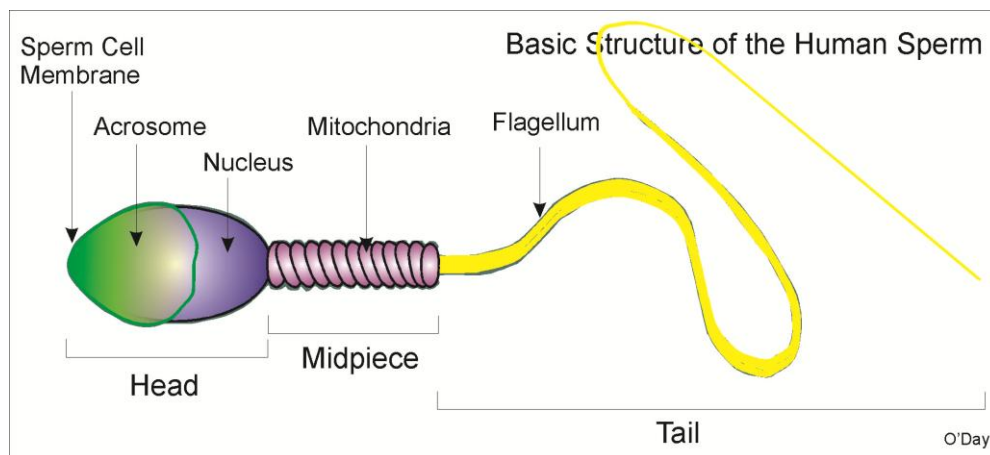
### Here's a list of the known functions of Sertoli cells:

- Surround developing sperm cells
- Synchronize and regulate the events of spermatogenesis
- Secrete critical proteins (e.g., growth factors, androgen-binding protein, inhibin) that are important for testes function and spermatogenesis
- Secretion of tubule fluid
- Phagocytosis of residual bodies so cellular constituents can be recycled
- Control release of sperm cells

### The Human Sperm Cell

The ultimate goal of spermatogenesis is the production of spermatozoa or sperm cells. To fully understand the complexity and significance of this process, we first should examine exactly what the sperm cell looks like and the function of each of its components. Later we'll re-examine this information in more detail when we discuss fertilization. There are three main regions in the sperm cells:

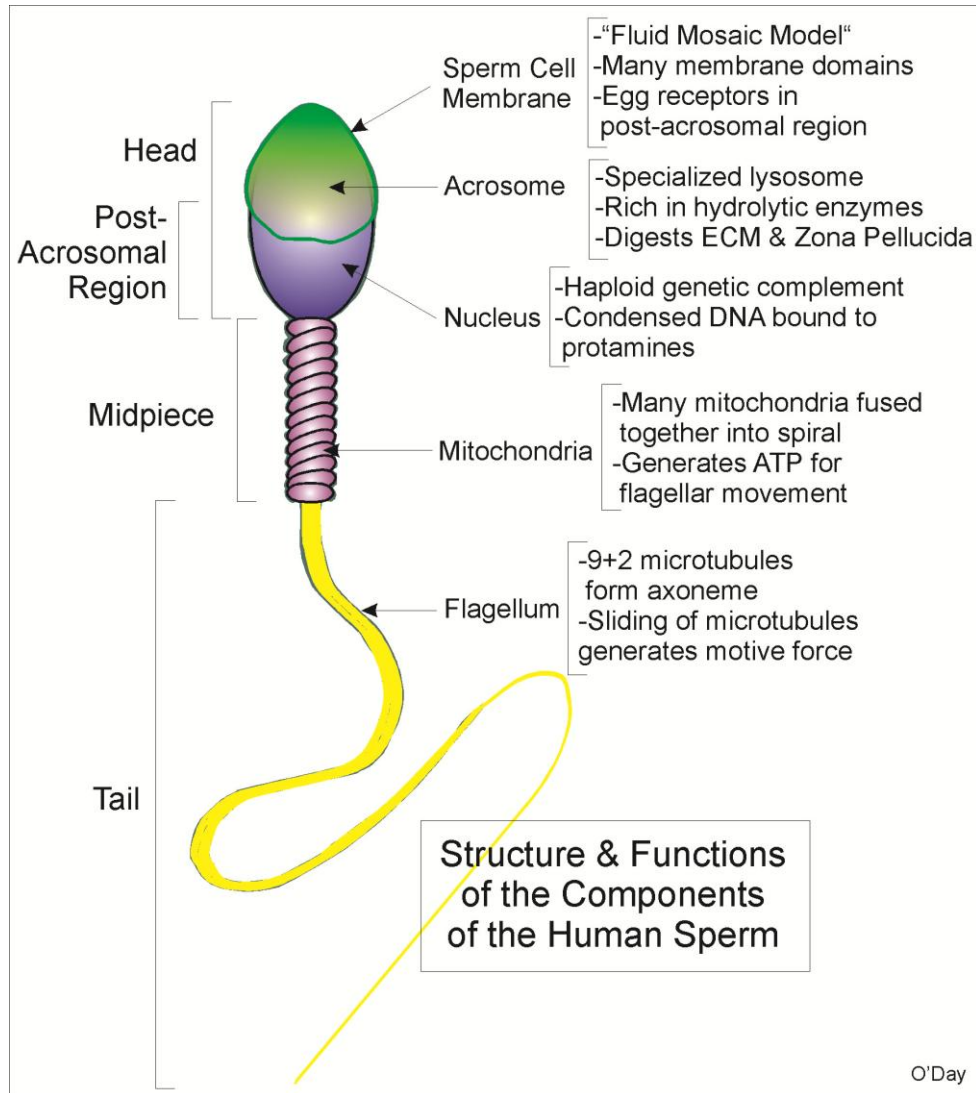
- **Head:** Front end where the haploid nucleus resides covered by a single membrane sac (bag) of enzymes. A pair of centrioles lies just behind the sperm nucleus.
- **Midpiece:** The middle region of the sperm mainly dominated by a spiral complex of mitochondria that are fused together.
- **Tail:** This is essentially a flagellum with some specializations not seen in non-mammalian flagella.



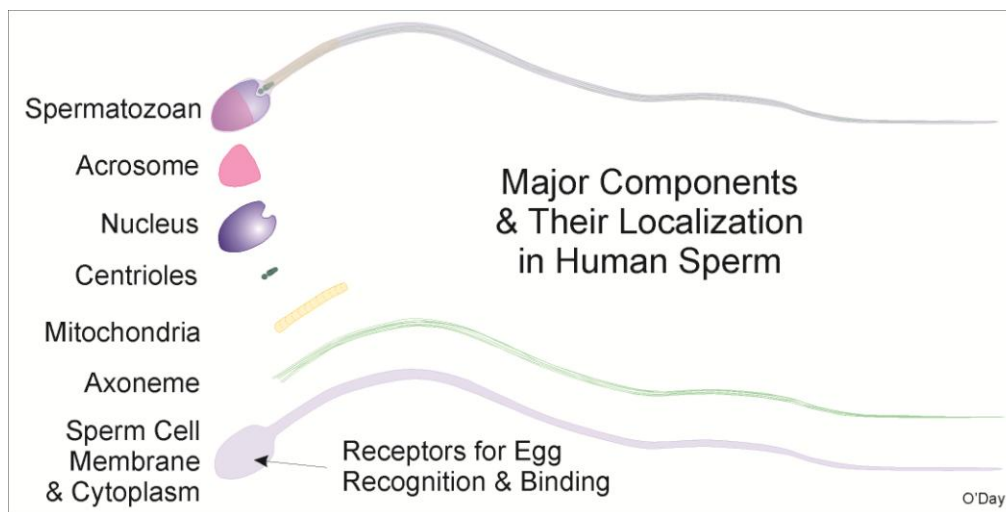
### Major Components of Sperm Cells & Their General Functions

Each of the components of the sperm has a specific function. Their overall job is to get their payload, the haploid male nucleus, into the egg cytoplasm where it can fuse with the female pronucleus to form the diploid, zygote nucleus.

## Male Anatomy and Spermatogenesis



Here's another way of looking at the components that make up a sperm cell.



## Male Anatomy and Spermatogenesis

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Here are the major sperm components and their basic functions:

- **Sperm Cell Membrane:** contains receptors for recognizing the egg. Remember, all cells are completely surrounded by a cell membrane (sometimes called the plasma membrane). Plant cells and many microbes have cell walls--animal cells **do not** have cell walls.
- **Acrosome:** A specialized lysosome containing digestive enzymes for penetration of the material surrounding the egg.
- **Nucleus:** haploid sperm nucleus will fuse with haploid egg nucleus forming 2N zygote nucleus.
- **Centrioles:** organize axoneme (microtubules) of the flagellum.
- **Flagellum:** whip-like "tail" of sperm functions in sperm motility; motive force for sperm involves sliding of axonemal microtubules as is typical for all flagella and cilia in all organisms that possess them.
- **Mitochondria:** provide energy (ATP) for sperm motility

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