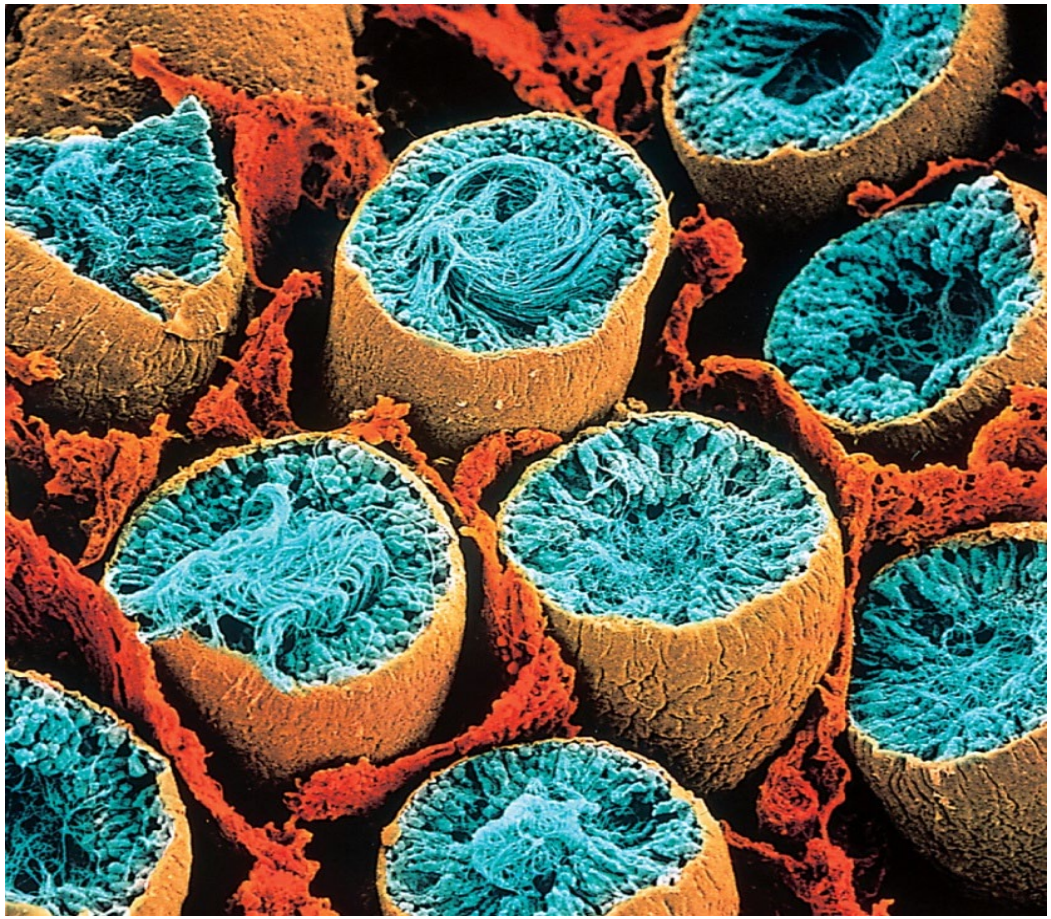
(Chapters 27 & 28)

Sexual Reproduction, Female Reproductive System, and Male Reproductive System



Sexual Reproduction

The essence of sexual reproduction is bi-parental

Child receive “combination” of genes from two parents

Child is not genetically identical to either parent

Parent's gonadal tissue produce gametes (sperm and eggs) by meiosis (haploid cell division)

Sperm and eggs are haploid cells (23 chromosomes) / the union of gametes forms diploid cell (46 chromosomes) // the first diploid cell is called the zygote

“We will die, but our genes will live on in a different container, our offspring”. Unknown Author

Overview of Reproductive System

Purpose of Sexual Reproduction

Perpetuate the species

Exchange genetic information between female and male

Allow for the expression of dominate and recessive genes

Male reproductive system

produce sperm

sperm = male gamete

deliver sperm to female's reproductive system

Female reproductive system

produce egg

egg = female gamete

more cyclical than male reproductive system

female reproductive system receives sperm

egg provides all the nutrients for the zygote

female nurtures the embryo / fetus (conceptus)

nourishes the offspring with mammary gland after postpartum

therefore, the female reproductive system is more complicated!

Gender Characteristics

Secondary sex characteristics = features that distinguish male and female form

- play a role in mate attraction
- male and female both have apocrine glands that produce pheromones at puberty to attract a mate
- both sexes develop pubic and axillary hair
- female puberty characteristics = redistribution of body fat with breast enlargement, and relatively hairless appearance of the skin
- male puberty characteristics = facial hair, coarse and visible hair on the torso and limbs, relatively muscular physique, deeper voice

Primary VS Secondary Sex Organs

Primary sex organs

> gonadal tissue produce gametes (ovum and sperm)

> female / ovaries produce ovums (eggs)

> male / testes produce sperm

Secondary sex organs

> organs other than the gonads

> necessary for reproduction

> females // uterine tubes, uterus, and vagina

> males // penis, glands, and ducts

Endocrine Control of Puberty

Puberty is initiated when nuclei in hypothalamus mature and start to secrete gonadotrophin releasing hormone (GnRH)

Female occurs at 10 to 14 years of age

Male occurs at 12 to 16 years of age

At puberty - GnRH stimulates anterior pituitary to release two “gonadotropes”

> follicle stimulating hormone (FSH)
> luteinizing hormone (LH)

FSH & LH target tissue is different in males and females

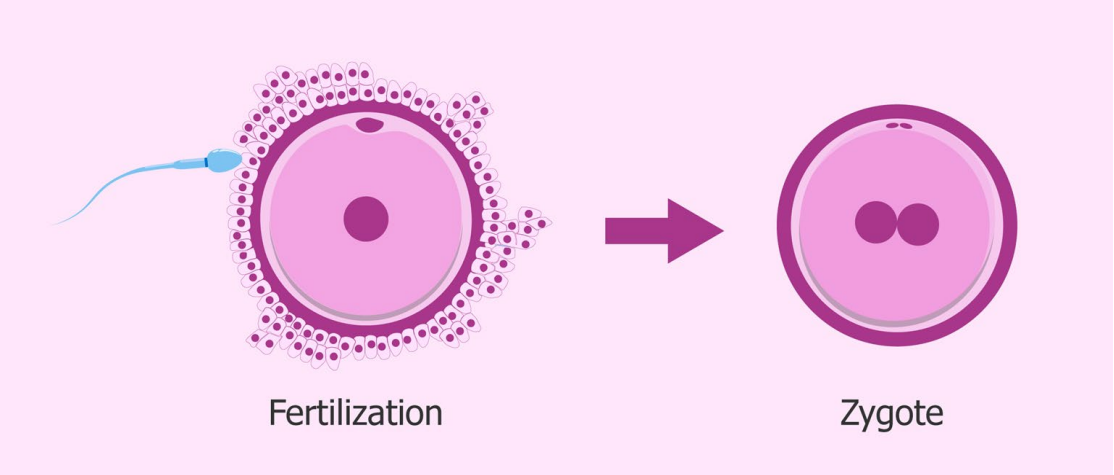
- females = ovaries
- males = testes

What is the first human diploid cell?

The sperm is a haploid cell (23 chromosomes) /// Males have an organ (the penis) to deliver sperm into the female reproductive tract

The ovum (egg) is a haploid cell (23 chromosomes) /// Females' vagina receives male gametes (sperm)

Zygote = union of male and female gametes (46 chromosomes) /// union occurs in the infundibulum of the female's fallopian tube /// it is the first diploid cell!



The Gametes

Sperm (spermatozoon immature sperm)

The sperm's flagella provides motility

The sperm contributes only it's DNA to zygote / 23 chromosomes / no organelles!!!

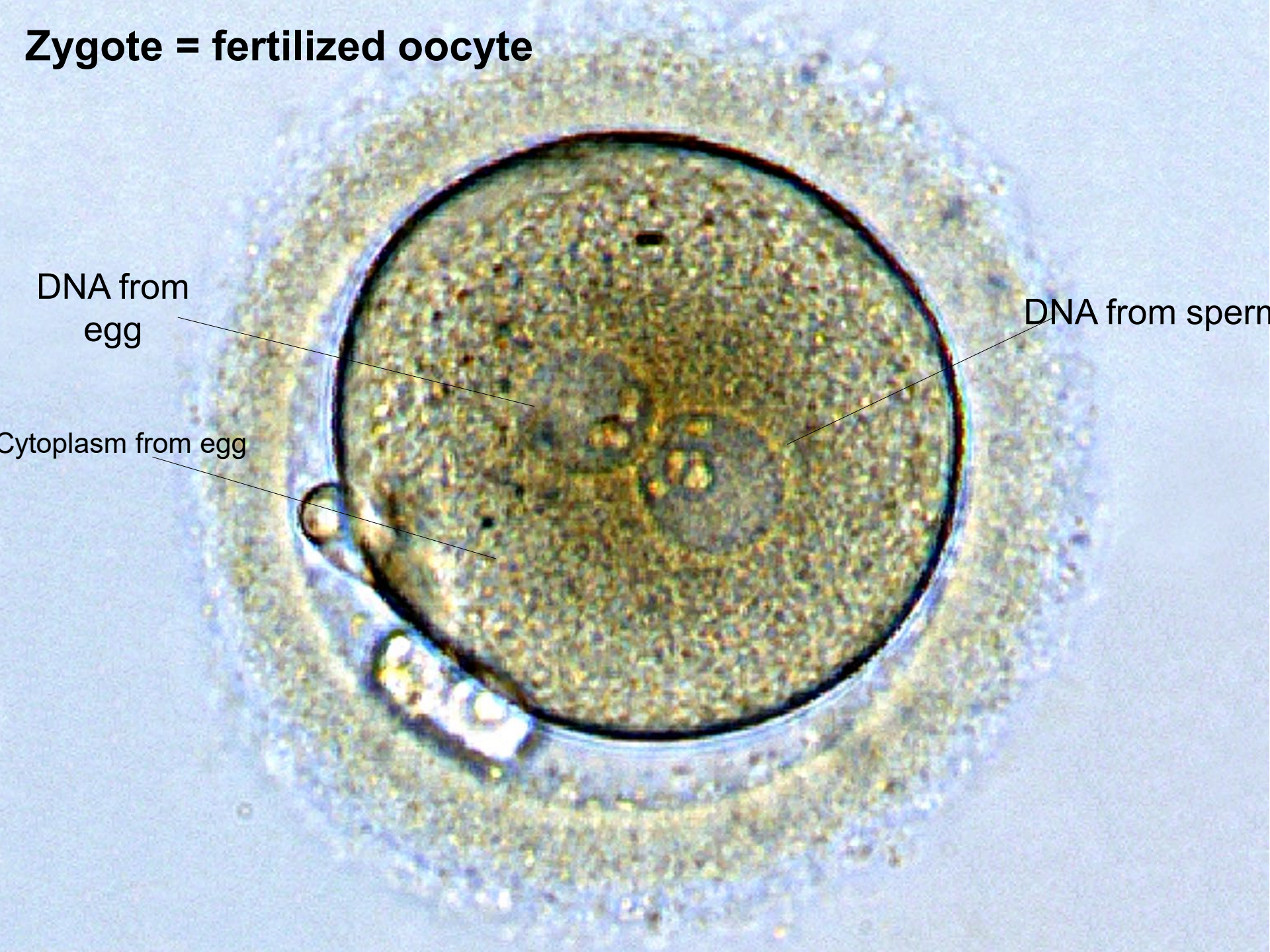
Egg (also called the ovum)

Provides all the cytoplasm for the first diploid cell (the zygote), including all the organelles plus 23 chromosomes from

Provides all the nutrients for developing zygote to blastocyte

In mammals, female is the parent providing a sheltered internal environment and prenatal nutrition for the embryo

Zygote = fertilized oocyte



Sex Determination

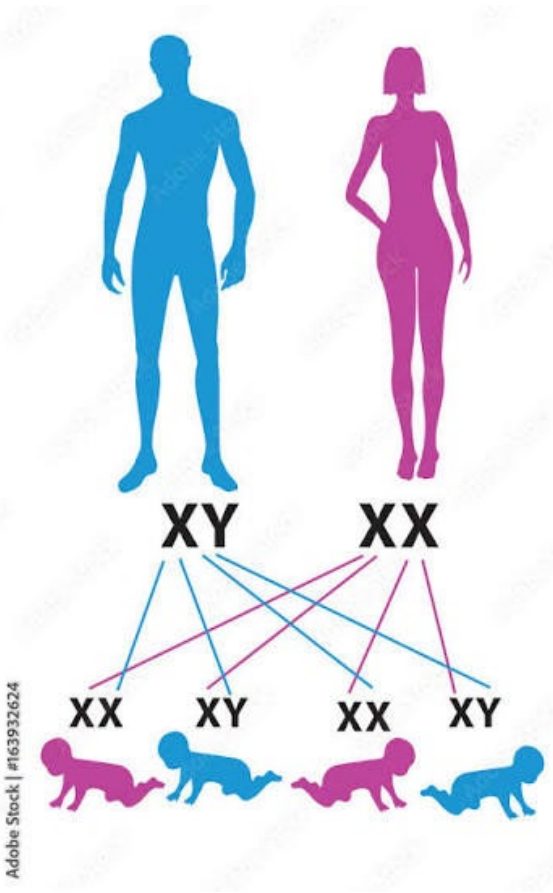
Human cells contain 23 pairs of chromosomes (46 chromosomes!)

- 22 chromosome pairs are called autosomes
- 1 chromosome pair called sex chromosomes

- Sex gene is either an X or a Y
- If sex gene pair in chromosome = XY = males
- If sex gene pair in chromosome = XX = females

The male's chromosome have an allele pair (genes) coed as Y and X // only one gene will be selected to be carried by the sperm // X or Y

The female chromosome have an allele pair (genes) with only the X gene // females may only transmit the X gene in the ovum



The sex chromosomes pair are “split” /// each gamete will receive only one of the alleles /// when the zygote forms – it will have one sex gene from each parent

Chromosomal Sex Determination

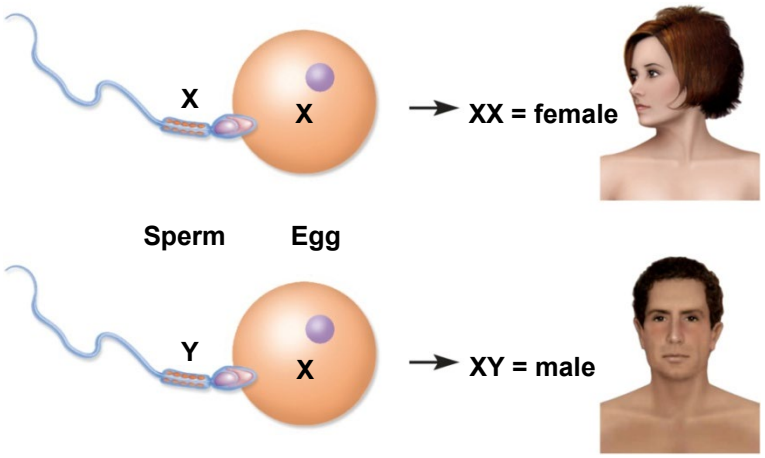
The punnet square illustrates the four possible outcomes

Sperm may contribute either X or Y

Egg (female) may only provide “X” chromosome

If X carrying sperm fertilizes the egg then fetus = female

If Y carrying sperm fertilizes the egg then fetus = male

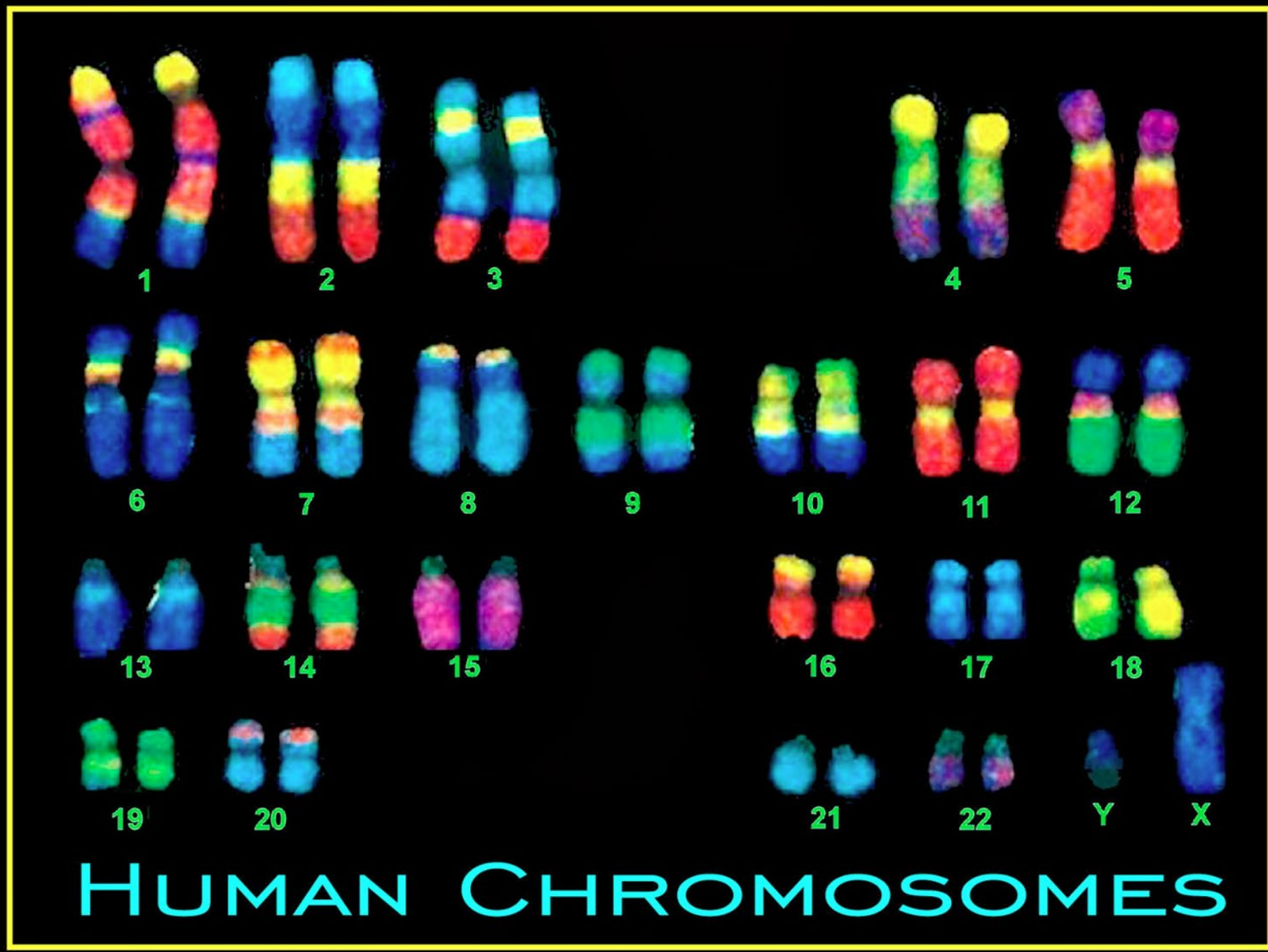


	X	Y
X	X X	X Y
X	X X	X Y

Punnet Square

Chromosomes

- Humans have 46 chromosomes (**diploid** =2N)
- 2 of them are **sex chromosomes** (the last pair)
  - X and Y→ they determine what sex you are
    - XX = female
    - XY = male
- 44 of them are **autosomes**
  - they do **not** determine the sex of an individual.


1
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22
Y
X
HUMAN CHROMOSOMES

Meiosis

Meiosis is haploid cell division /// meiosis reduces the chromosome number by half

Type of cell division seen only in the formation of gametes // occurs in the gonads // females = ovaries producing eggs // males = testes produce sperm

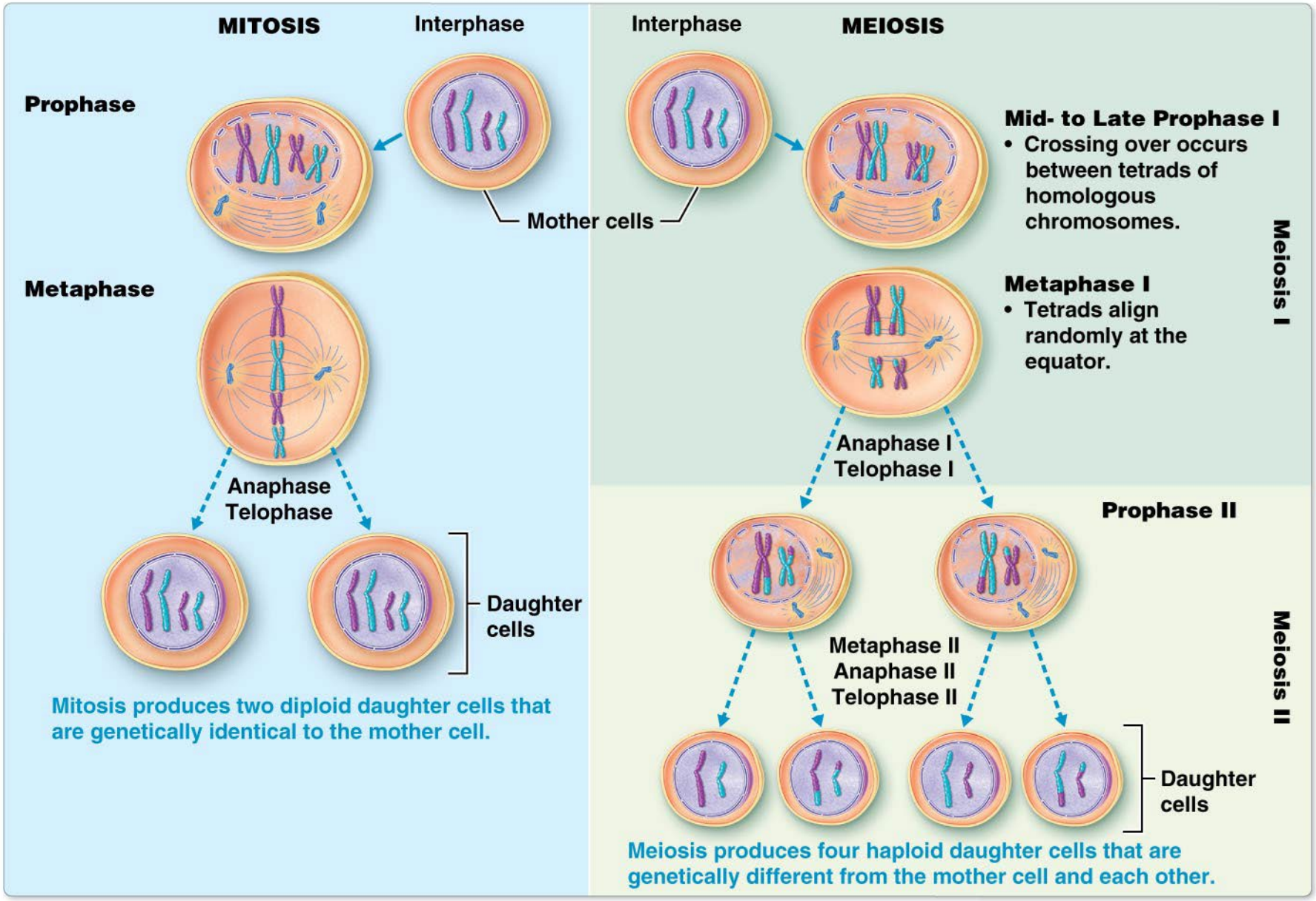
Humans reduce chromosome number from 46 to 23 chromosomes (diploid to haploid)

Sperm and egg haploid cells unite to form a zygote with 46 chromosomes

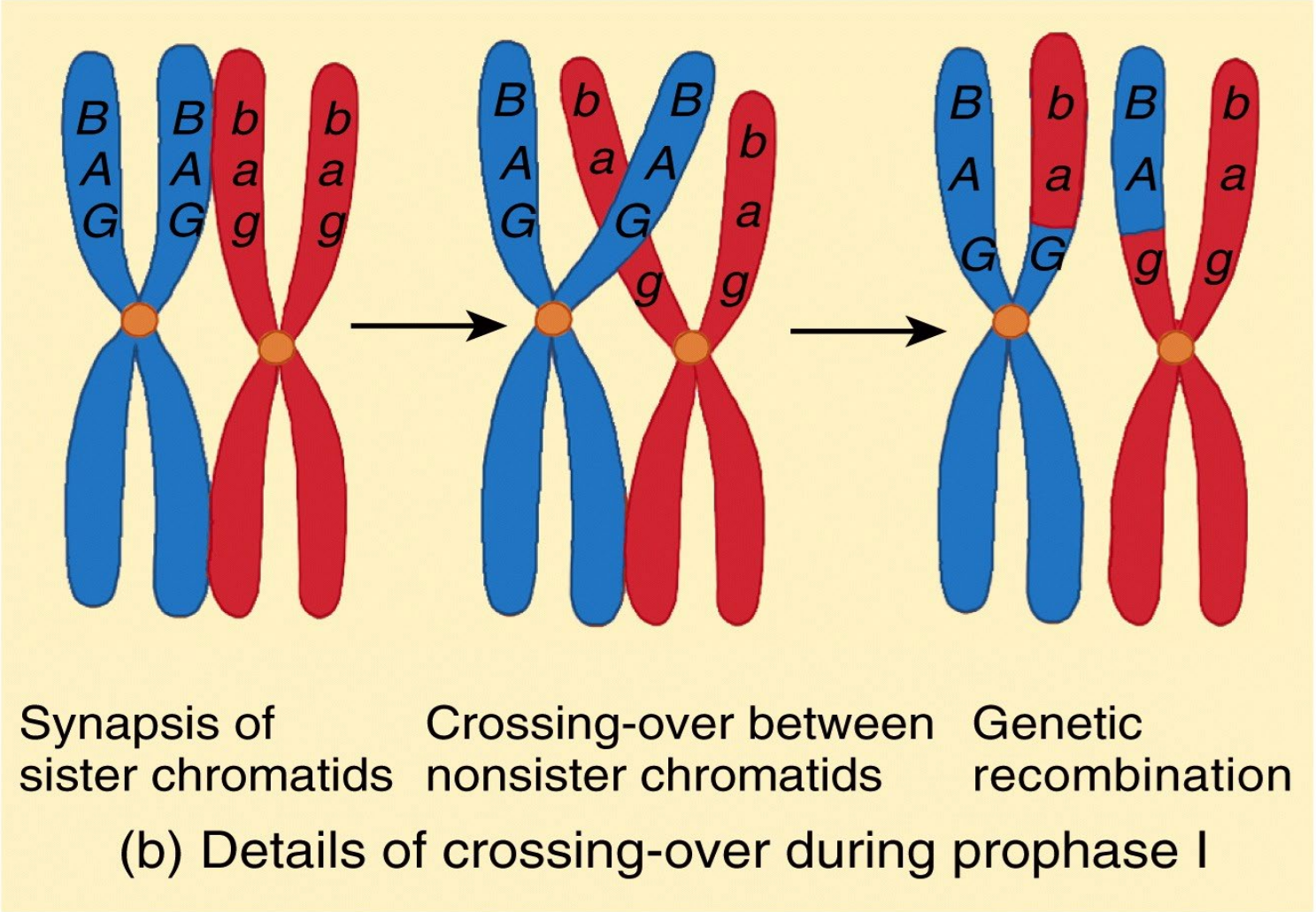
Note: mitosis conserves the chromosomal number /// epithelial cells use mitosis to make copy of itself. /// the somatic cells

Think of meiosis as following the phases of mitosis twice but only duplicating the chromosomes in the "S phase" once. This then reduces the chromosome number by half.

Comparing Mitosis and Meiosis



Crossing-Over is an important event because it increases the possibility for maximizing the mixing of the genes between the male and female chromosomes.



First Stage of Meiosis

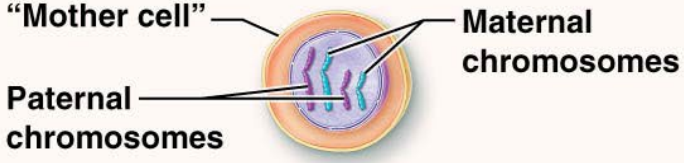
For simplicity, the cell is shown with only two pairs of homologous chromosomes.

Male gonadal tissue produce four viable haploid cells (sperm) but female gonadal tissue produce only one viable haploid cell (the ovum) and three polar bodies that die by apoptosis.

BEFORE BIRTH

Cells before DNA Replication

- This is what the cell would look like if the chromatin condensed into chromosomes before the DNA replicated.



MEIOSIS I

Early Prophase I

- Chromosomes form with two sister chromatids.

Mid- to Late Prophase I

- During synapsis, homologous chromosomes form tetrads and **crossing over** occurs.

Metaphase I

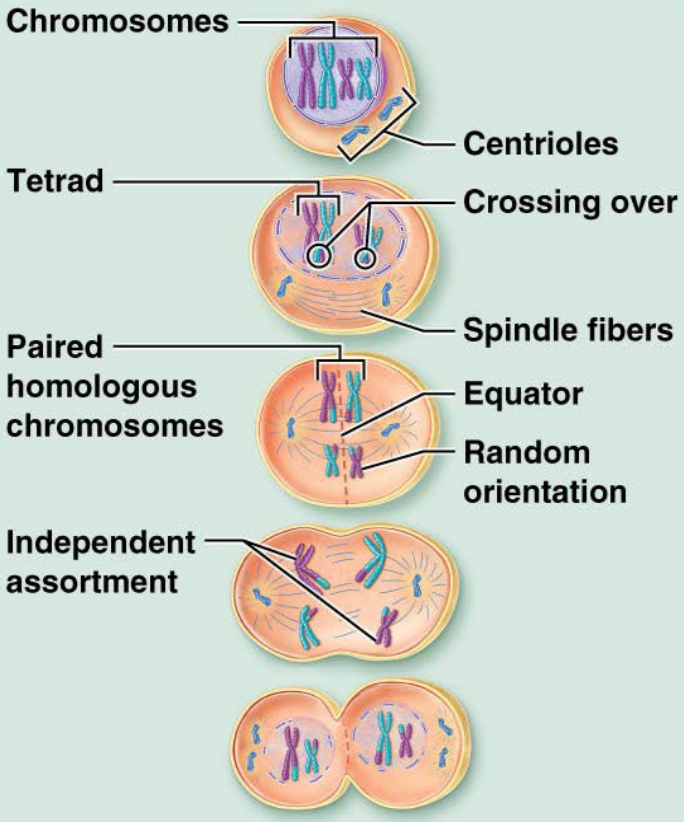
- Tetrads align randomly at equator (random orientation).

Anaphase I

- Random orientation in metaphase I leads to **independent assortment.**

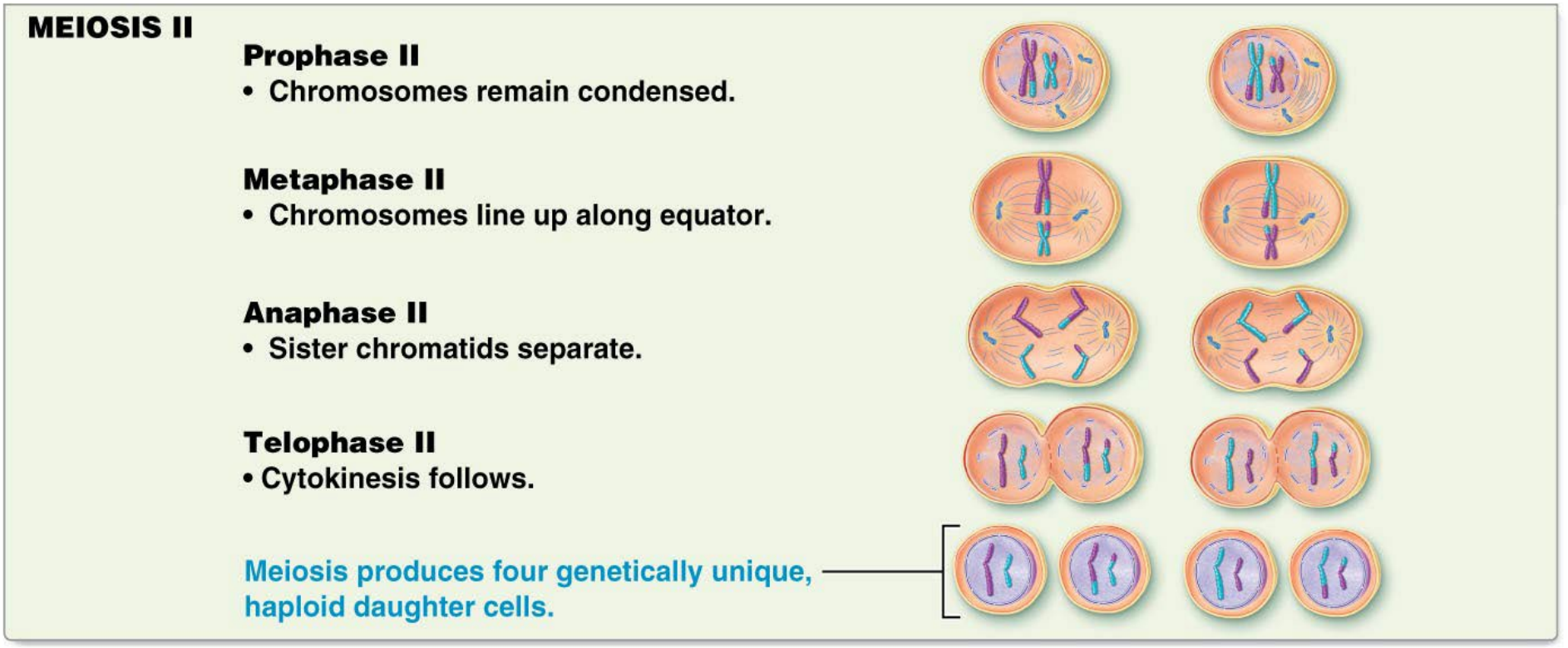
Telophase I

- Cytokinesis may follow, resulting in two genetically different haploid cells with sister chromatids still attached.



Second Stage of Meiosis

For simplicity, the cell is shown with only two pairs of homologous chromosomes.



Stages of Meiosis

BEFORE BIRTH

Cells before DNA Replication
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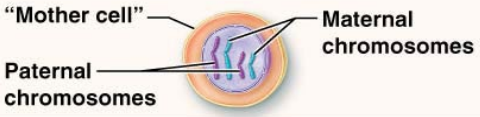

MEIOSIS I

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- Chromosomes form with two sister chromatids.

Mid- to Late Prophase I
- During synapsis, homologous chromosomes form tetrads and **crossing over** occurs.

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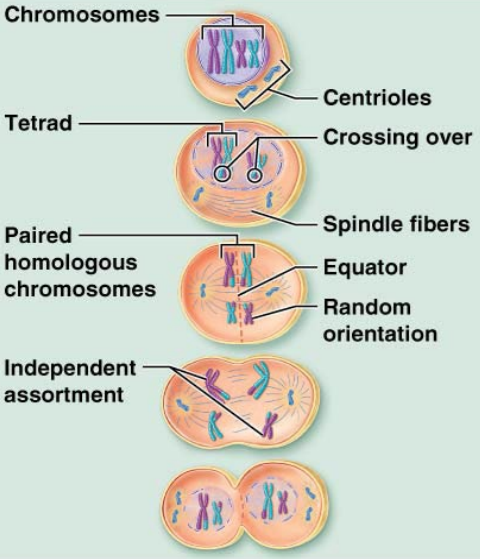
Anaphase I
- Random orientation in metaphase I leads to **independent assortment.**

Telophase I
- Cytokinesis may follow, resulting in two genetically different haploid cells with sister chromatids still attached.



MEIOSIS II

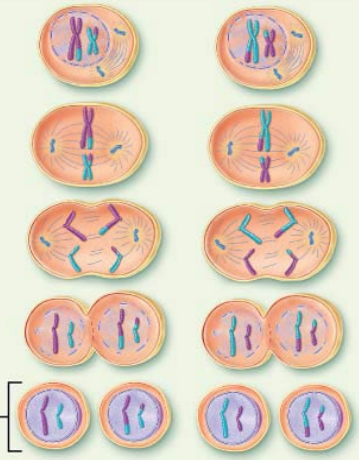
Prophase II
- Chromosomes remain condensed.

Metaphase II
- Chromosomes line up along equator.

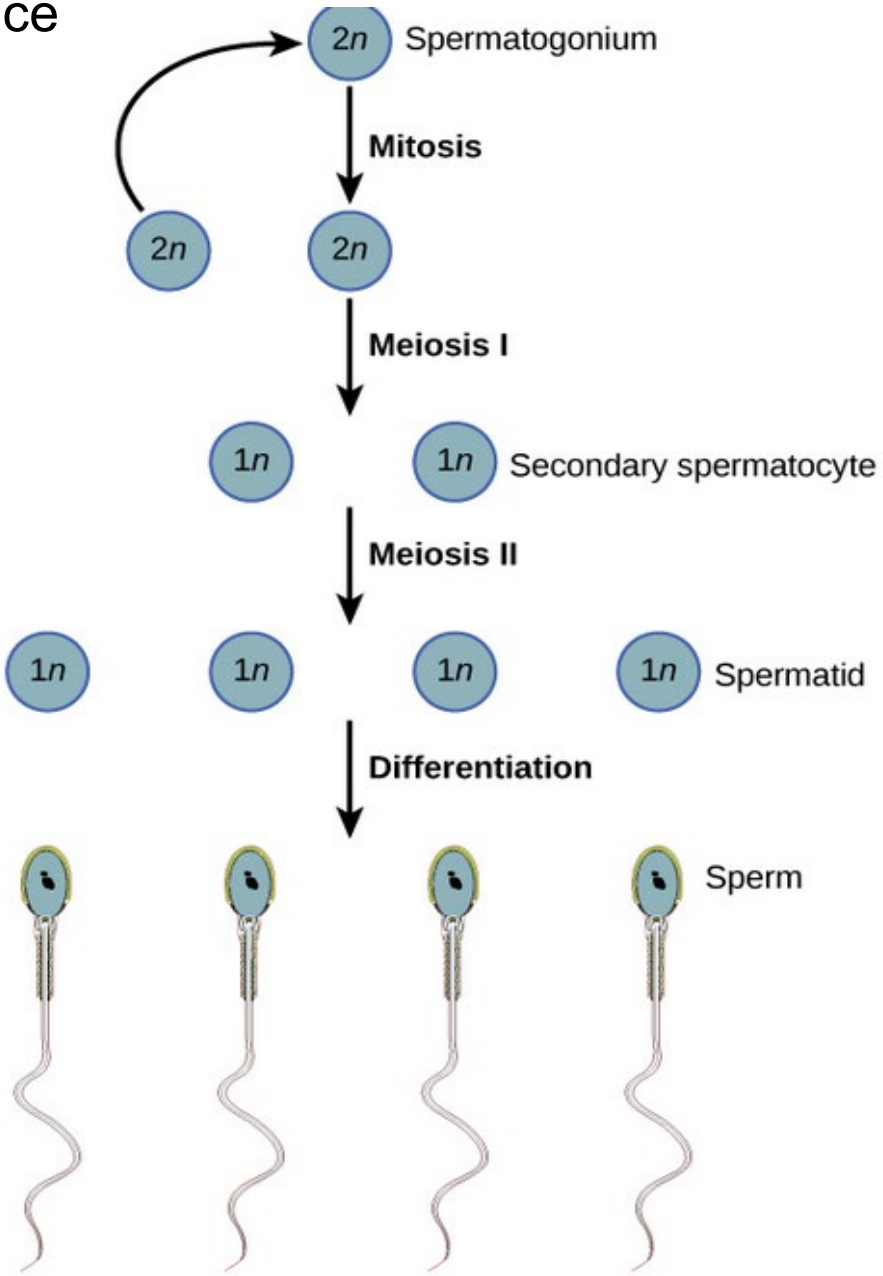
Anaphase II
- Sister chromatids separate.

Telophase II
- Cytokinesis follows.

Meiosis produces four genetically unique, haploid daughter cells.

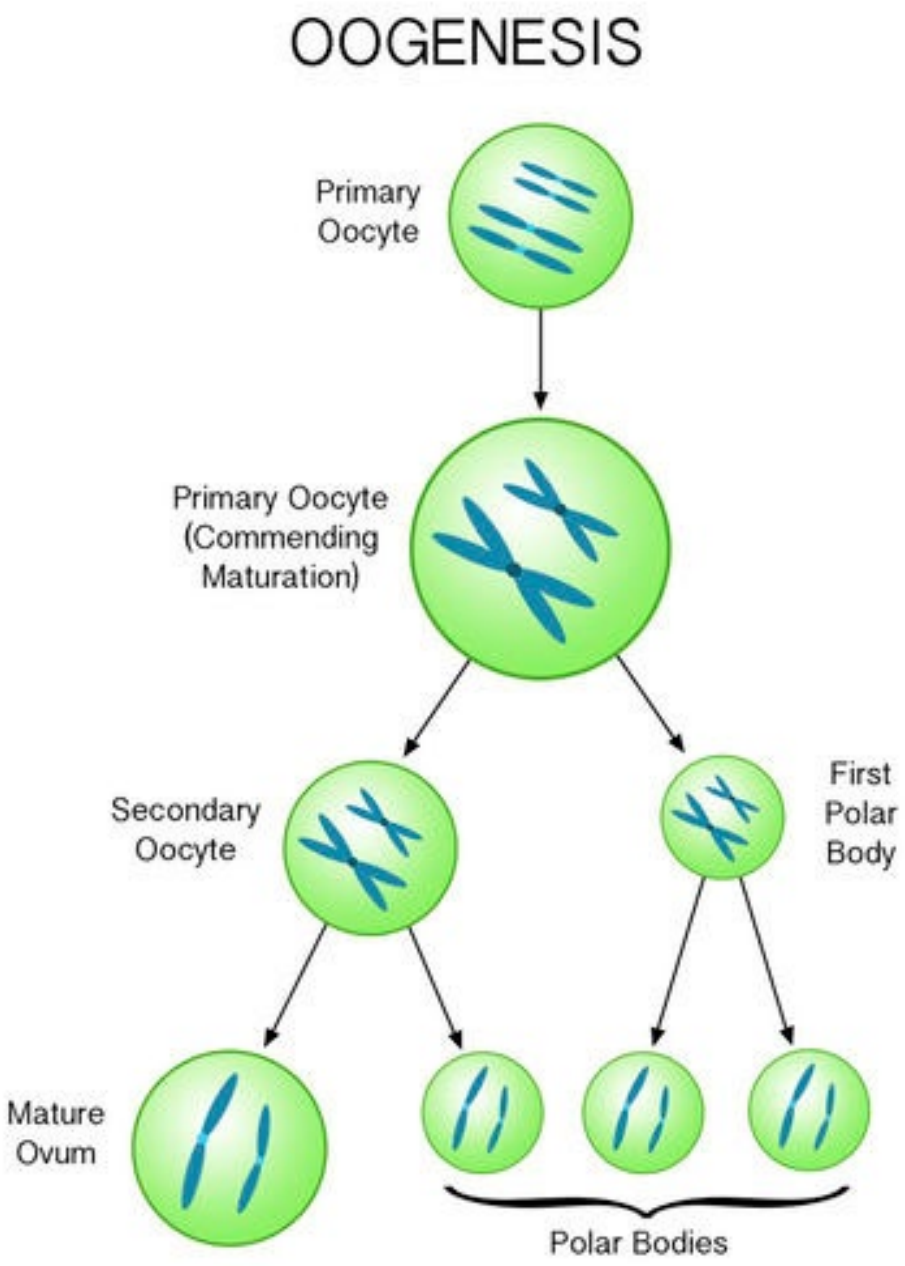


Meiosis in male gonadal tissue produce four viable sperm.

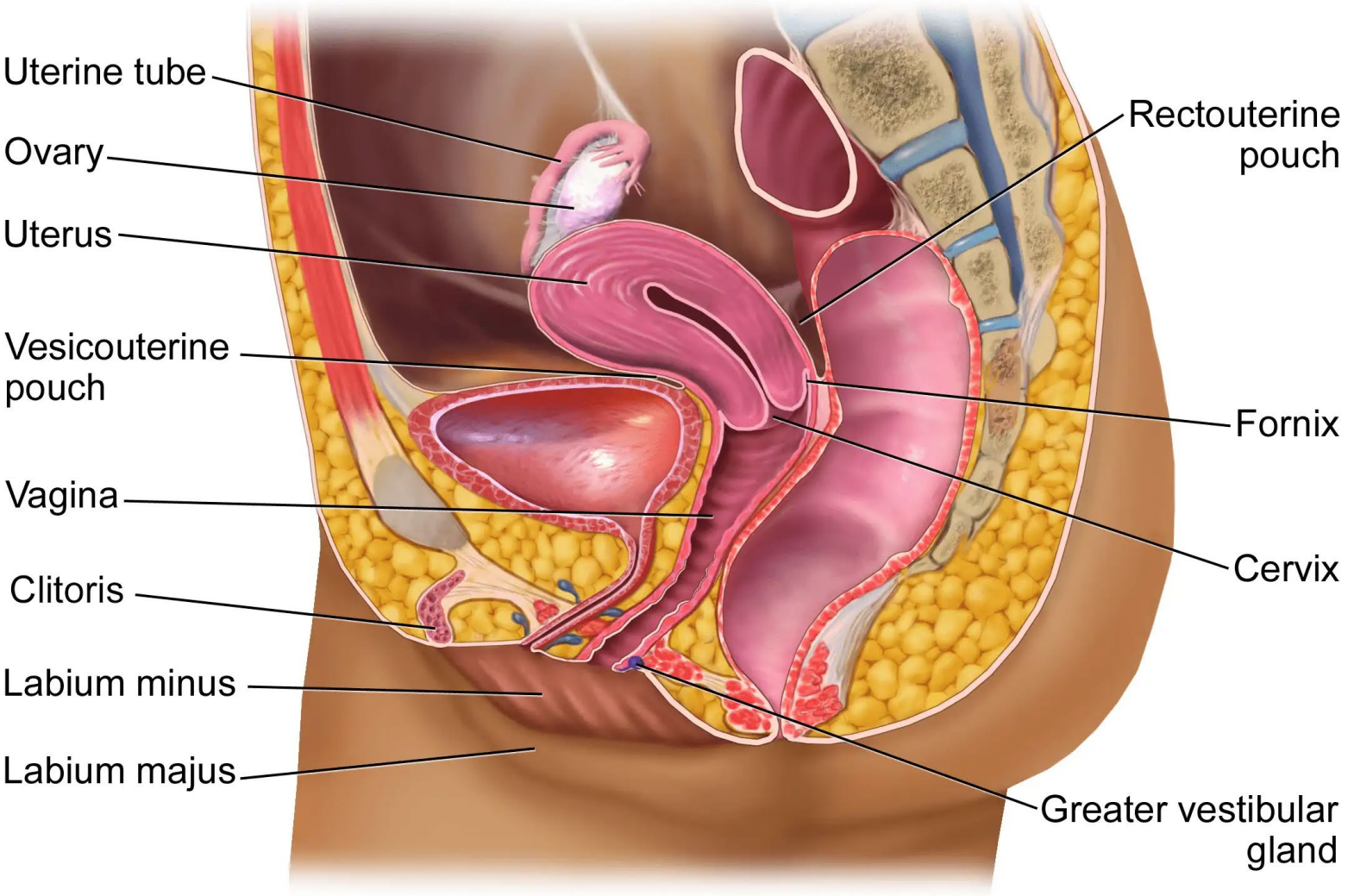


Meiosis in female gonadal tissue produce one mature ovum and three polar bodies.

It is not possible to fertilize the polar bodies and they die by apoptosis.



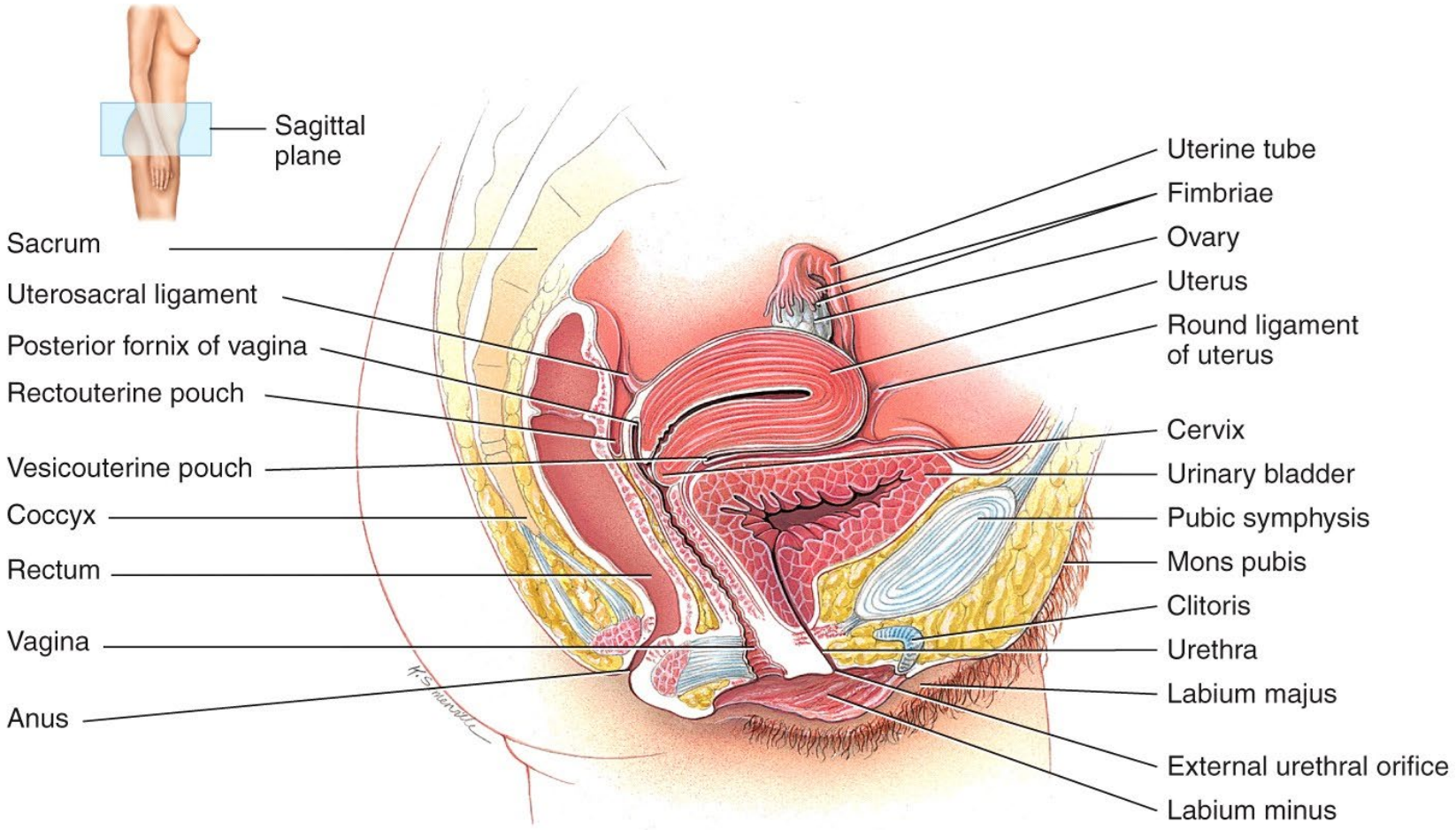
Female Reproductive System



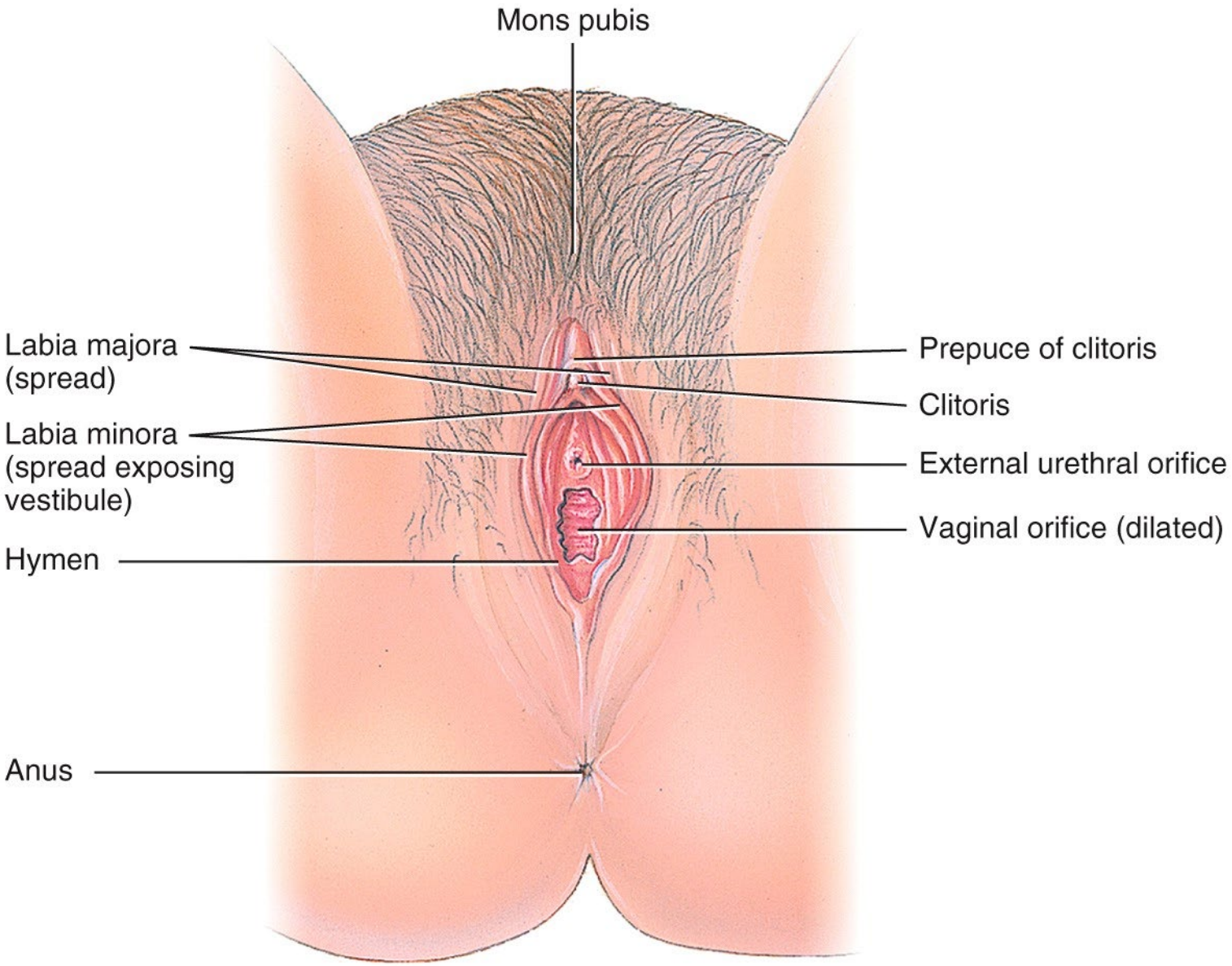
Female Reproductive Organs

Primary sex organ = ovaries // produce female gamete (egg)

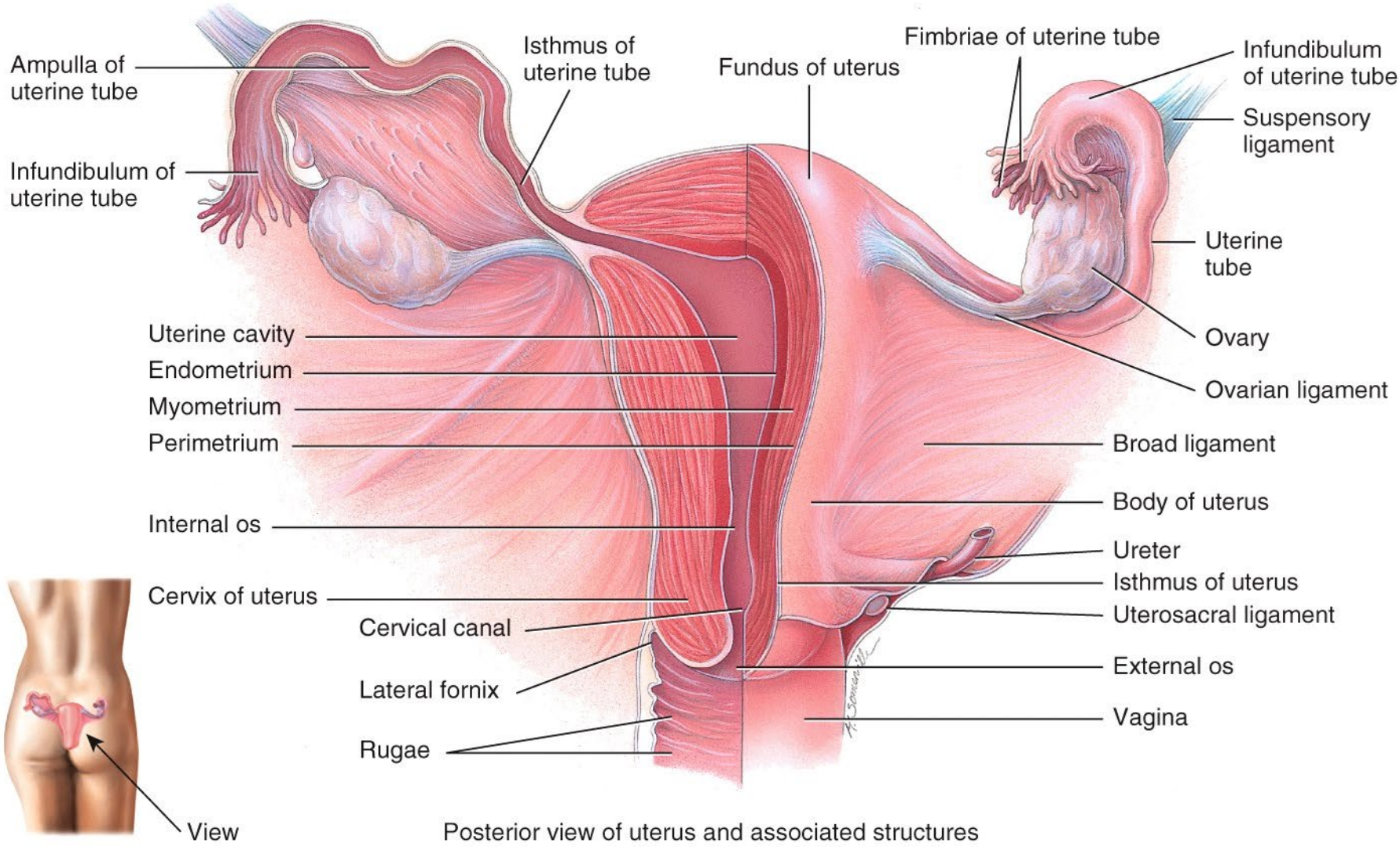
Secondary sex organs = fallopian tubes, uterus, vagina



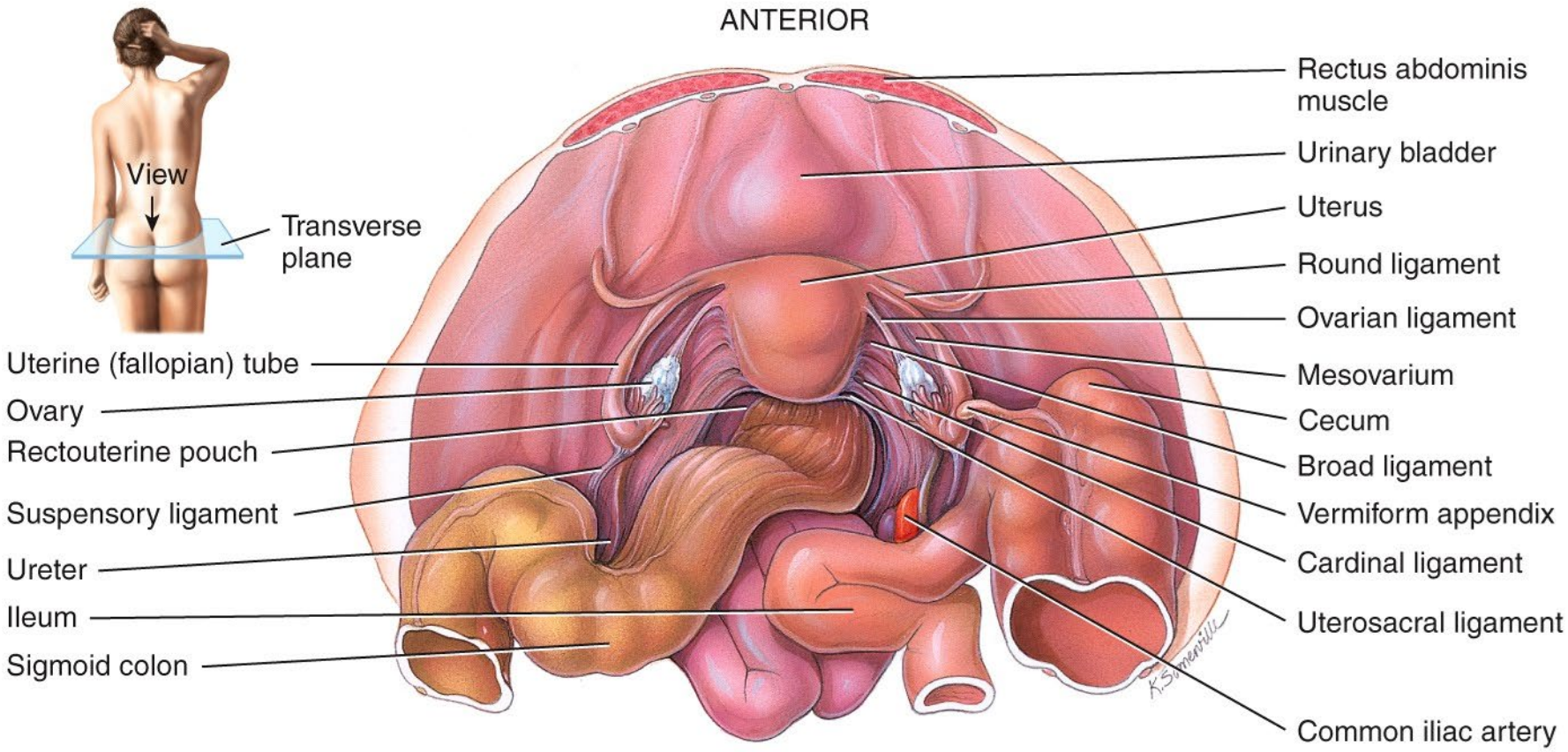
(a) Sagittal section



(c) Inferior view

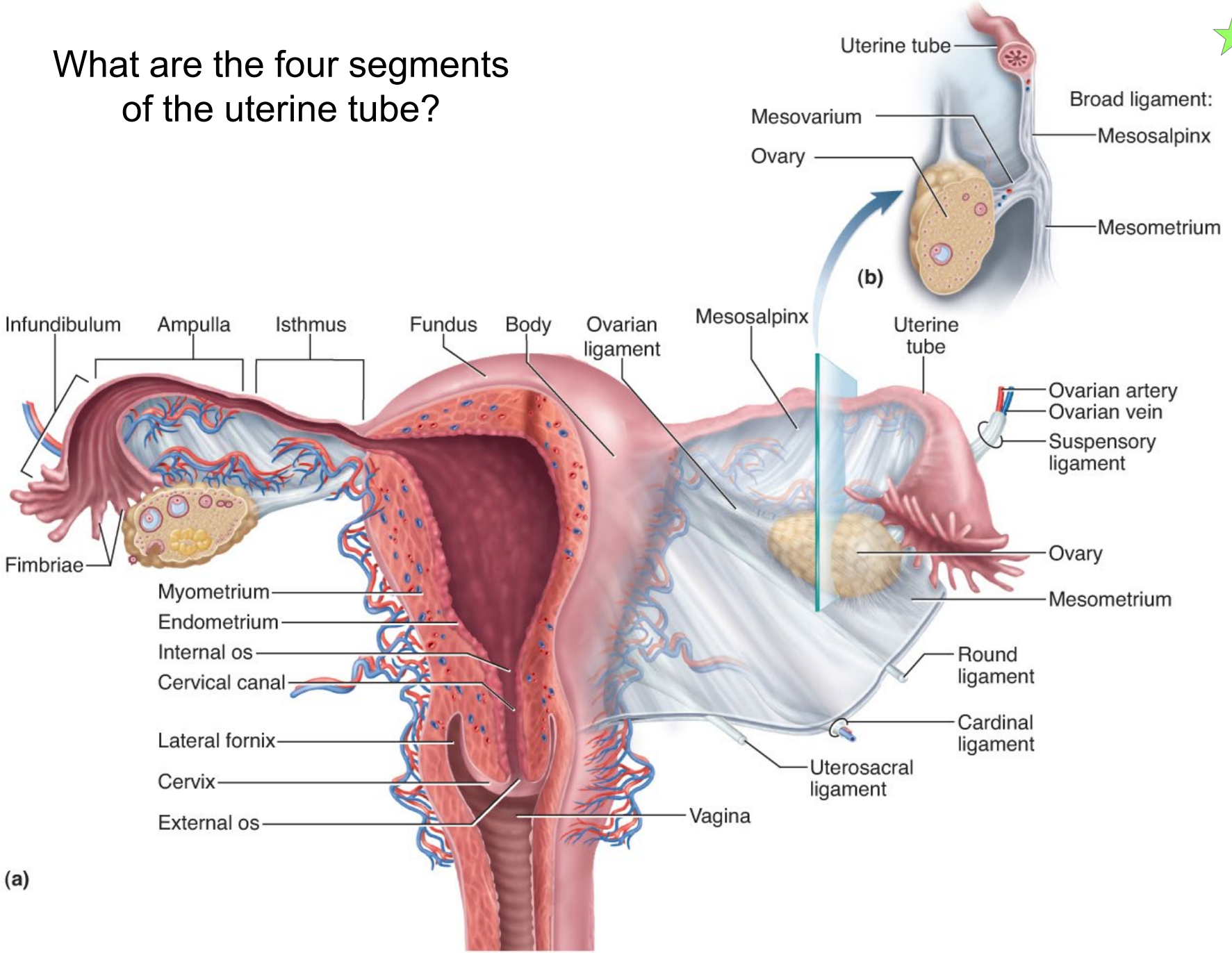


Posterior view of uterus and associated structures

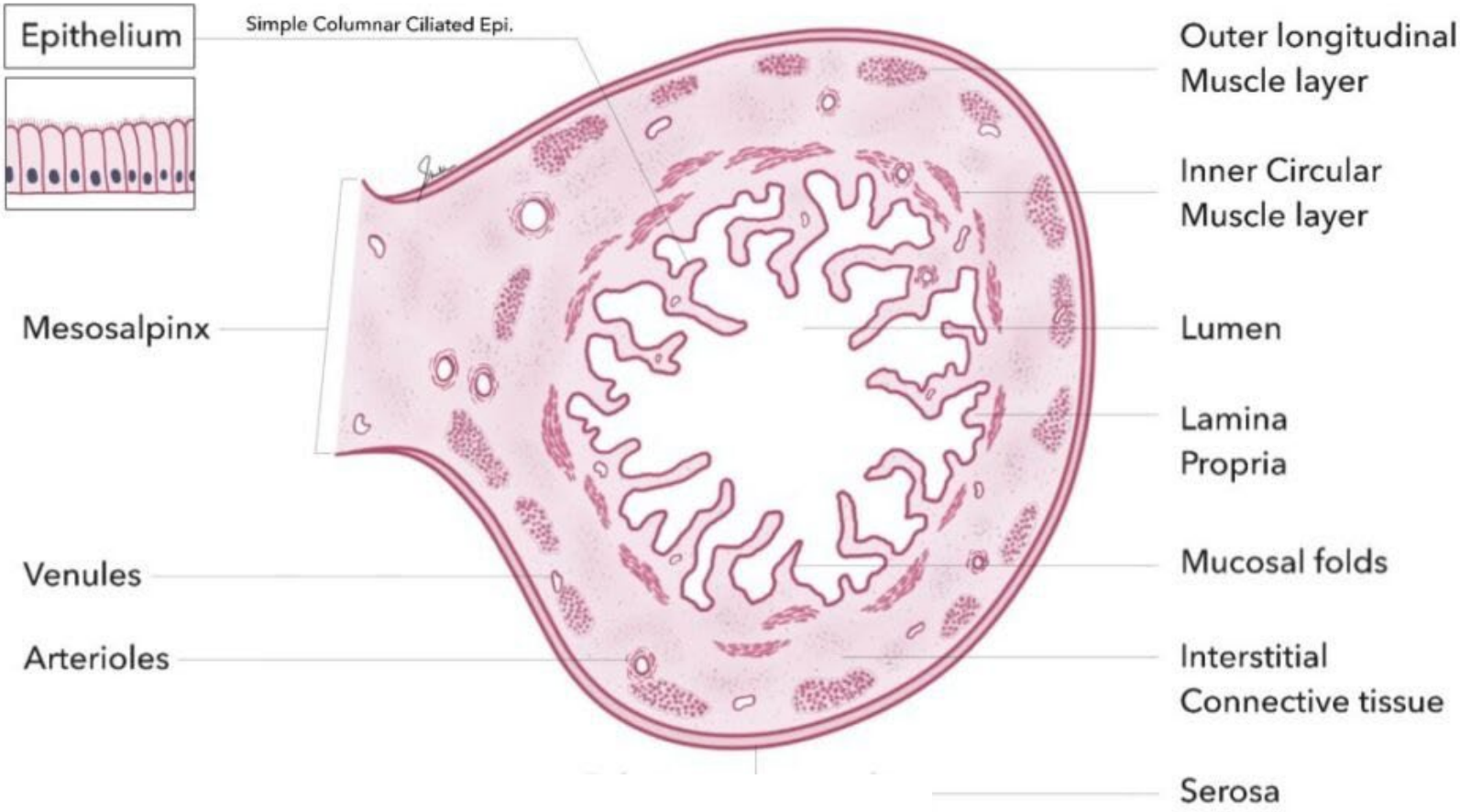


Superior view of transverse section

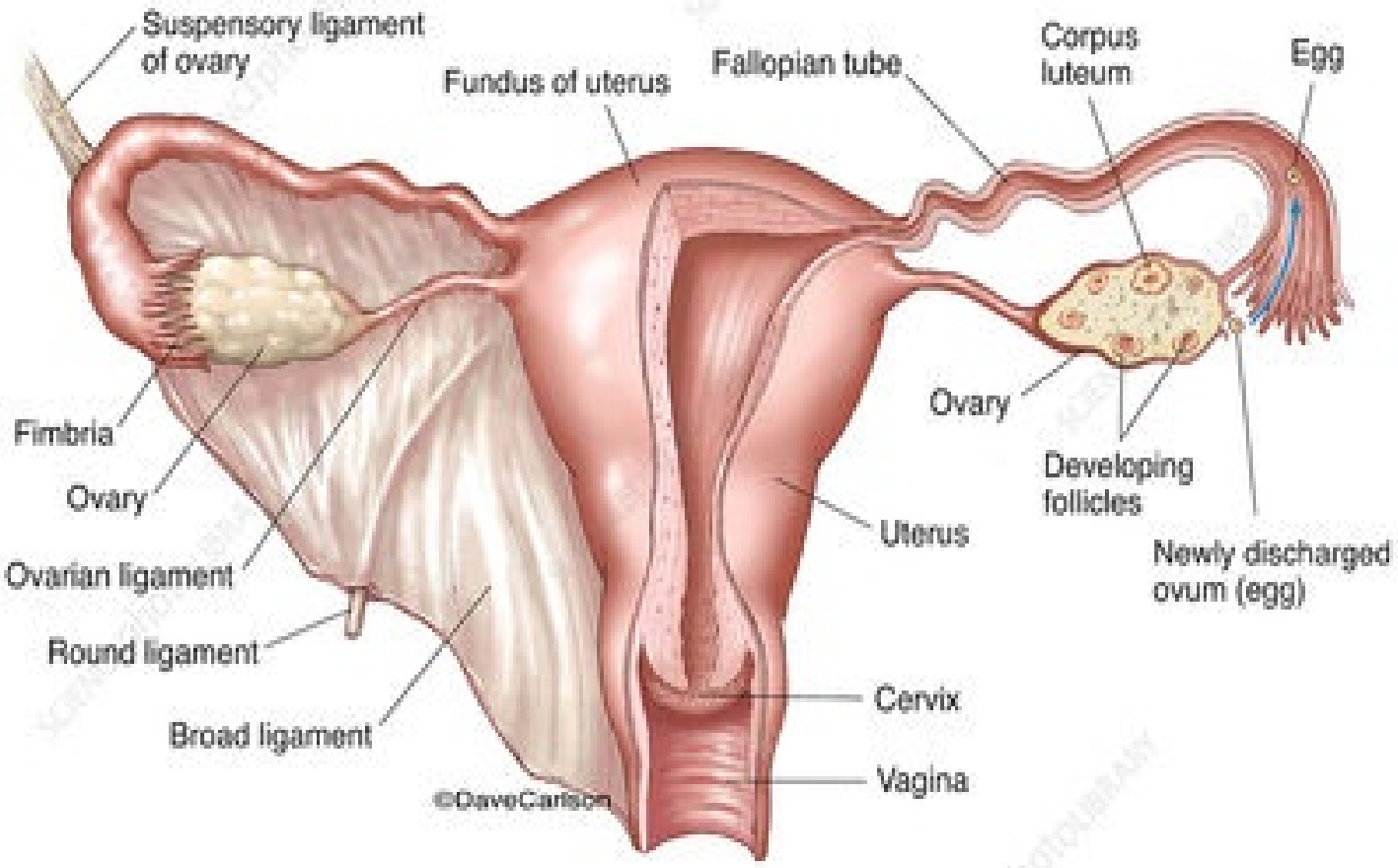
What are the four segments of the uterine tube?



Fallopian Tube



Internal organs of the female reproductive system.



The Uterus

Lumen is roughly triangular

- upper two corners are the openings to the uterine tube
- lower apex is internal os
- uterus is not a hollow cavity /// a potential space in the non-pregnant uterus

Cervical canal connects the lumen to vagina

- internal os – superior opening of the canal into the body of the uterus
- external os – inferior opening of the canal into the vagina

Cervical glands – secretes mucus that prevents the spread of microorganisms from the vagina to the uterus /// cervical plug = estrogen reduces viscosity and progesterone increases the viscosity

The Uterus

Uterus – thick muscular (smooth muscle) chamber that opens into the roof of the vagina

Usually tilts forward over the urinary bladder

Location where conceptus develops /// provides a source of nutrition and expels the fetus at the end of its development

Pear-shaped organ

- fundus – broad superior curvature
- body (corpus) – middle portion
- cervix – cylindrical inferior end

Uterine Wall Layers
(serosa / myometrium / endometrium)

External layer covered by serosa (visceral serous membrane) = outer layer

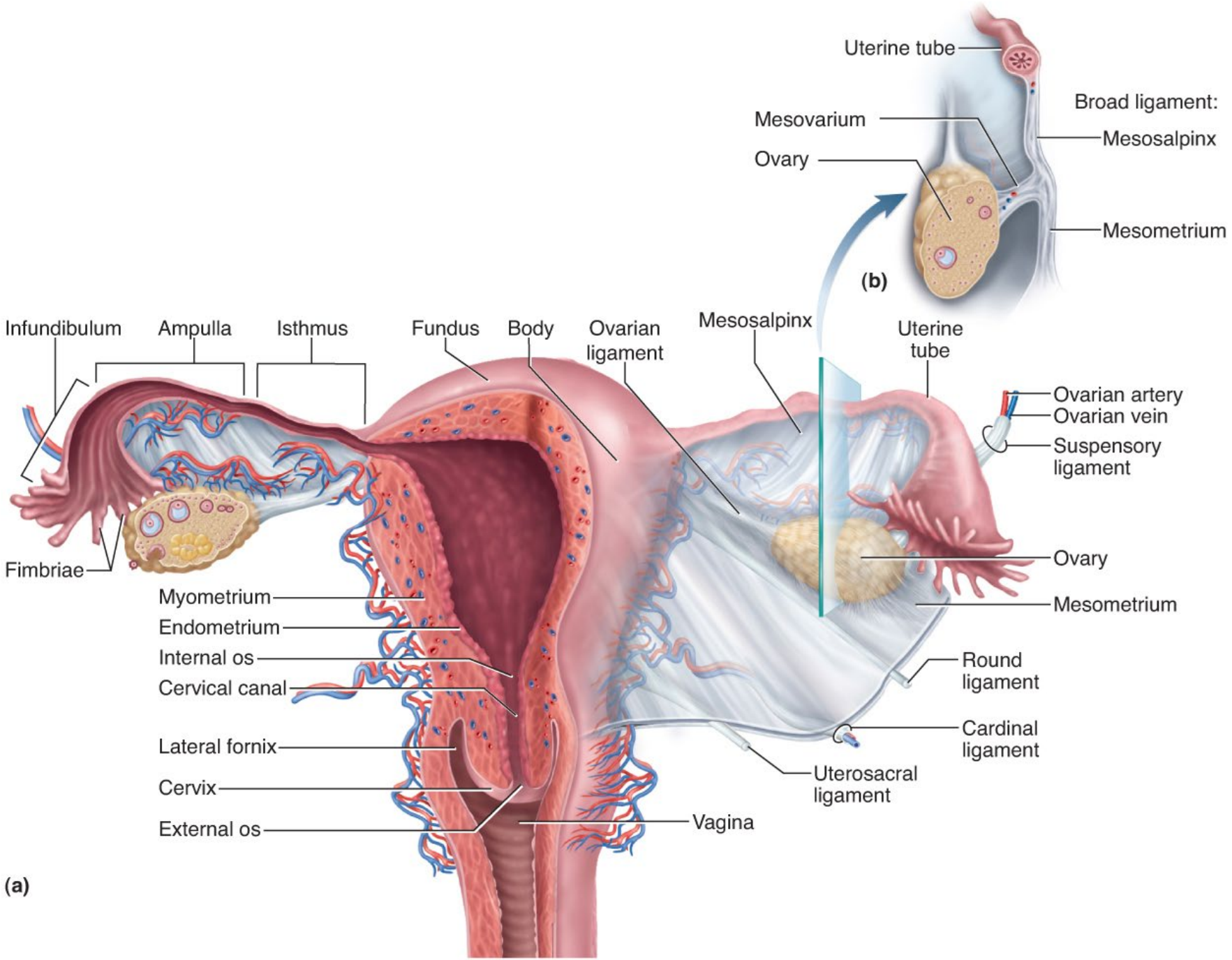
Myometrium = middle muscular layer // constitutes most of the uterine wall

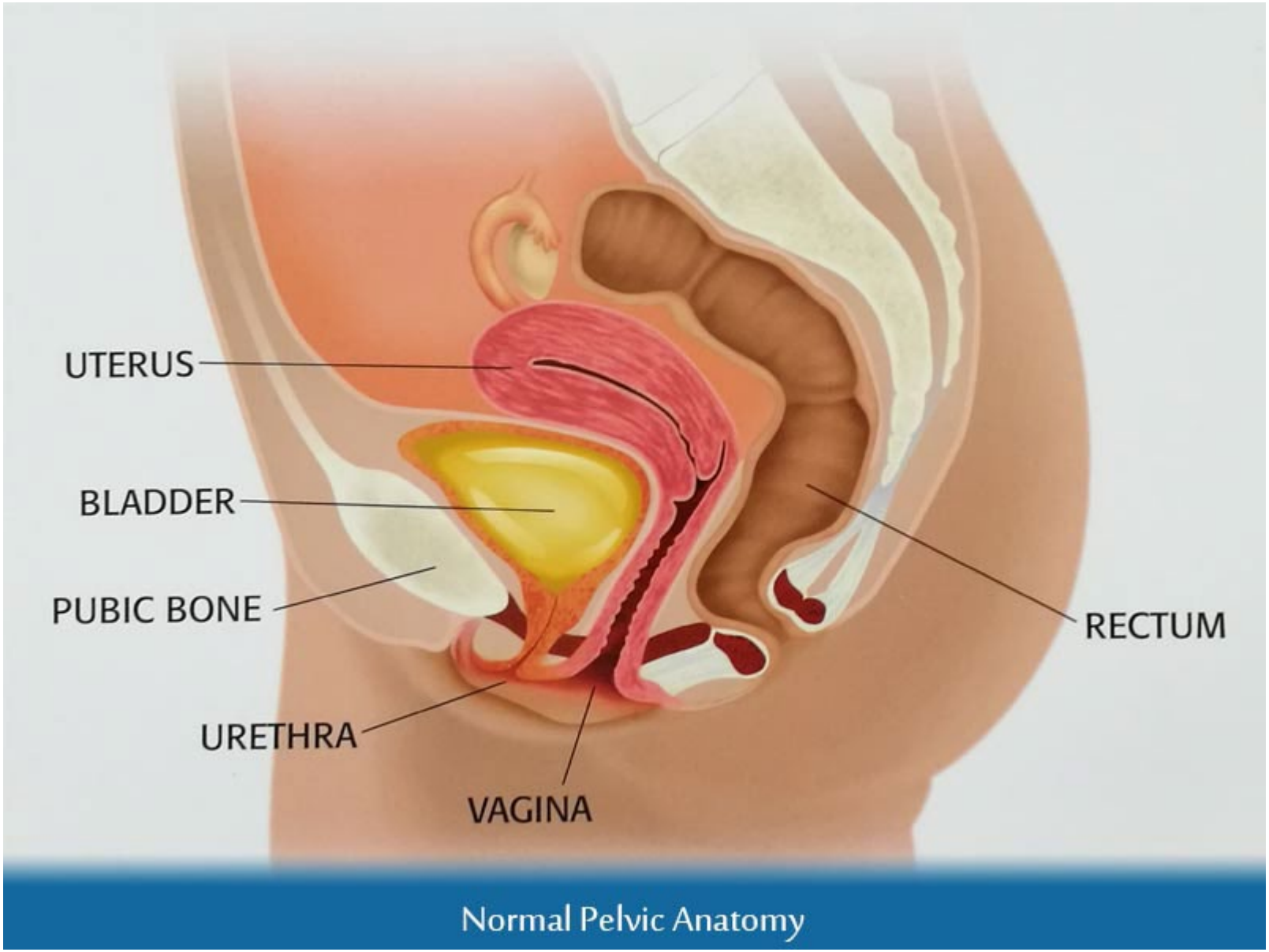
Composed mainly of smooth muscle

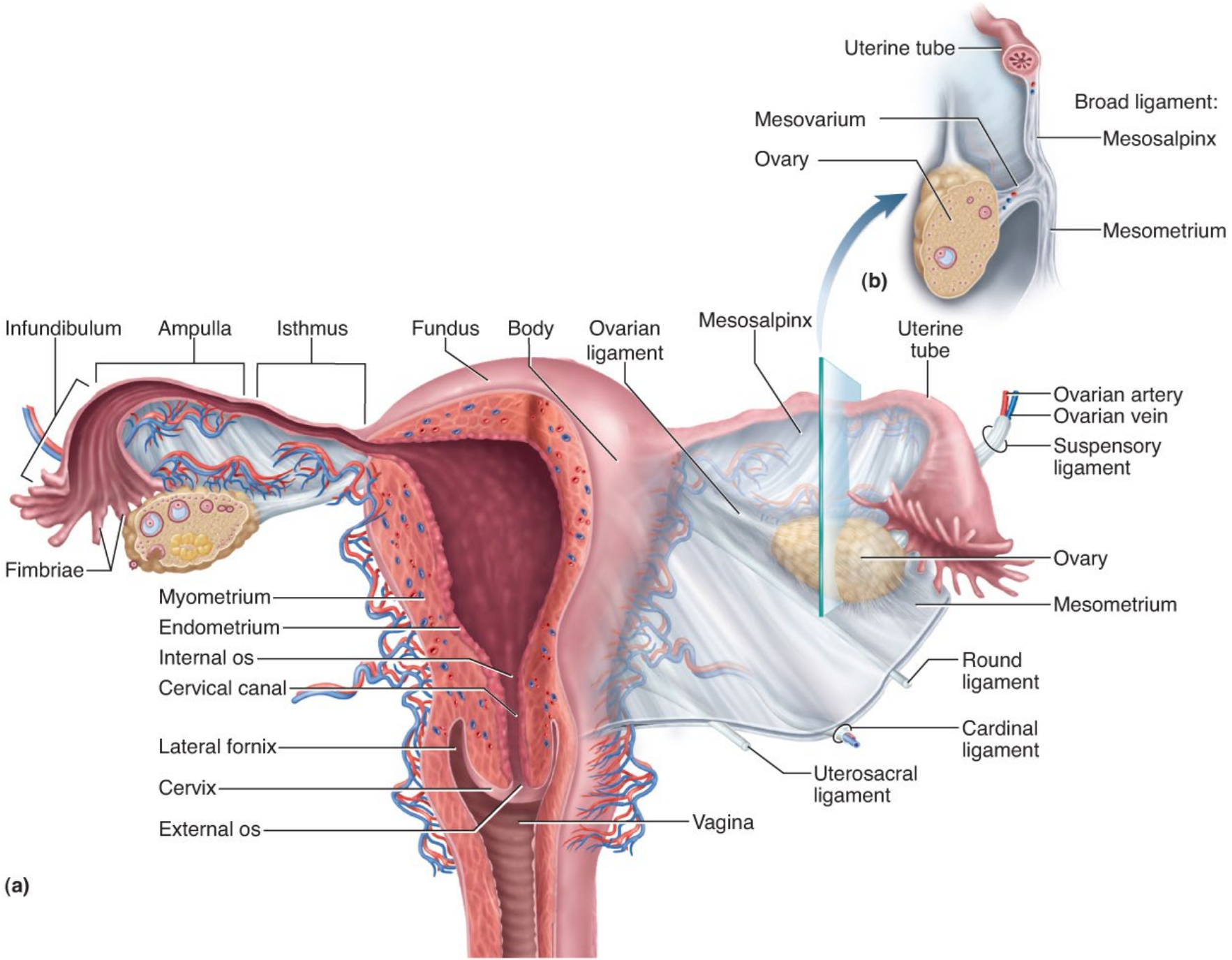
sweep downward from fundus and spiral around the body /// less muscular and more fibrous near cervix ///

produces labor contractions, expels fetus

Endometrium = simple columnar epithelium lining the interior of the uterus (see upcoming slides) // mucosa


Uterine tube
Broad ligament:
Mesosalpinx
Mesovarium
Ovary
Mesometrium
(b)
Infundibulum
Ampulla
Isthmus
Fundus
Body
Ovarian ligament
Mesosalpinx
Uterine tube
Ovarian artery
Ovarian vein
Suspensory ligament
Fimbriae
Ovary
Myometrium
Mesometrium
Endometrium
Internal os
Round ligament
Cervical canal
Cardinal ligament
Lateral fornix
Uterosacral ligament
Cervix
External os
Vagina
(a)


UTERUS
BLADDER
PUBIC BONE
URETHRA
VAGINA
RECTUM
Normal Pelvic Anatomy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Uterine tube
Ovarian artery
Ovarian vein
Suspensory ligament
Fimbriae
Ovary
Myometrium
Mesometrium
Endometrium
Internal os
Round ligament
Cervical canal
Cardinal ligament
Lateral fornix
Uterosacral ligament
Cervix
External os
Vagina
(a)

Endometrium

Endometrium = the mucosa of the uterus // two layers

Endometrium = simple columnar epithelium, compound tubular /// glands, and a stroma populated with leukocytes, /// macrophages, and other cells.

Stratum functionalis – superficial half, shed each menstrual period

Stratum basalis - deep layer, stays behind and regenerates a new stratum functionalis with each menstrual cycle

During pregnancy, the endometrium is the site of attachment of the conceptus /// the placenta grows “out of the conceptus” /// forms interphase between maternal tissue and conceptus // the placenta is the organ that exchanges nutrients and waste products between conceptus and mother

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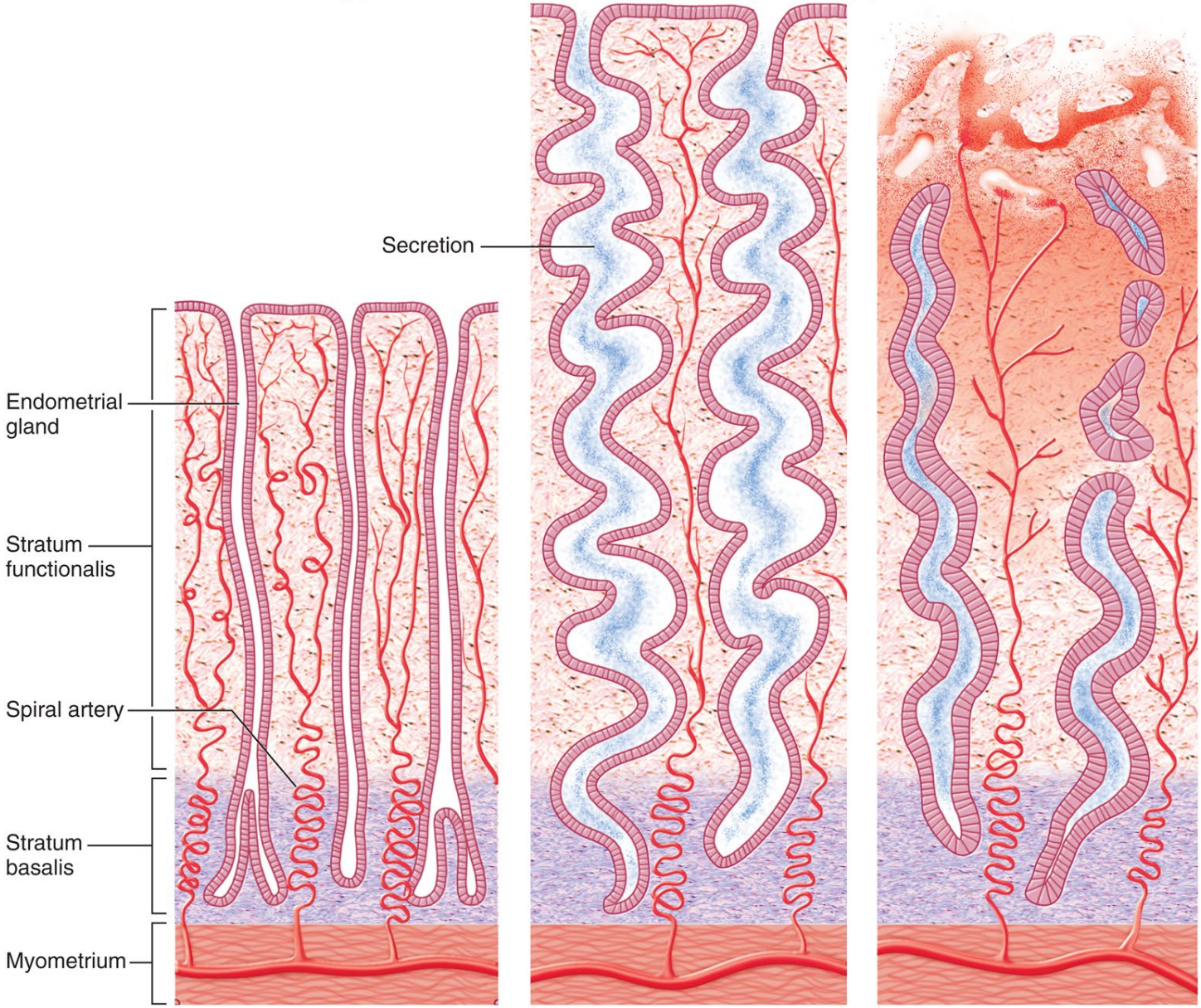
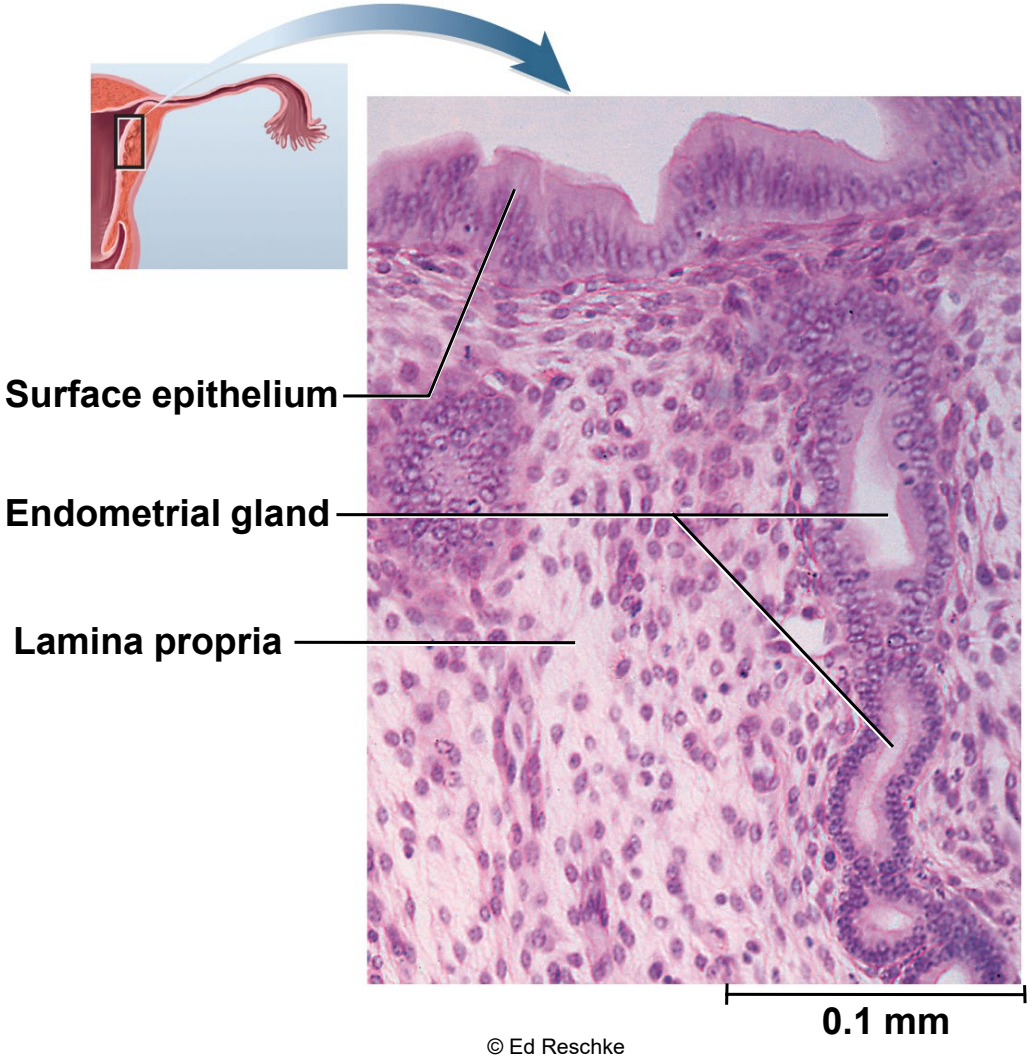


Histology of Endometrium



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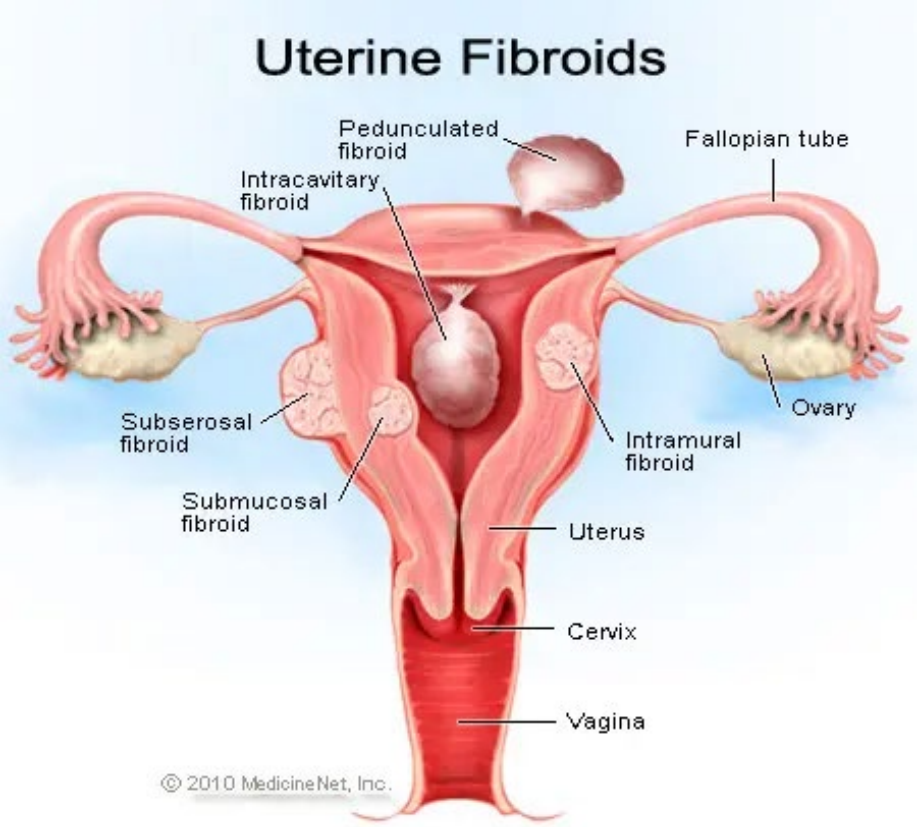
Endometrium



Uterine fibroids are **Noncancerous (benign) tumors** that grow in the uterus. They are very common, especially during a woman's reproductive years, and can vary in size and number.

While many women with fibroids experience no symptoms, some may have heavy periods, pelvic pain, or pressure.



What are uterine fibroids?

> Fibroids are made of muscle and other tissues that grow in and around the uterine wall.

> They can be located within the uterine wall (intramural), inside the uterine cavity (submucosal), or on the outer surface of the uterus (sub-serosal).

> Some fibroids are connected to the uterus by a stalk (pedunculated).

> Fibroids are generally not cancerous and do not increase the risk of uterine cancer.

Symptoms of uterine fibroids:

>Heavy or prolonged menstrual bleeding: This is a common symptom, especially with submucosal fibroids.

>Pelvic pain or pressure: This can range from a dull ache to a feeling of fullness or pressure in the lower abdomen.

>Frequent urination or difficulty emptying the bladder: Larger fibroids can press on the bladder.

>Constipation or pain during bowel movements: Fibroids can sometimes press on the bowel.

>Painful intercourse: Some women experience pain or discomfort during sexual activity.

>Infertility or pregnancy complications: In some cases, fibroids can affect fertility or increase the risk of miscarriage or premature birth.

Causes of uterine fibroids:

>The exact cause of fibroids is unknown, but they are influenced by hormones (estrogen and progesterone) and genetics.

>Fibroids tend to grow during the reproductive years when hormone levels are high and may shrink after menopause.

Risk factors for uterine fibroids:

>Age: Fibroids are more common in women in their 30s and 40s.

>Race/ethnicity: Black women are more likely to develop fibroids at a younger age and experience more severe symptoms.

>Family history: Having a mother or sister with fibroids increases the risk.

>Obesity and high blood pressure: These conditions may also be associated with an increased risk.

>Vitamin D deficiency: Low vitamin D levels may be a risk factor.

Diagnosis of uterine fibroids:

>Pelvic exam: A doctor can feel for enlarged uterus or fibroids during a pelvic exam.
>Ultrasound: Ultrasound is a common and readily available imaging test that can help visualize fibroids and determine their size and location.
>Other imaging tests: MRI or other imaging tests may be used to further evaluate fibroids.

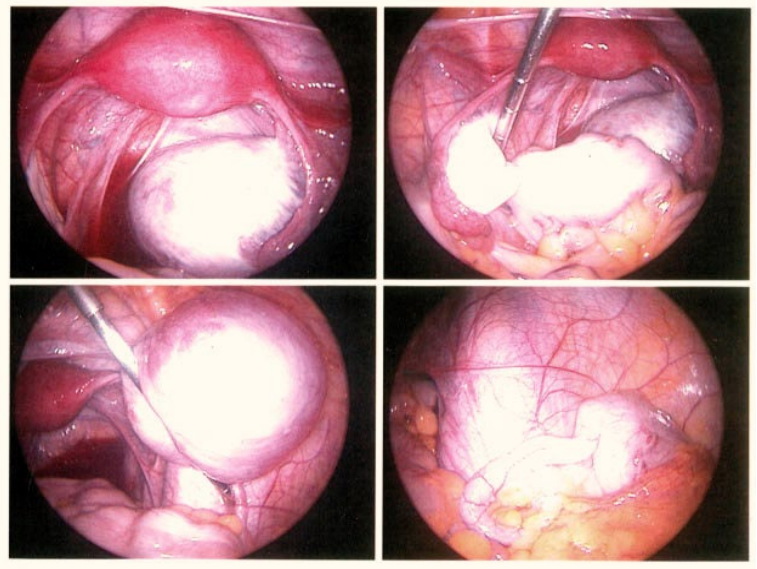
Treatment of uterine fibroids:
>M**edications:** Medications can help manage symptoms such as heavy bleeding and pain.
>Surgical and non-surgical procedures: If medications are not effective, procedures like uterine artery embolization, myomectomy (surgical removal of fibroids), or hysterectomy (surgical removal of the uterus) may be considered.

Watchful waiting: If fibroids are not causing symptoms, treatment may not be necessary, and the fibroids may shrink on their own after menopause.

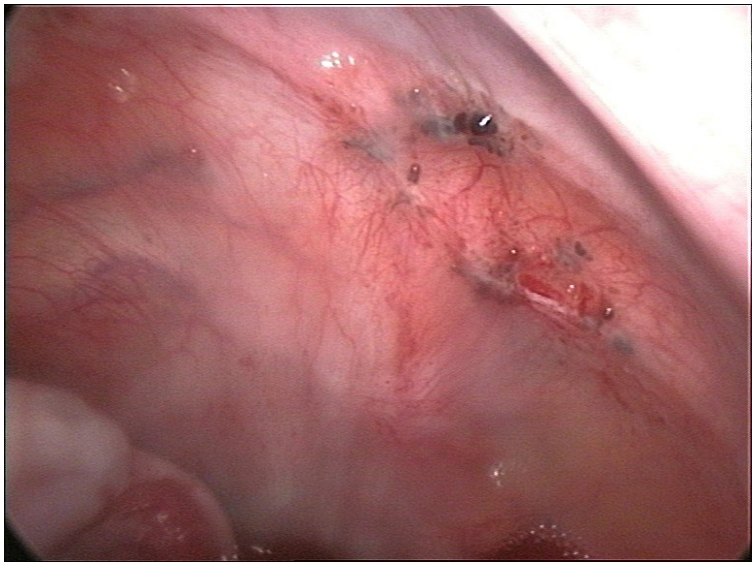
Endometriosis

Endometriosis (en-doe-me-tree-O-sis) is an often-painful disorder in which tissue that normally lines the inside of your uterus — the endometrium — grows outside your uterus.

Endometriosis most commonly involves your ovaries, fallopian tubes and the tissue lining your pelvis.

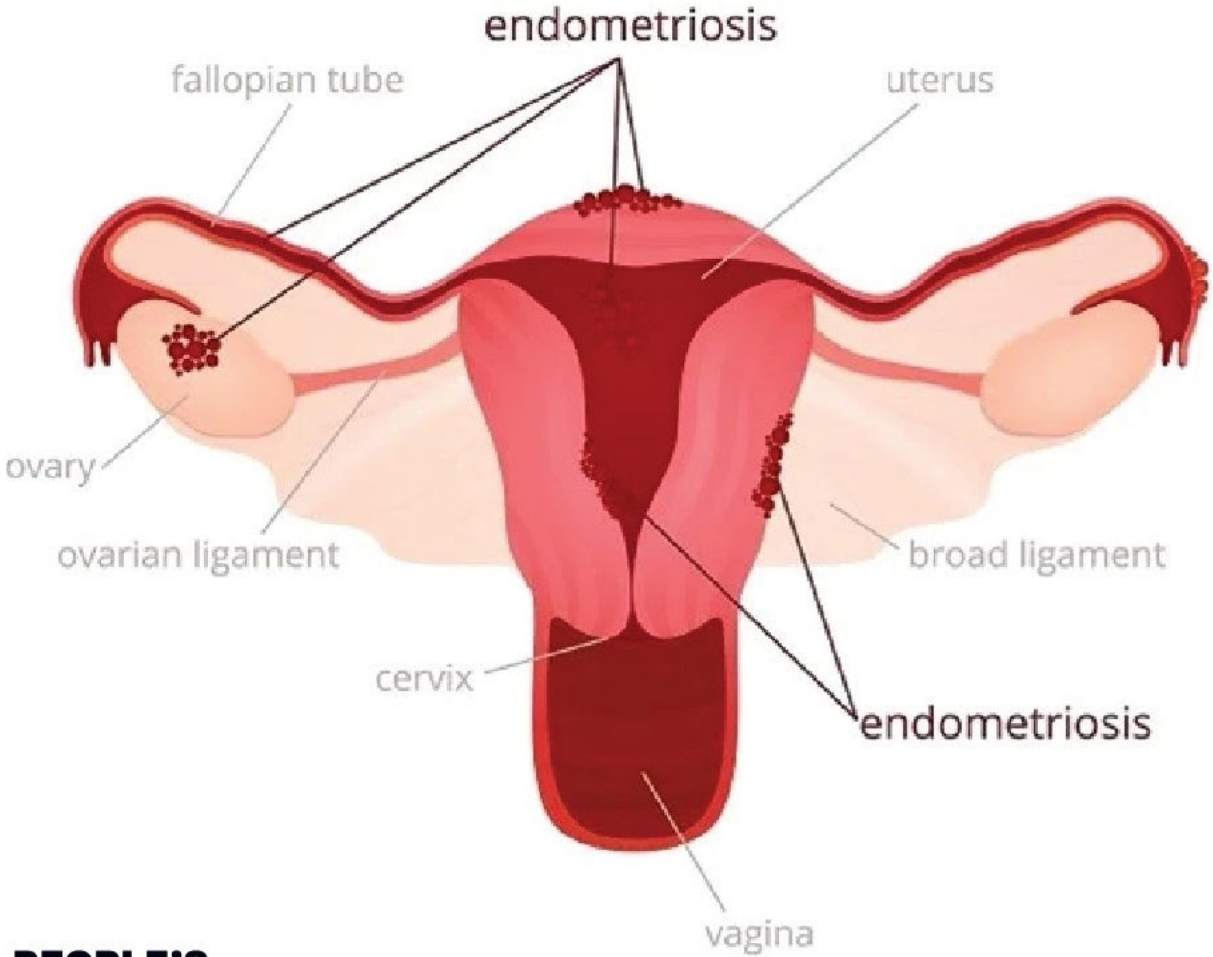


Endometriotic cyst on ovary



Endometriotic lesions at the peritoneum of the pelvic wall

ENDOMETRIOSIS



PEOPLE'S COMMUNITY CLINIC

Hormones regulate the female reproductive system. You will need to describe site of production, target tissues, and outcomes for these hormones.

–Gonadotropin Releasing Hormone
–Follicle stimulating hormone (FSH)
–Luteininzing hormone (LH) or interstitial cell stimulating hormone (ICSH)
–Human chorionic gonadotropin (hCG)
–Prolactin
–Oxytocin
–Estrogen
–Progesterone
–Inhibin
–Testosterone
–Relaxin

Most of these hormones have functions in both male and female reproductive physiology, however. These hormones may have different target tissues resulting in different types of outcomes in female and male reproductive physiology.

Gonadotropin Releasing Hormone

This hormone starts the sexual cycle in both males and females

GRH produced by nuclei in the hypothalamus // these nuclei mature more slowly

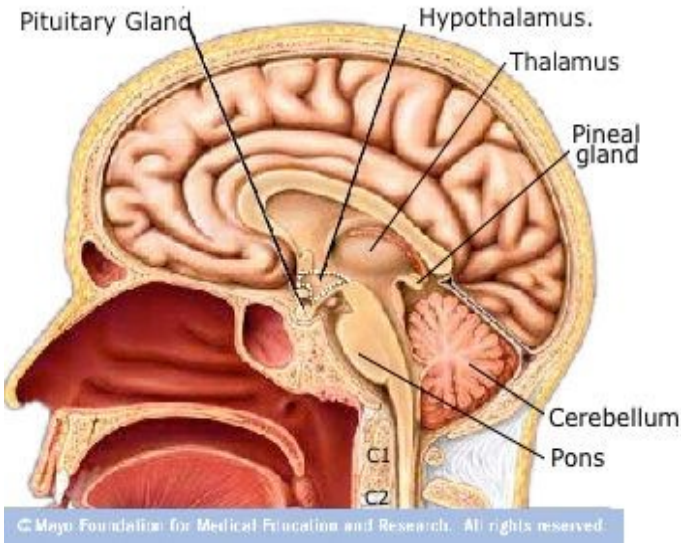
Hormone secretions begins after nuclei completes development – this initiates puberty

GRH target tissue is anterior pituitary (via portal system)

Stimulates release of follicle stimulating hormone and luteinizing hormone from anterior pituitary

GRH has similar function in male and female physiology....however

LH and FSH different target tissue in genders // female ovaries // male testes



GRH is released later in males and earlier in females

Female occurs at 10 to 14

Male occurs at 12 to 16

Follicle Stimulating Hormone (FSH) - Females

FSH produced by anterior pituitary

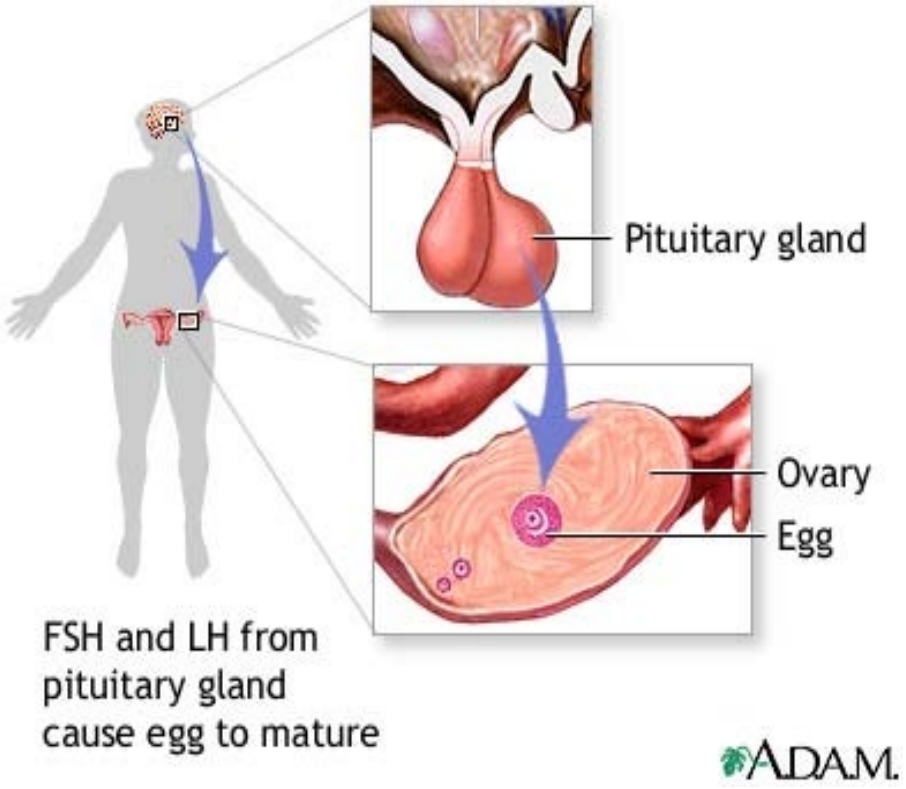
Target tissue = primoidal eggs in ovaries

Stimulates growth of follicles (early stages of ovum = egg)

Stimulate follicles to secrete estrogen

Only one follicle will be up-regulated with FSH receptors // follicular phase

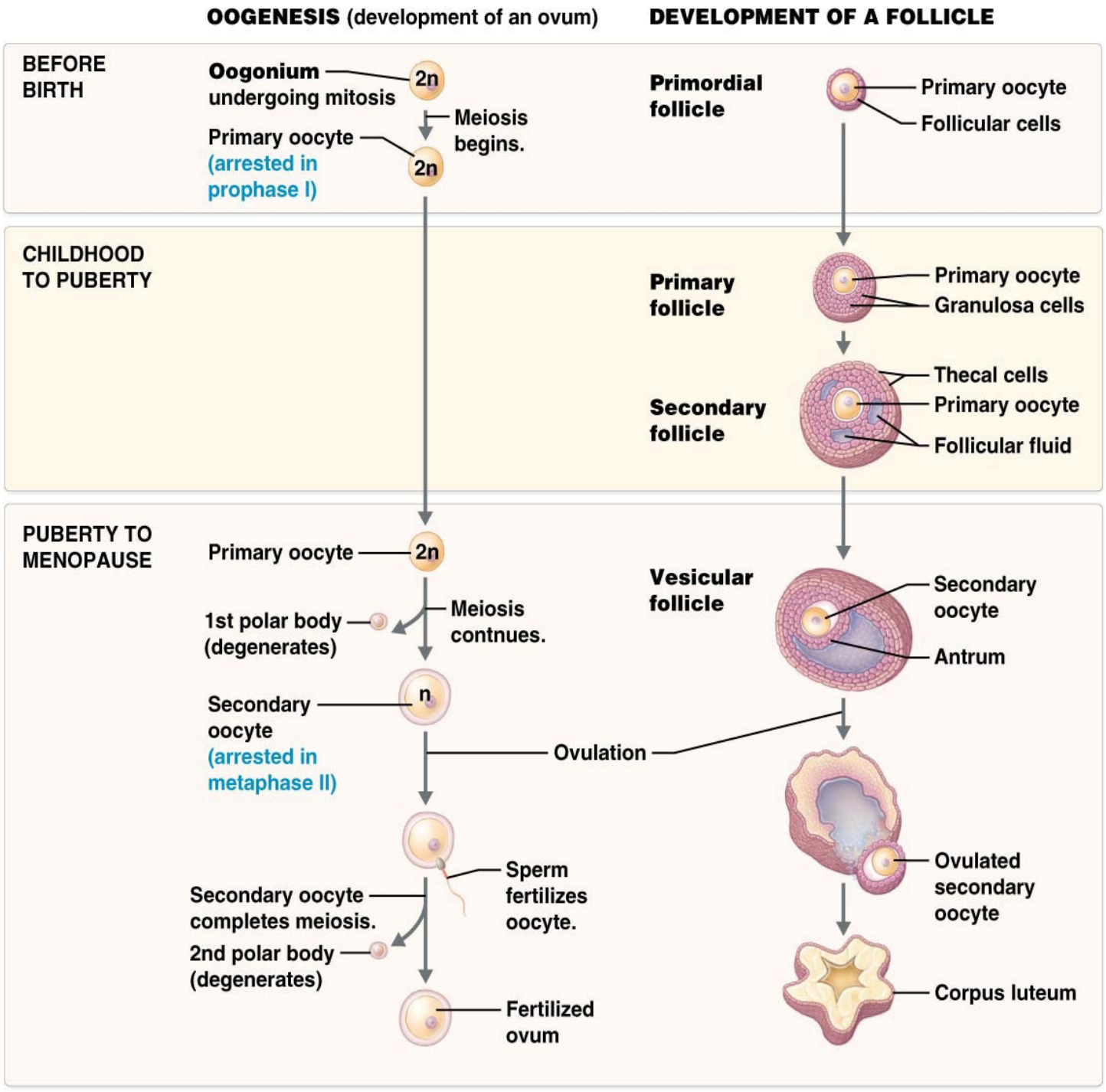
The follicle with the most receptors continues to grow and will become a Graafian follicle // the egg in this follicle to be fertilized!



There are 8 million oogoniums before birth (4 million primary oocytes per ovary).

By puberty, the number of primary oocytes will reduce to 400,000 per ovary. // 90% die by apoptosis.

Only about 400 primary oocytes will reach maturity and ovulate during a woman's reproductive lifetime.



Luteininzing hormone (LH) - Females

LH produced by anterior pituitary

Target tissue = mature egg in ovary

Spike in LH production near day 14 initiates ovulation

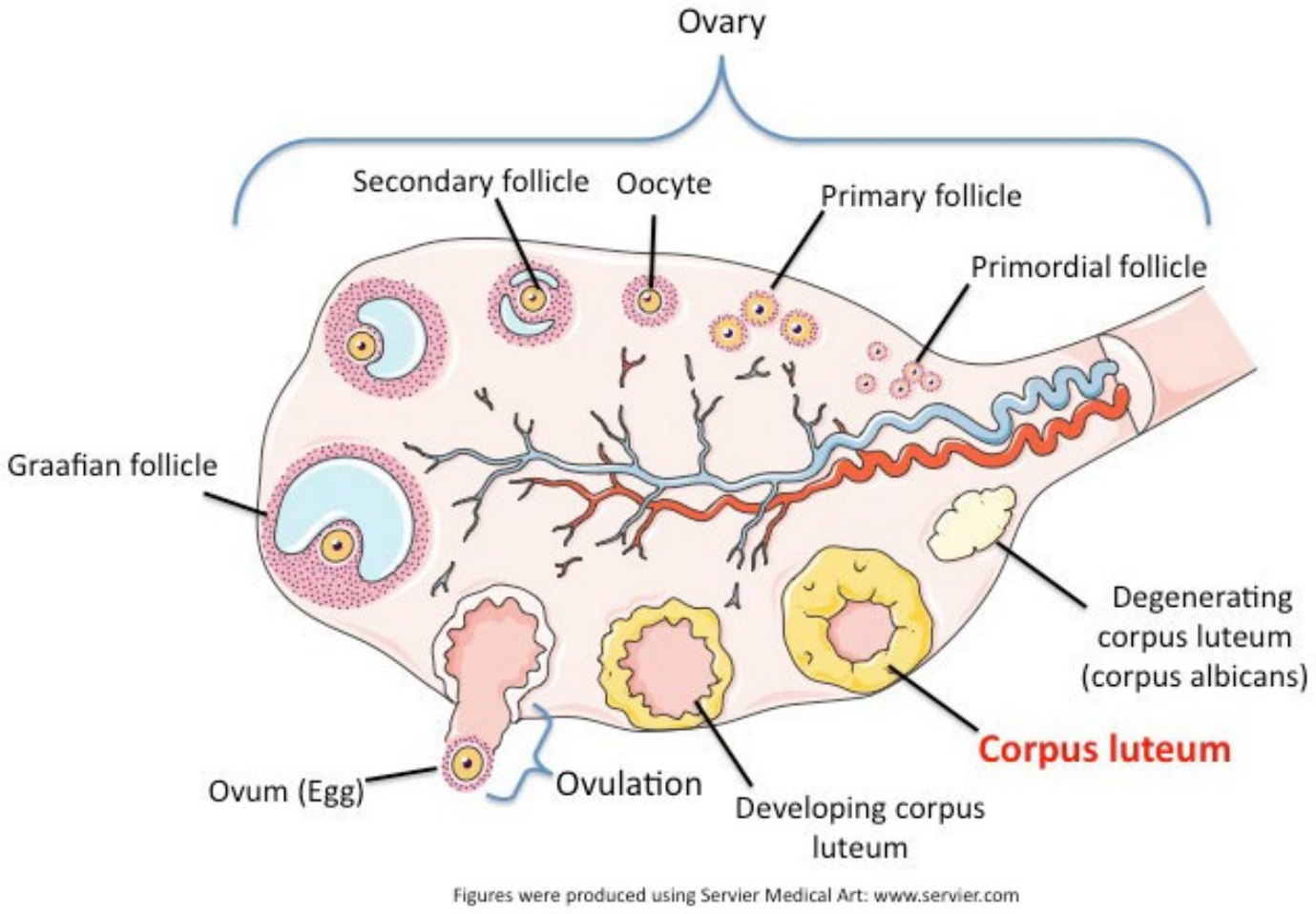
LH also binds to follicular cells remaining on surface of ovary and converts follicular cells into corpus luteum

Corpus luteum secretes inhibin, relaxin, progesterone (and small amount of estrogen)

This starts the luteal phase of the ovarian cycle / second 14 days of ovary cycle

Stages In Egg Development

FSH during first 14 days // LH surge causes release of egg (ovulation) and formation of the corpus luteum.



Corpus luteum secretes inhibin, relaxin, progesterone (and small amount of estrogen)

Estrogen - Female

Released from different tissues at different times during the sexual cycle and throughout pregnancy (follicles, corpus luteum, placenta)

FSH stimulate primordial follicles in ovary to produce estrogen

After ovulation, corpus luteum produces estrogen as well as progesterone, relaxin, and inhibin

After CL stops producing hormones then placenta begins to produces estrogen, relaxin, and progesterone (as well as other hormones)

Estrogen has multiple functions:

- development of secondary sexual characteristics
- tissue growth in mammary glands
- responsible for proliferation phase of the menstrual (uterine) cycle
- makes cervical canal less viscous ("opens cervical canal" // allow sperm to enter uterus)
- mimics the effects of aldosterone (water retention)

Progesterone - Female

Released from different tissues at different times during the sexual cycle and pregnancy

Produced first by corpus luteum and later by placenta

Maintains endometrium /// need to determine if egg will be fertilized and if a placenta can be established

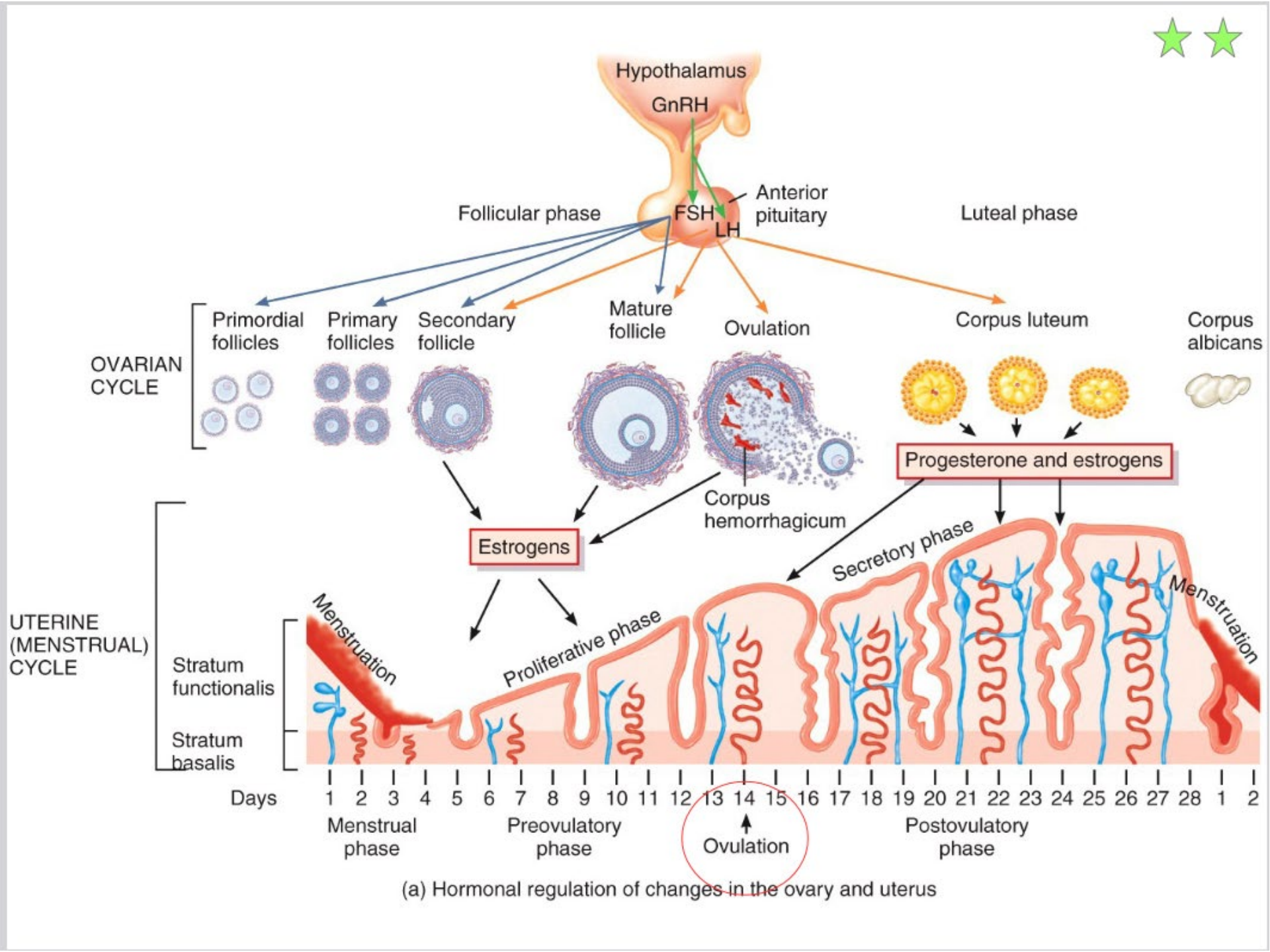
Responsible for secretory phase of the menstrual cycle

If placenta is established, then placenta will produce progesterone and corpus luteum is no longer needed – becomes corpus albicans

Multiple functions: development of secondary sexual characteristics / tissue growth in mammary glands (ducts) / secretory phase of the menstrual cycle

Diuretic effect – water loss // opposite effect of estrogen

Makes cervical canal more viscous // "the cervical plug"



(a) Hormonal regulation of changes in the ovary and uterus

Morula reaches end of fallopian tube after 72 hours (3rd day).

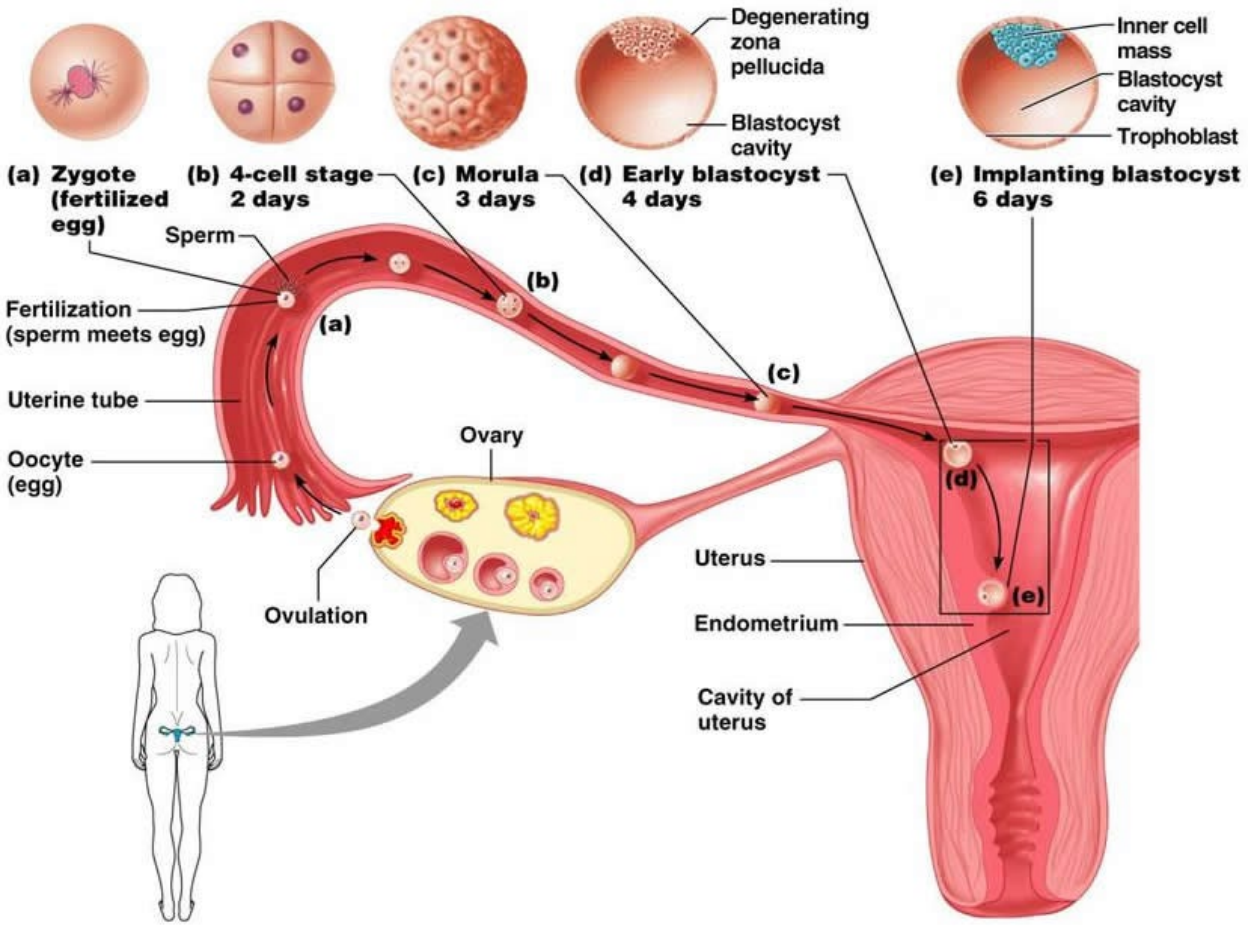
Blastocyst stays in uterus lumen for seven days.

Uterine mucosa sweats nutrients (uterine milk) to “feed” blastocyte

Implants into endometrium on day 10.

Placenta is not functional until after the eighth week.

By the **end of the eighth week**, the embryo has developed the basic structures of all major organs and begins to take on a more recognizable human shape, marking the official transition to the fetal stage



Blastocyste secretes human chorionic gonadotropin by the fourth day after fertilization // this stimulates corpus luteum to continue progesterone secretion to maintain stratum faciculus // hCG maybe detected in the woman’s urine and is used as the home pregnancy test

Human chorionic gonadotropin (hCG) - Female

Produced by blastocyte (fertilized egg first becomes a zygote then undergoes mitosis to become a blastocyte)

Able to measure HCG in blood and in urine four days after fertilization of ovum // this is the home pregnancy test

Target tissue is corpus luteum // Stimulates CL to continue to production of progesterone

Progesterone required to maintains endometrium (maintains pregnancy)

After placenta developed, placenta will continue to secrete progesterone

Corpus luteum is no longer required to secrete progesterone // corpus luteum turns into corpus albicans (scar tissue)

Blastocyte attaches to endometrium at day 10 to initiate the formation of the placenta

Placenta is the organ used to exchange nutrients and metabolic waste between mother and conceptus // nicknamed the fetus first organ

Placenta fully developed at week 8 – before this time the conceptus gets nutrients from digested endometrial cells and "uterine milk" /// secretions from endometrial glands

As the placenta develops, it secretes several hormones that maintain pregnancy and alter female physiology

–Estrogen

–Progesterone

–Human chorionic gonadotropin (hCG) – stops secretion after wk 12

–Relaxin

–Placental prolactin

–Placental lactogen

–Other recently discovered hormones not included

What is the fertility window?

The fertile window is the period during which it is possible to become pregnant after sex.

This is the day of ovulation plus the time sperm can live inside the cervix before it fertilizes the egg. The ovum is only viable for 24 hours. Sperm are viable in female reproductive tract for up to seven days.

According to the American College of Obstetricians and Gynecologists (ACOG), a person can become pregnant if they have sex **anywhere from 5 days before until 1 day after ovulation.**

(Test Answer: 5 days before ovulation to 1 day after ovulation)

Depending on the menstrual cycle, the fertile window may vary from one person to another.

Prolactin - Female

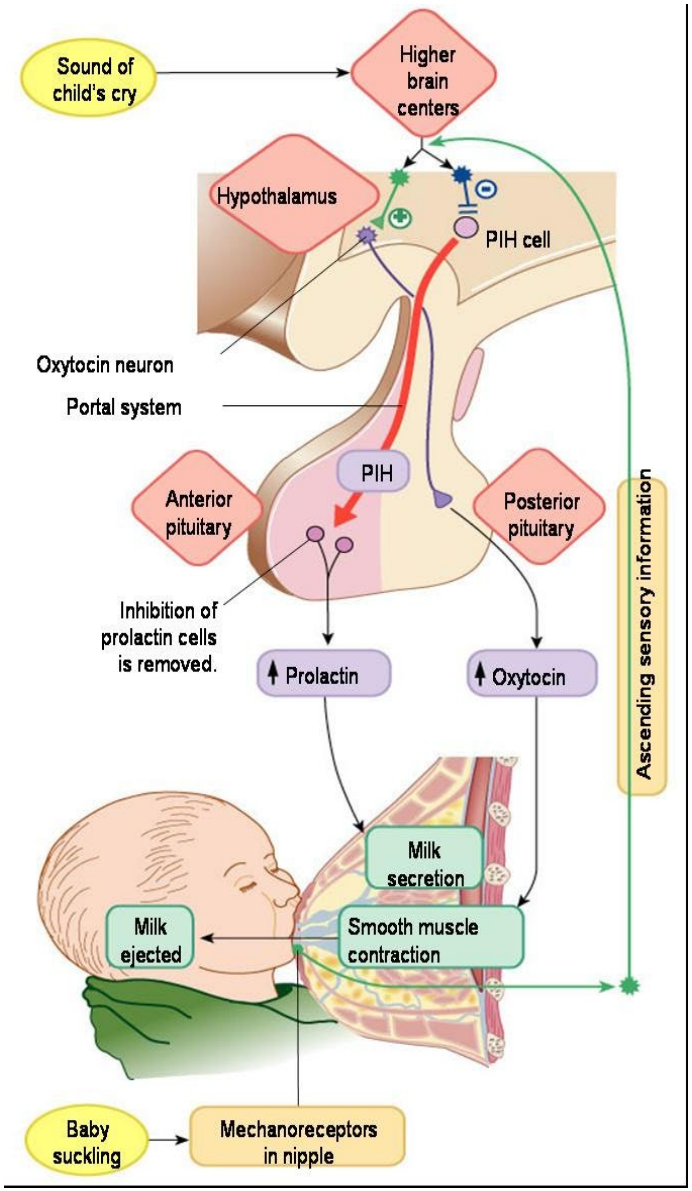
Released from anterior pituitary // normally inhibited until after birth

Target tissue = epithelial glandular cells of the mammary gland

Mammary gland needs to be "primed" by estrogen and progesterone // cell differentiation and cell growth

This occurs during pregnancy

Prolactin stimulates the glands' ability to make milk



Oxytocin - Female

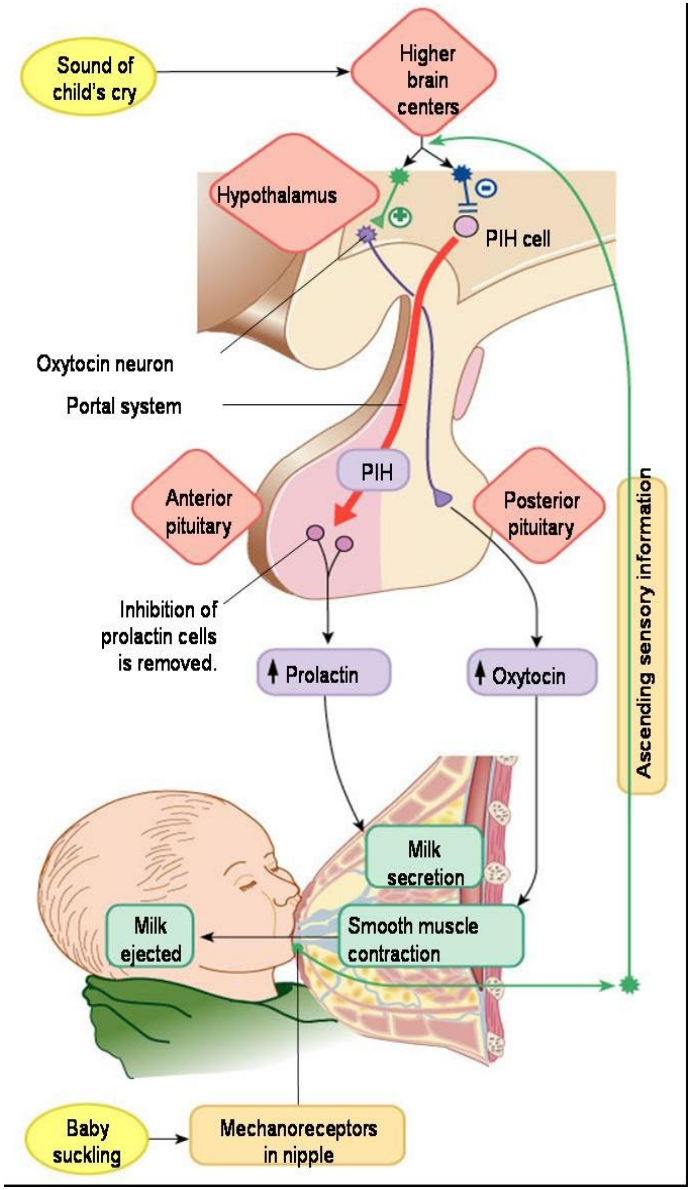
Released from posterior pituitary

Two different "neuroendocrine reflexes"

Receptors located on myometrium of uterus // parturition reflex

Receptors located on smooth muscle associated with mammary gland // milk let down reflex

Receptors in brain // emotional bonding // psychological bonding between mother and baby



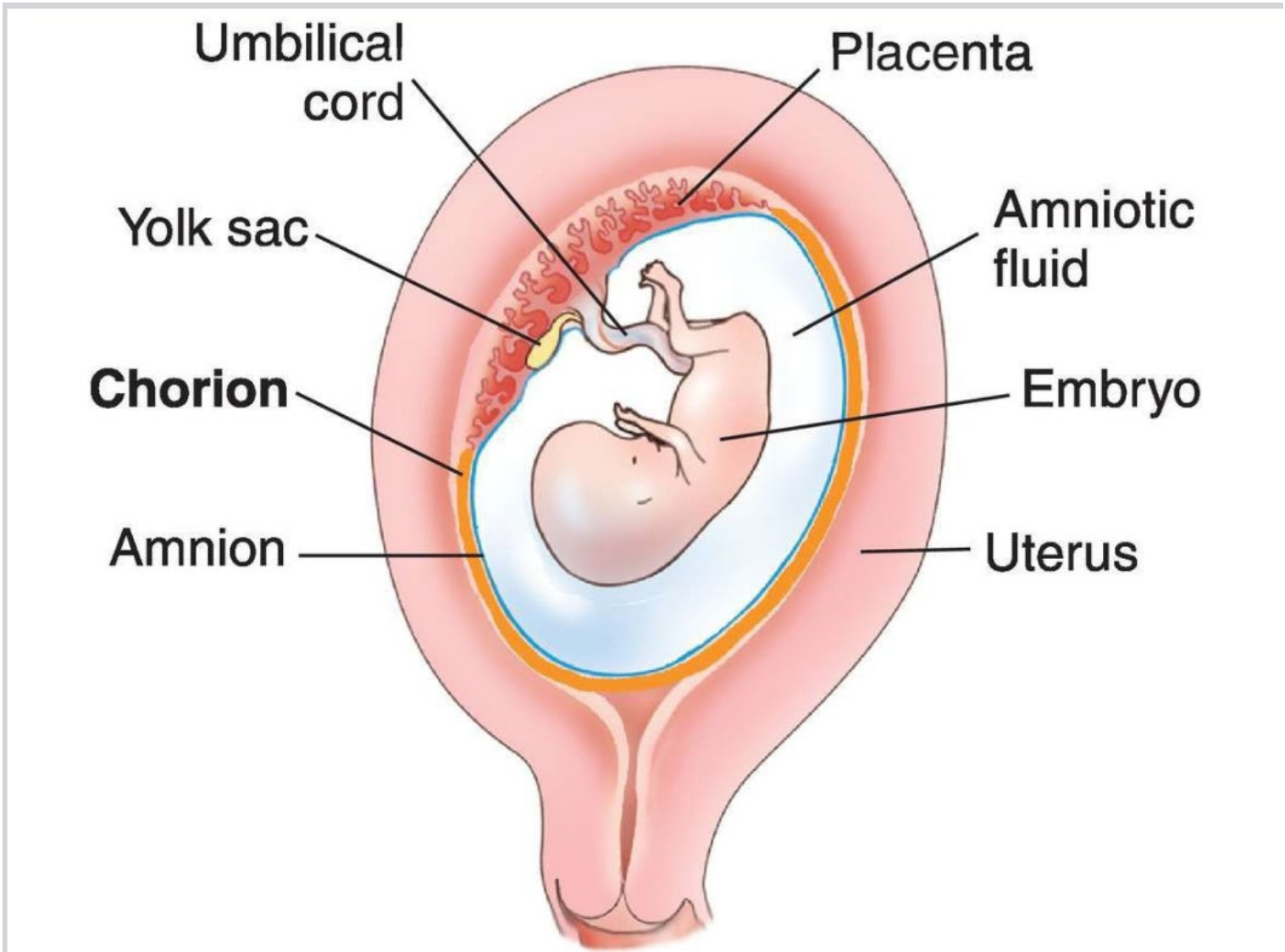
Inhibin - Female

- Secreted by corpus luteum
- Target tissue - anterior pituitary
- Inhibits the release of FSH // this delays the start of a new cycle (note – estrogen also inhibits FSH)
- The delay is needed to determine if zygote will implant in endometrium and to determine if the pregnancy is still viable

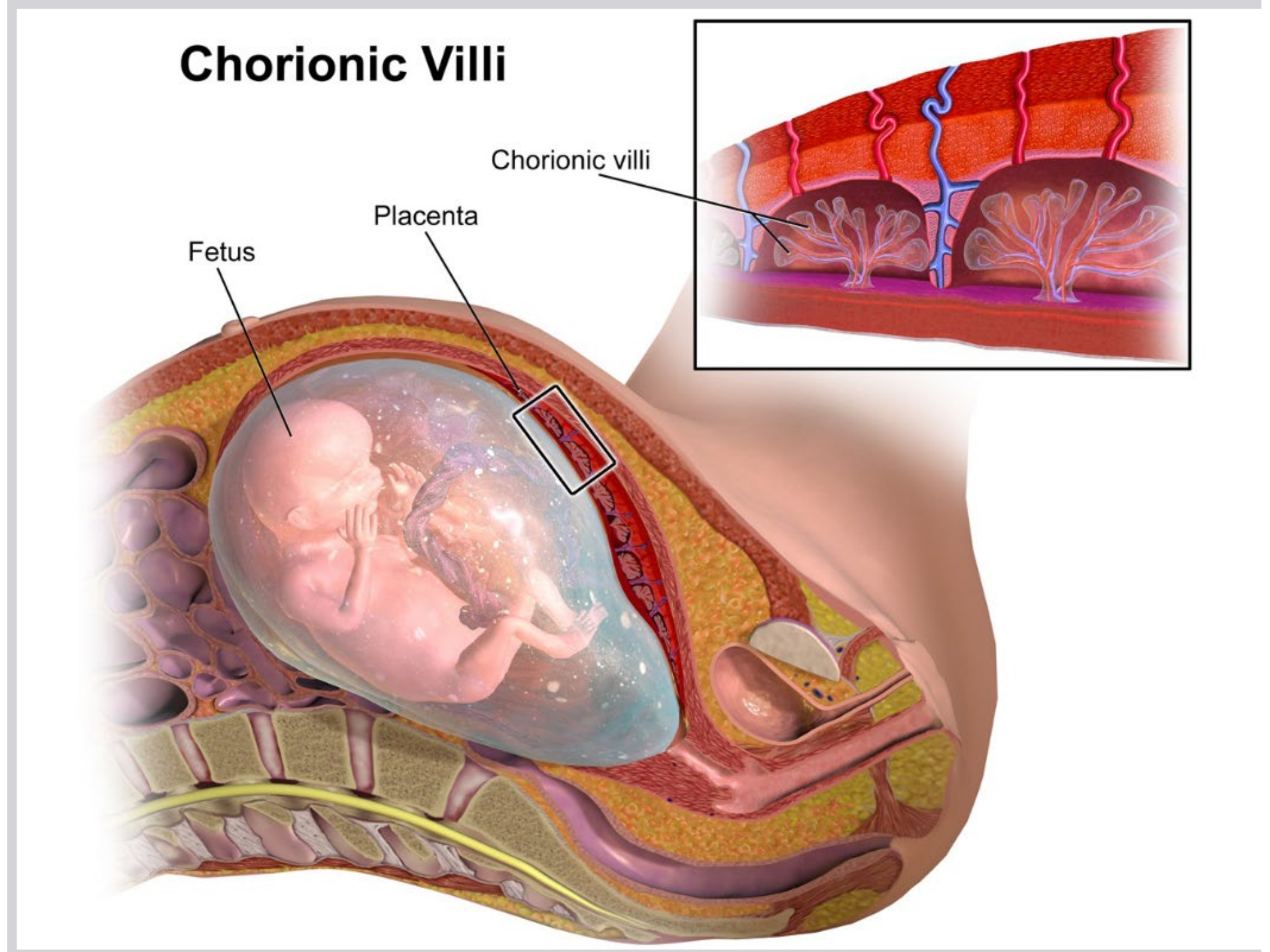
Relaxin - Female

- Produced first by corpus luteum and then later by placenta
- First effect is to “quiet” uterine contraction // therefore aids in the implantation of blastocyte
- Late in pregnancy (just before parturition), the hormone “softens” the connective tissue in the pelvic girdle // this prepares the pelvic girdle for parturition

Uterus and Placenta



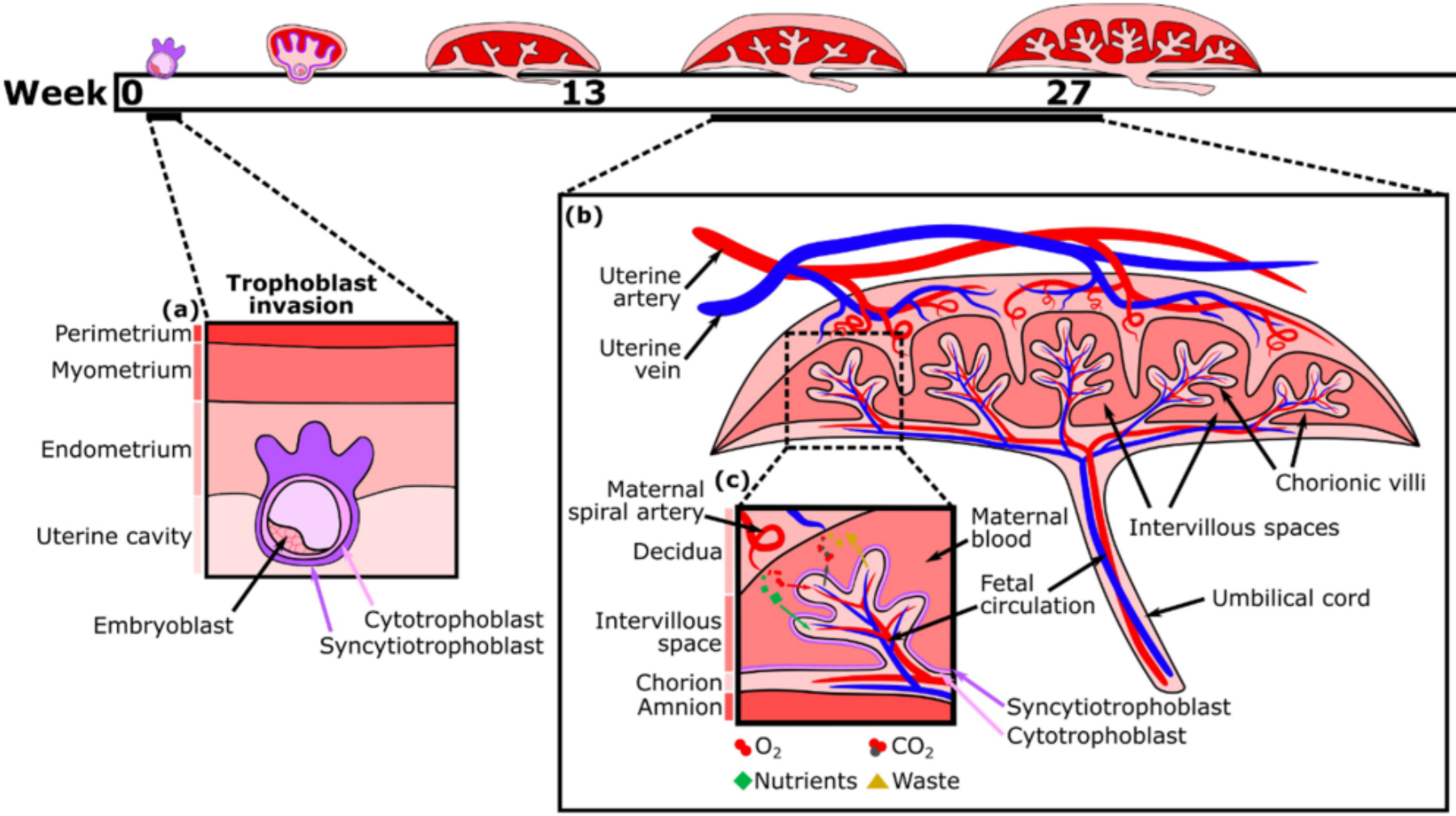
Chorionic Villi

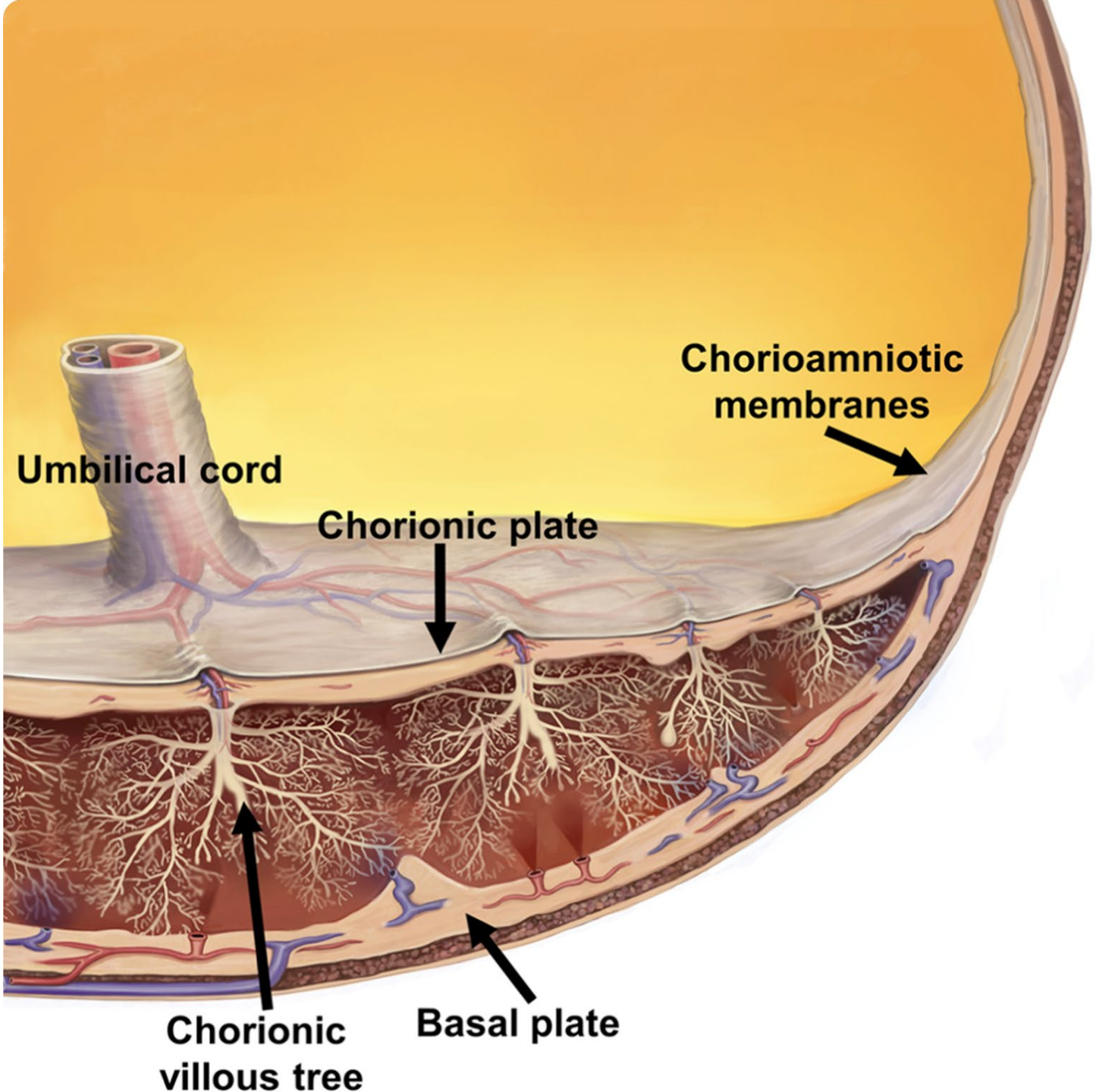


The placenta is the “baby's first organ”

It is the embryonic tissues from the embryo that grows into the maternal endometrium to form union with maternal blood vessels.




Week
0
13
27
40
(a)
Trophoblast invasion
Perimetrium
Myometrium
Endometrium
Uterine cavity
Embryoblast
Cytotrophoblast
Syncytiotrophoblast
(b)
Uterine artery
Uterine vein
Chorionic villi
Intervillous spaces
Umbilical cord
(c)
Maternal spiral artery
Decidua
Intervillous space
Chorion
Amnion
Maternal blood
Fetal circulation
Syncytiotrophoblast
Cytotrophoblast
O_2
CO_2
Nutrients
Waste


Chorioamniotic membranes
Umbilical cord
Chorionic plate
Chorionic villous tree
Basal plate

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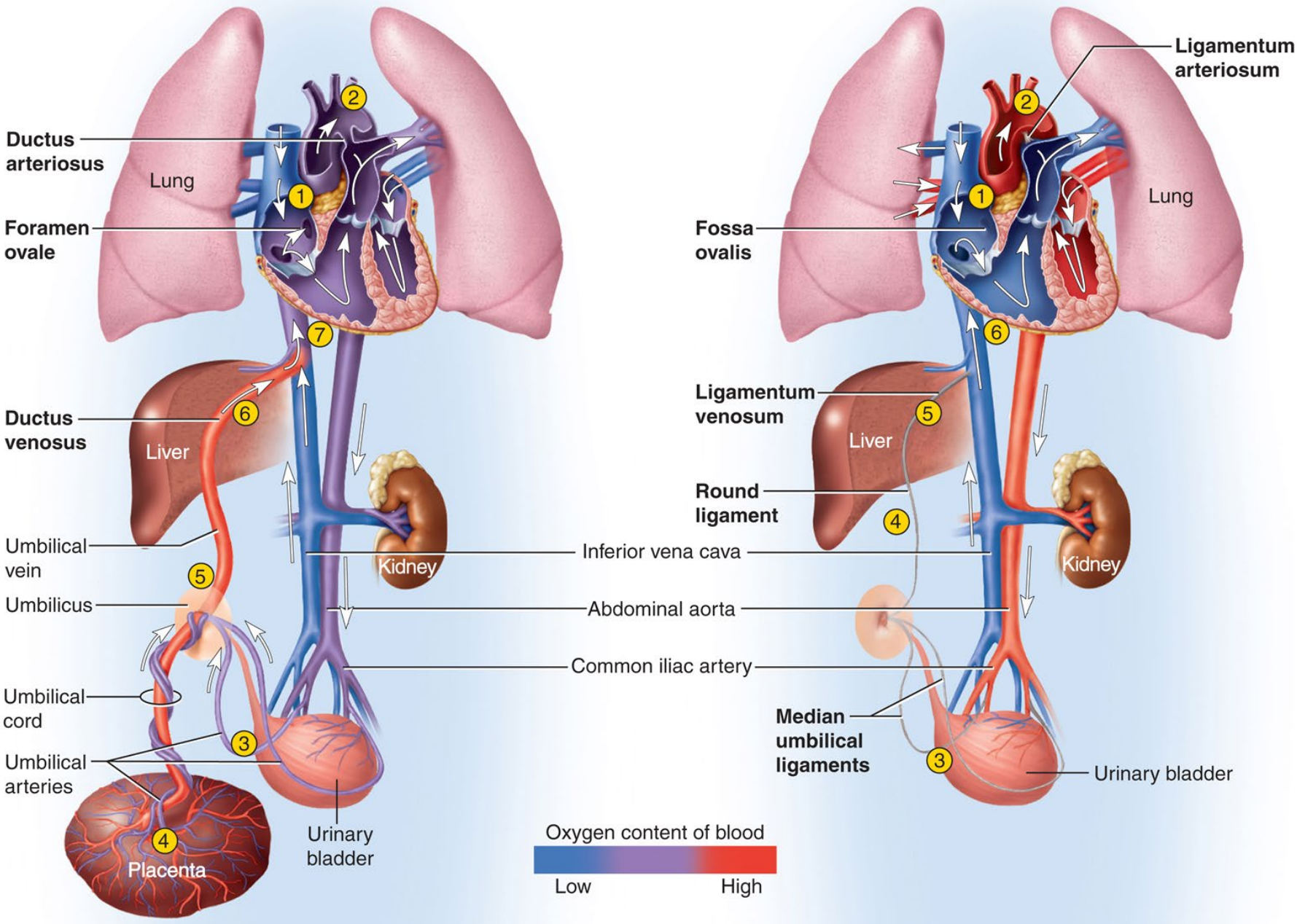

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As the placenta develops, it secretes several hormones that maintain pregnancy and alter female physiology

–Estrogen

–Progesterone

–Human chorionic gonadotropin (hCG) – stops secretion after wk 12

–Relaxin

–Placental prolactin

–Placental lactogen

–Other recently discovered hormones not included

What hormones are produced by the placenta?

The placenta produces estrogen and progesterone. Progesterone acts to maintain pregnancy by supporting the lining of the uterus (womb), which provides the environment for the fetus and the placenta to grow.

Progesterone prevents the shedding of this lining (similar to that which occurs at the end of a menstrual cycle), since this would result in pregnancy loss.

Progesterone also suppresses the ability of the muscular layer of the uterine wall to contract, which is important in preventing labor from occurring before the end of pregnancy.

Estrogen levels rise towards the end of pregnancy. Estrogen acts to stimulate the growth of the uterus to accommodate the growing fetus and allows the uterus to contract by countering the effect of progesterone. In this way, it prepares the uterus for labor

Estrogen also stimulates the growth and development of the mammary glands during pregnancy, in preparation for breastfeeding.

The placenta also releases other protein hormones. (see next slide).

What hormones are produced by the placenta?

The placenta also releases human chorionic gonadotrophin, human placental lactogen, placental growth hormone, relaxin and kisspeptin.

Human chorionic gonadotrophin is the first hormone to be released from the developing placenta. HCG was first secreted by the blastocyte at 72 hours and is measured in a pregnancy test.

HCG acts as a signal to the mother's body that pregnancy has occurred by maintaining progesterone production from the corpus luteum, a temporary endocrine gland found in the ovary.

The function of human placental lactogen is not completely understood, although, it is thought to promote the growth of the mammary glands in preparation for lactation. It is also believed to help regulate the mother's metabolism by increasing maternal blood levels of nutrients for use by the fetus.

A similar role is played by placental growth hormone, which predominates during pregnancy due to suppression of growth hormone produced by the maternal pituitary gland.

What hormones are produced by the placenta?

Relaxin causes the relaxation of pelvic ligaments and softening of the cervix at the end of pregnancy, which aids the process of labor

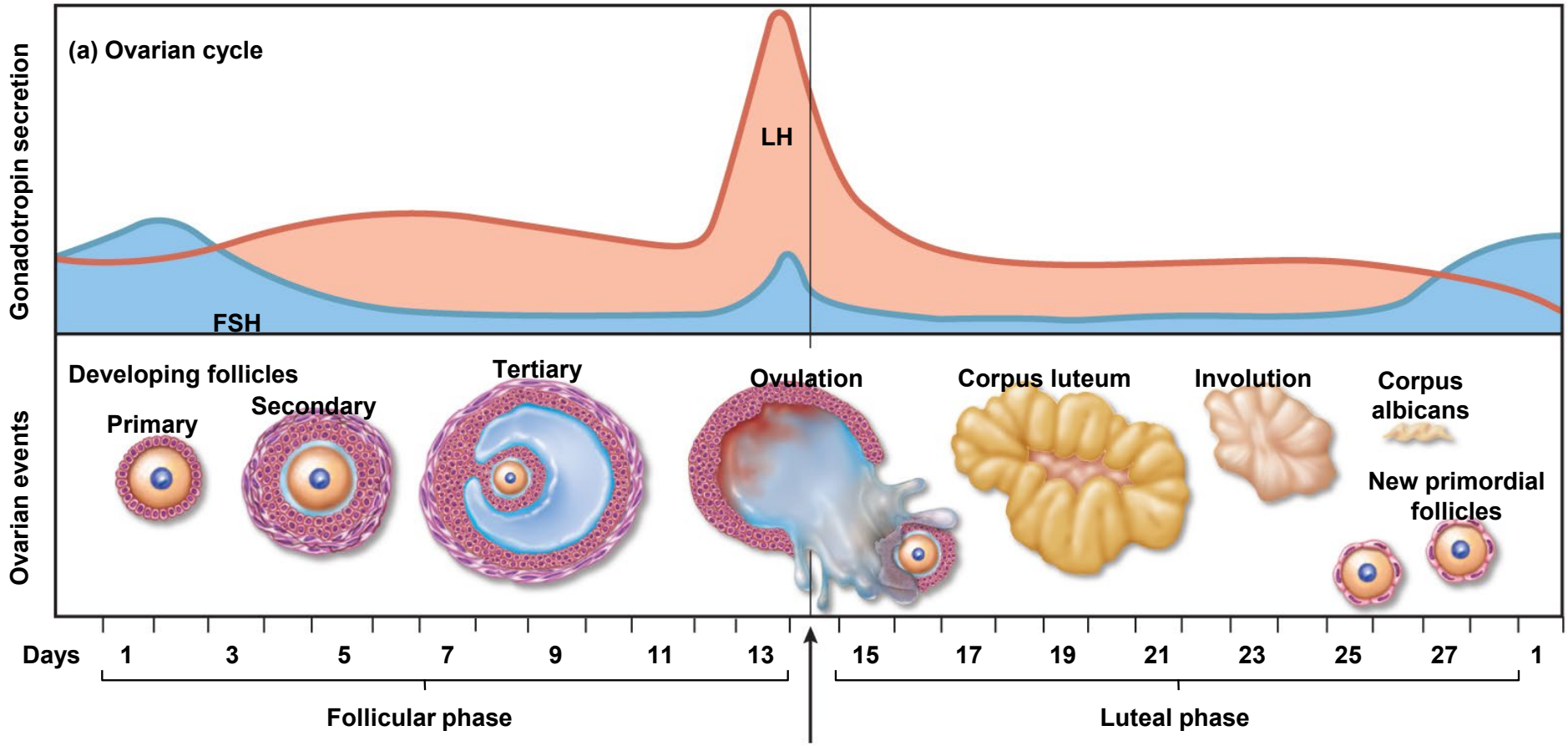
Kisspeptin is a recently identified hormone, which is important for many aspects of human fertility. In the placenta, kisspeptin appears to regulate placental growth into the lining of mother's womb (endometrium).

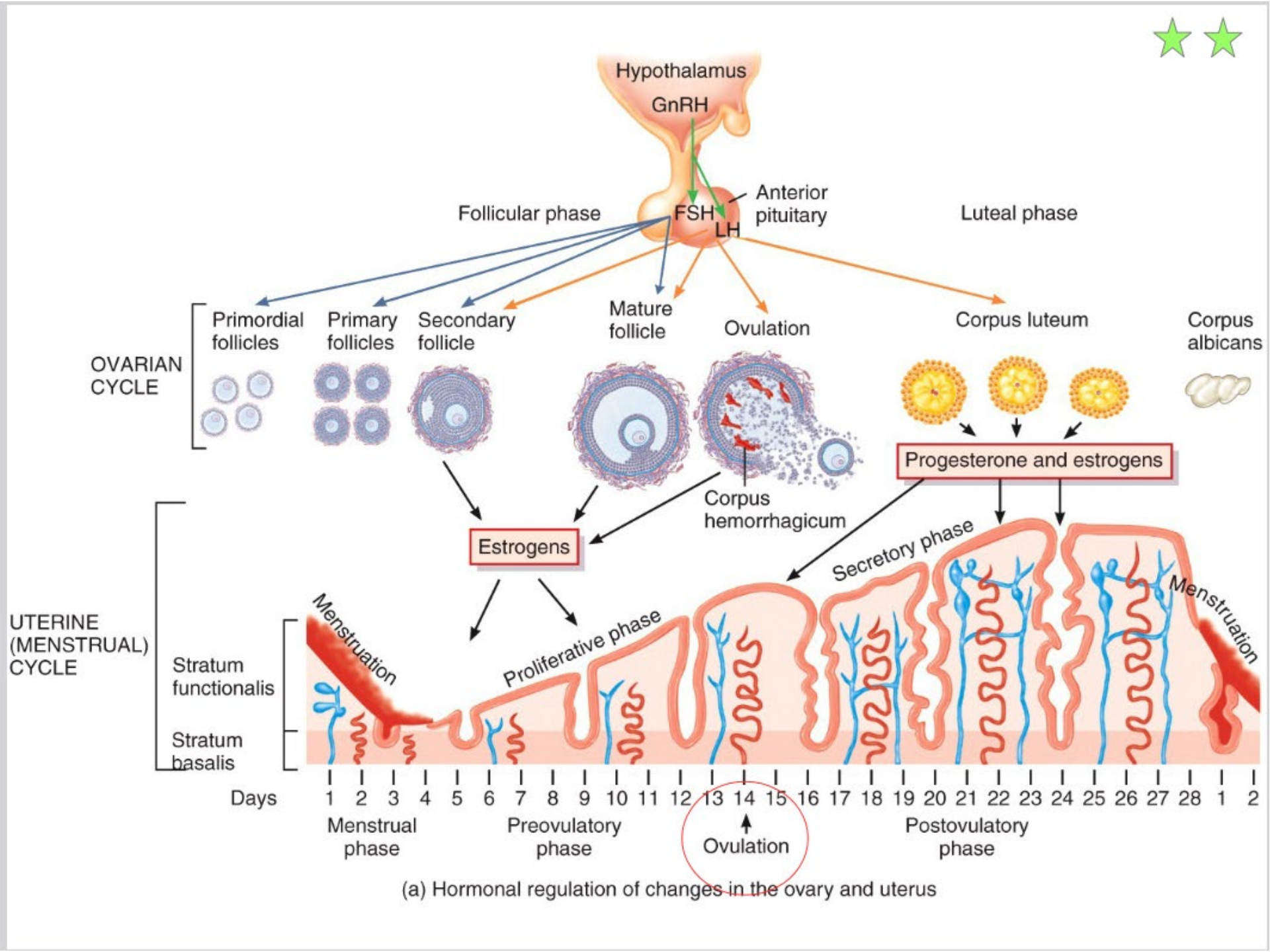
Several other peptide hormones have been recently identified to regulate blood vessel formation within the placenta, which is crucial in allowing the placenta to exchange nutrients from the mother to baby; these peptide hormones include soluble endoglin (sEng), soluble fms-like tyrosine kinase 1 (sFlt-1) and placental growth factor (PlGF).

Ovarian and Uterine Cycles

Ovaries Divided into Follicular & Luteal Phases

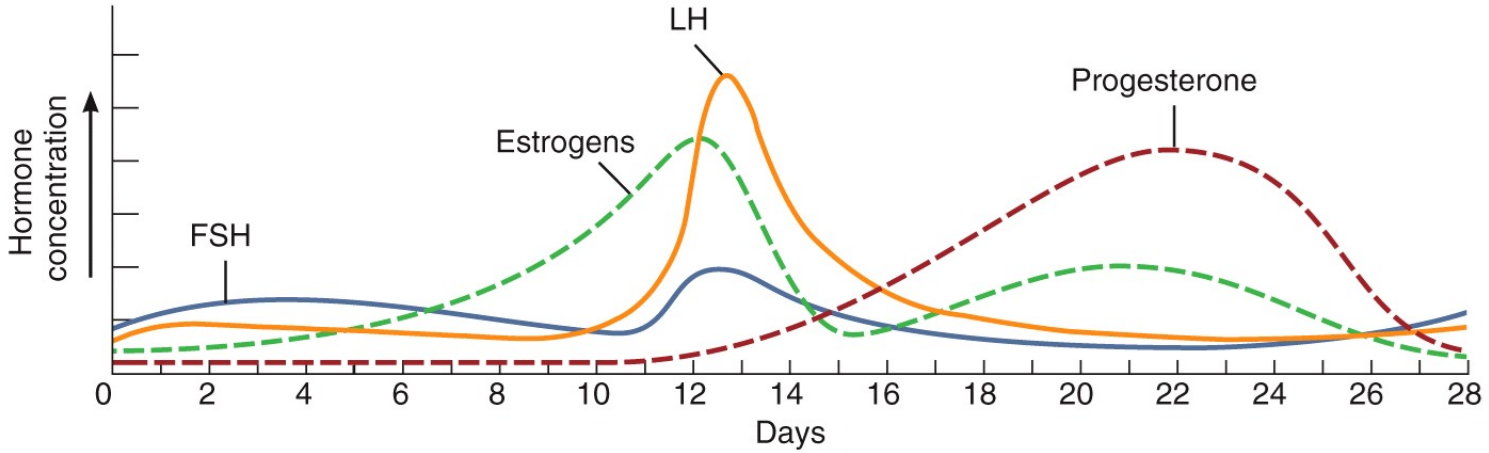
Uterus Divided into Proliferative & Secretory Phases





(a) Hormonal regulation of changes in the ovary and uterus

These Hormones Regulate Two Concurrent Cycles
The Ovarian Cycle and the Uterine Cycle



(b) Changes in concentration of anterior pituitary and ovarian hormones

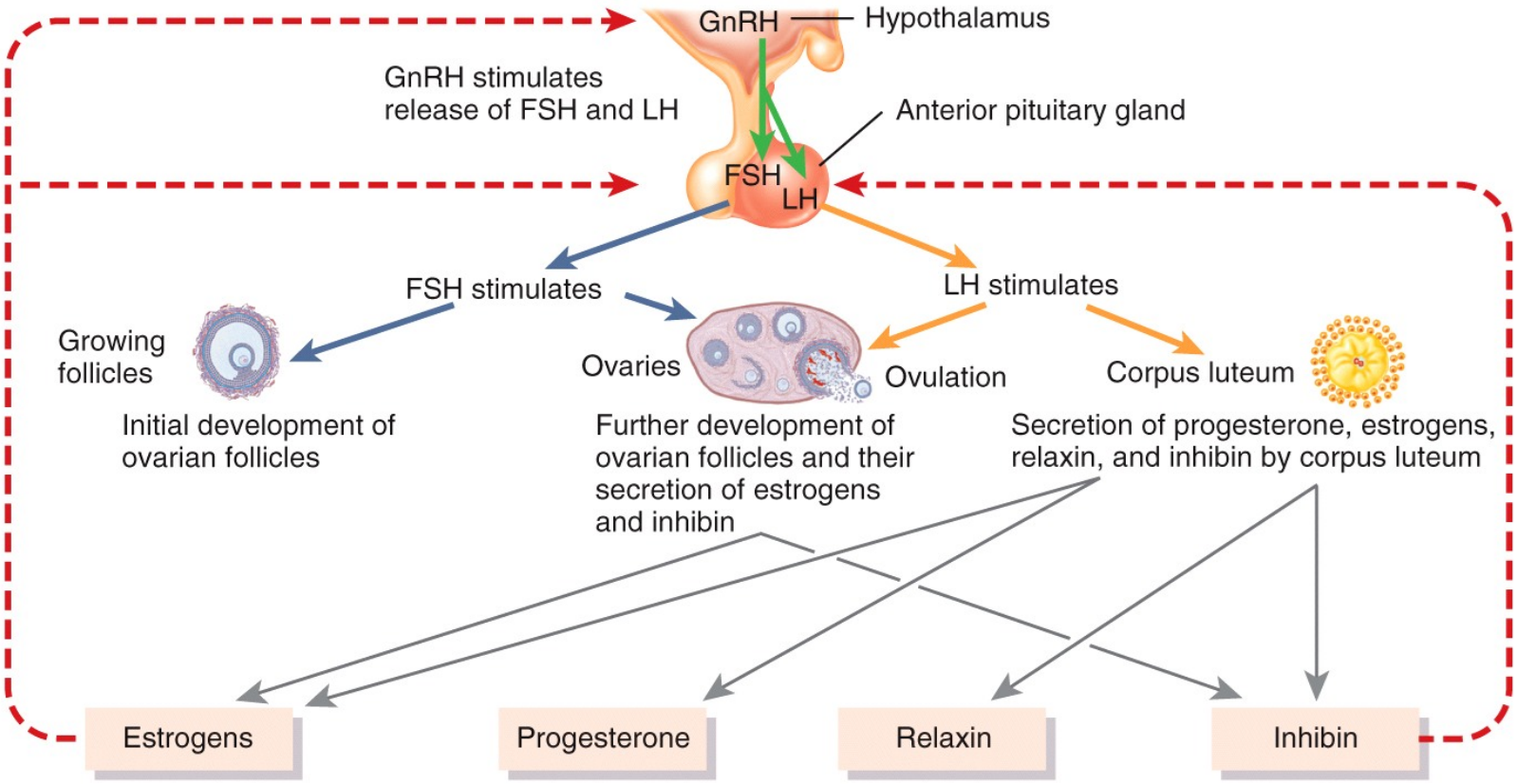
These secretions regulate both the ovarian cycle and the menstrual (uterine) cycle

The reproductive cycle describes what happens if a pregnancy occurs

The sexual cycle describes the events that occur if a pregnancy does not occur.

Ovarian Cycle

Study This Slide!



- Promote development and maintenance of female reproductive structures, feminine secondary sex characteristics, and breasts
- Increase protein anabolism
- Lower blood cholesterol
- Moderate levels inhibit release of GnRH, FSH, and LH

- Works with estrogens to prepare endometrium for implantation
- Prepares mammary glands to secrete milk
- Inhibits release of GnRH and LH

- Inhibits contractions of uterine smooth muscle
- During labor, increases flexibility of pubic symphysis and dilates uterine cervix

- Inhibits release of FSH and, to a lesser extent, LH

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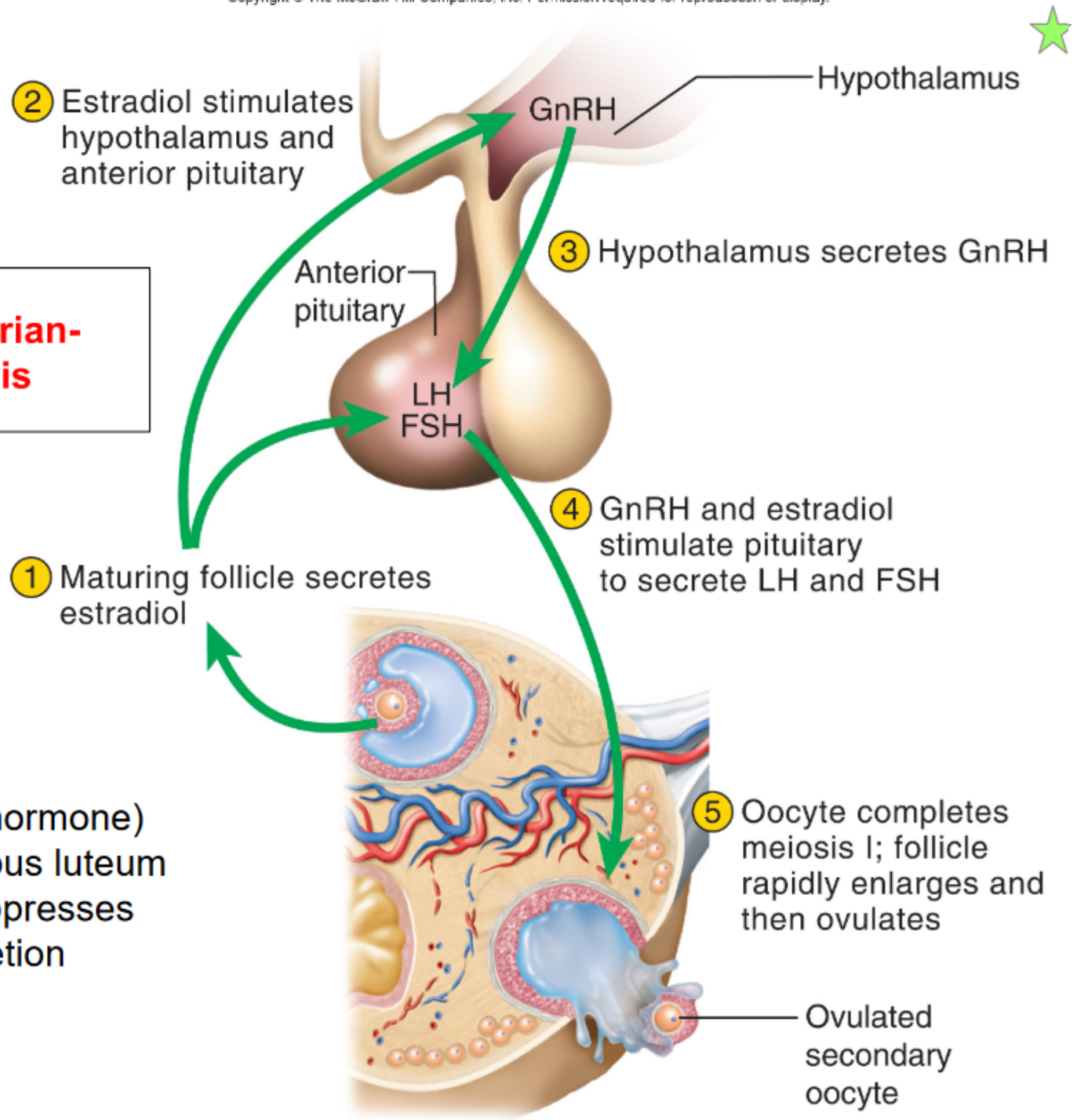
Pituitary-Ovarian-Uterine Axis



Note: Inhibin (hormone) secreted by corpus luteum selectively suppresses FSH secretion

The Menstrual or Uterine Cycle

The menstrual cycle is also referred to as the sexual cycle. It is approximately 28 days long and occurs when there is no pregnancy.

It is associated with changes in the tissues of the uterus

There are four phases: menstrual, proliferative, secretory, premenstrual.

The first phase starts on day one of the cycle with the discharge of blood

The menstrual cycle coincides with ovarian events associated with the development of the female gamete (ovum / egg)

Humans, chimpanzees, six species of bats, and elephant shrews are among the only animals on earth that have periods (i.e. mensis) !

All other mammals reabsorb their endometrium. Evolutionary physiologist study mensis to understand what might be the adaptive advantage of the period. (see The Point of a Period – Scientific American)



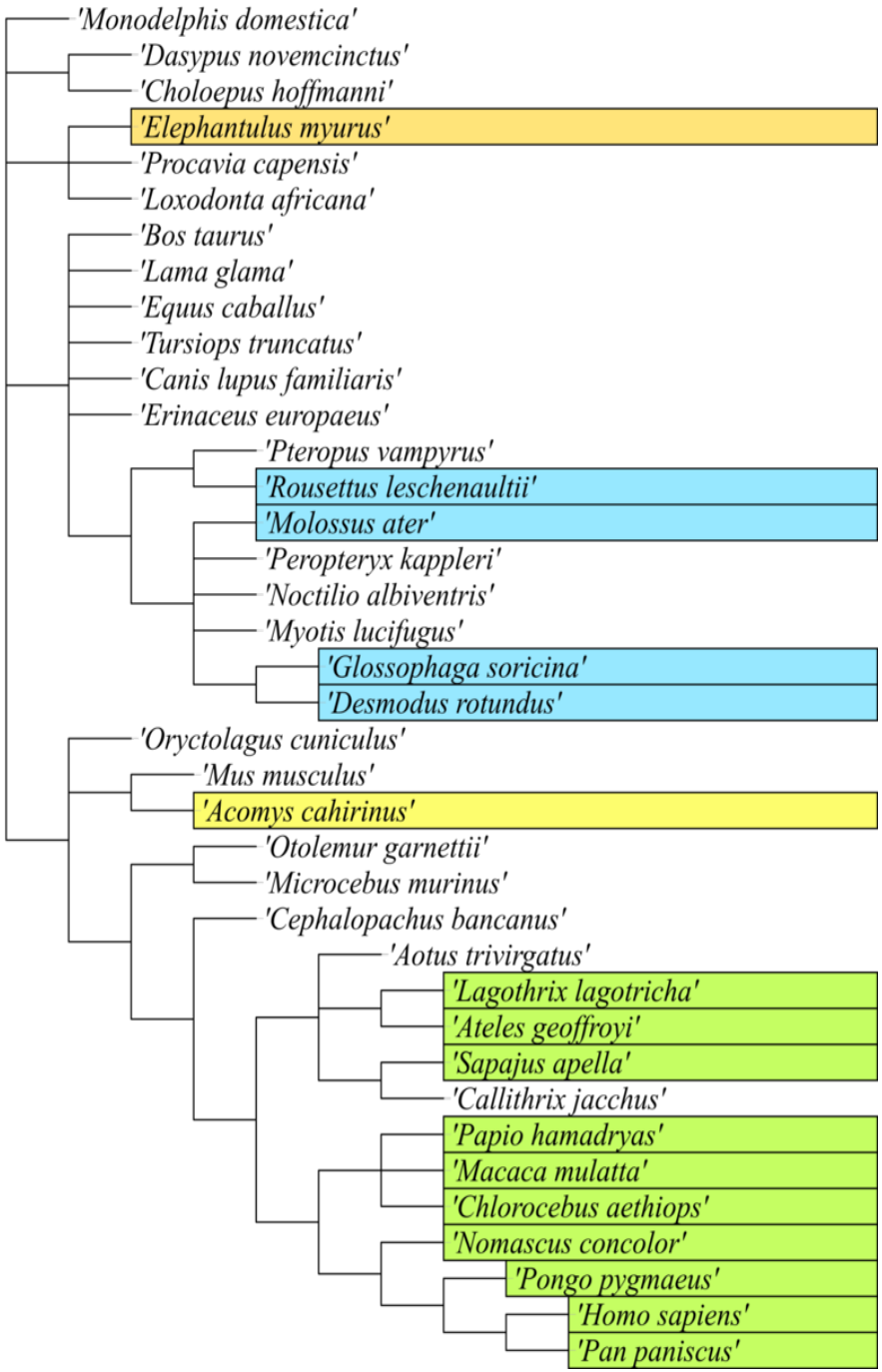






These animals are the only animals to have periods and shed their endometrium. They do not “exhibit” but hide when they are most fertile. Other mammals visually display estrus when they are in “heat” and a time when they are most likely to produce a fertilized egg.

Humans, chimpanzees, six species of bats, and elephant shrews are among the only animals on earth that have periods (i.e. mensis) !

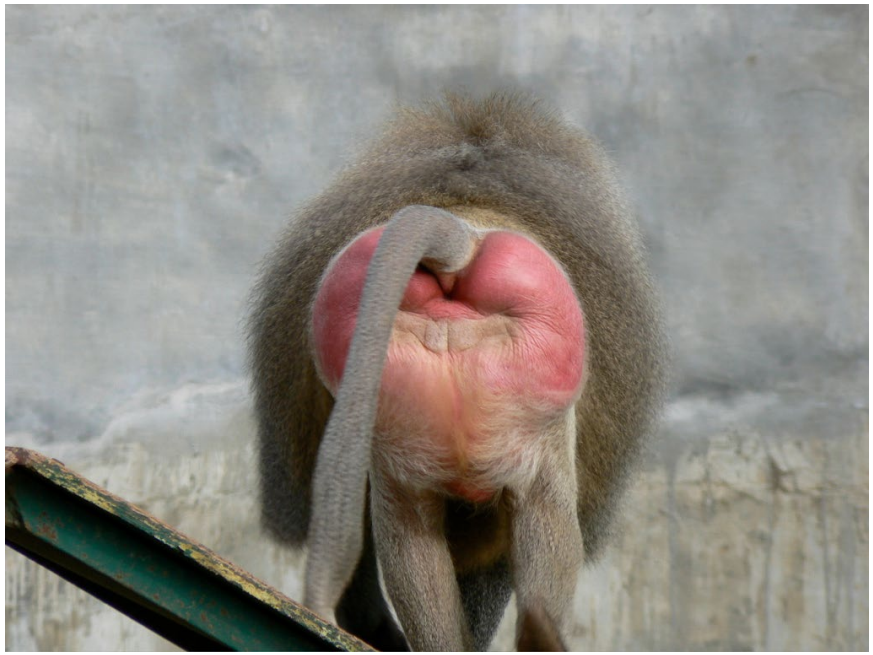


Phylogeny tree of menstruating and select non-menstruating mammals. Each color indicates a convergent evolutionary event: green, Primates; blue, Chiroptera; orange, Afrotheria; yellow, Rodentia.

Orange - Afrotheria – elephant shrews
Blue - Chiroptera – bats
Yellow - Rodentia – rodents
Green - primates

Many have questioned the evolution of overt menstruation in humans and related species, speculating on what advantage there could be to losing blood associated with dismantling the endometrium rather than absorbing it, as most mammals do.

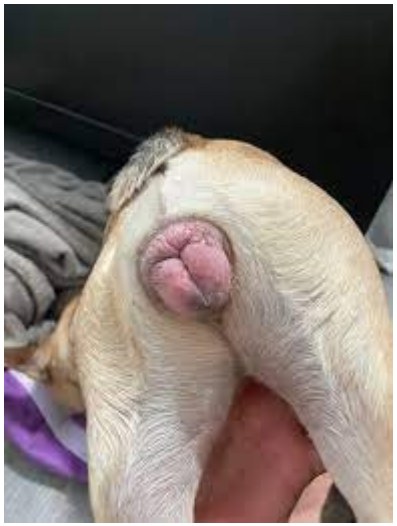
Leading hypothesis is energy conservation. Takes less energy to discard and reform endometrium than to maintain endometrium through receptive state.



Monkey

What is estrus?

Estrus is the period in the sexual cycle of female mammals, except the higher primates, during which they are in heat—i.e., ready to accept a male and to mate.

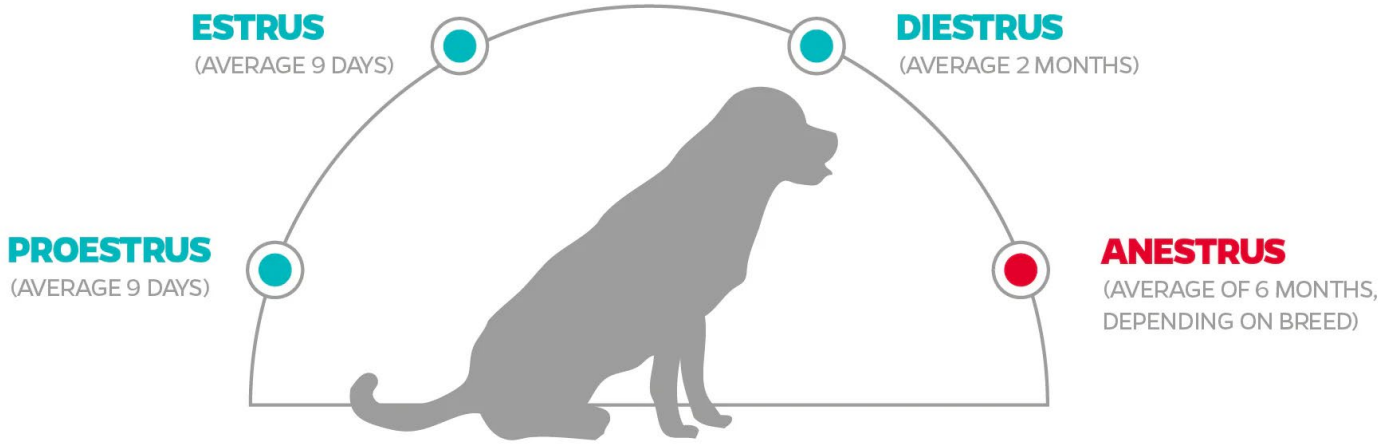


Dog

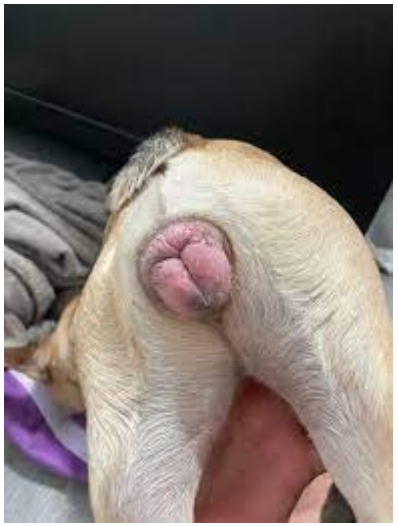


Horse

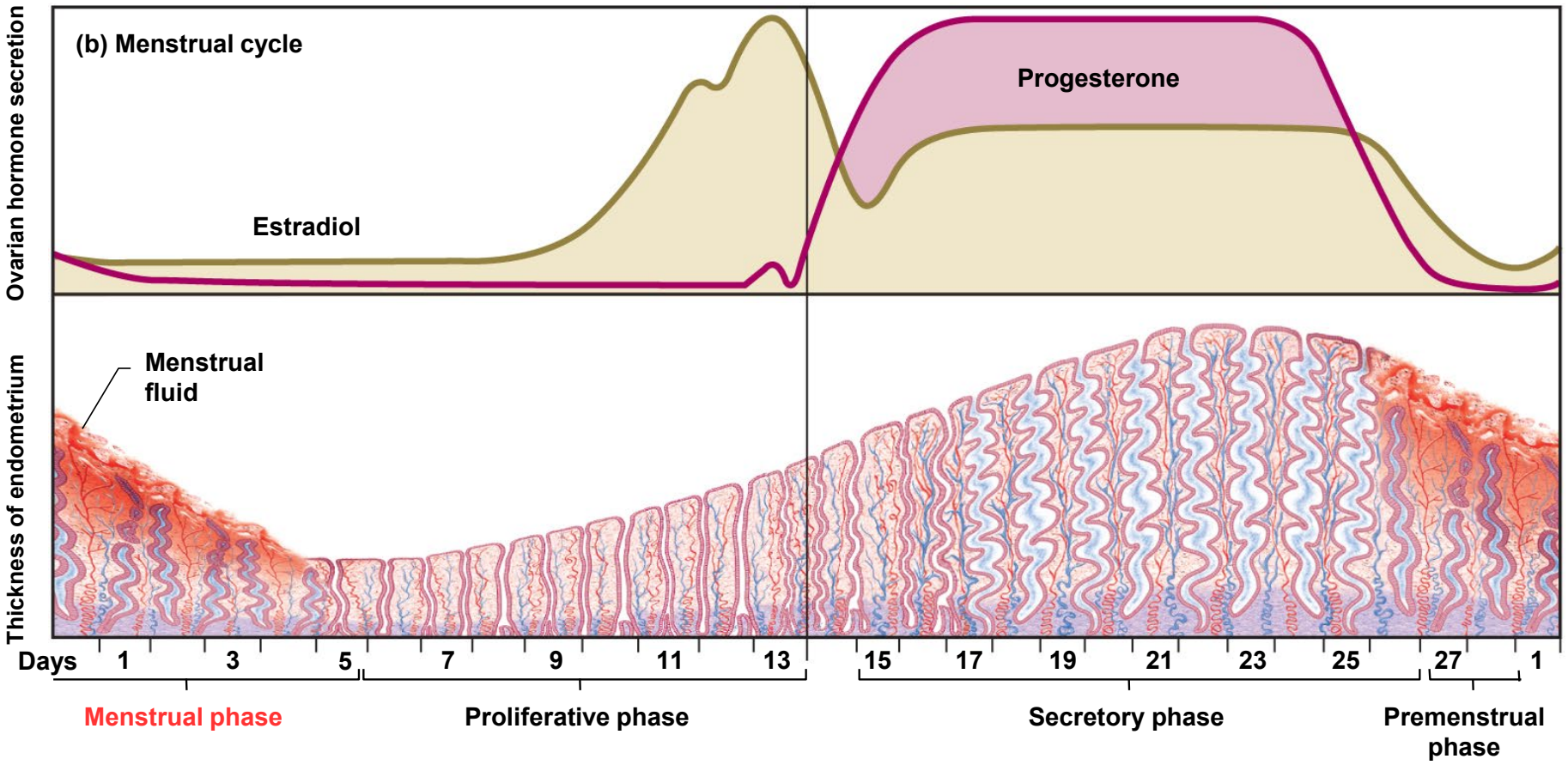
FEMALE DOG HEAT CYCLE



Estrus in dogs, commonly called "heat," is the stage of the estrous cycle when a female dog is fertile and receptive to mating. During this time, her body changes, and she may display physical signs like a swollen vulva and bloody discharge, as well as behavioral changes like increased urination and flirtatious behavior, while being unable to become pregnant. It is the fertile phase when ovulation occurs, and she will "stand" for a male.

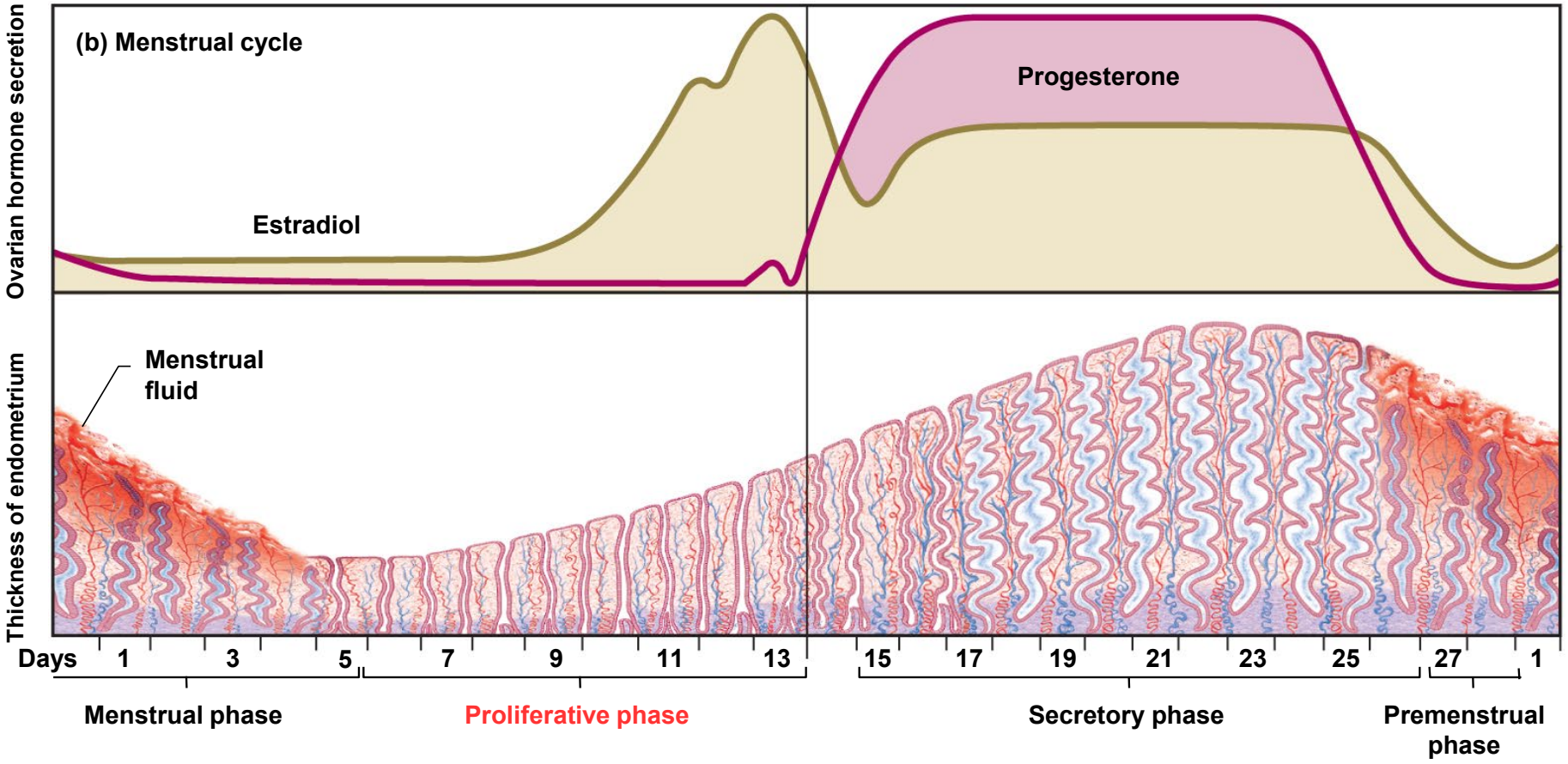


First Phase = Menstrual Phase



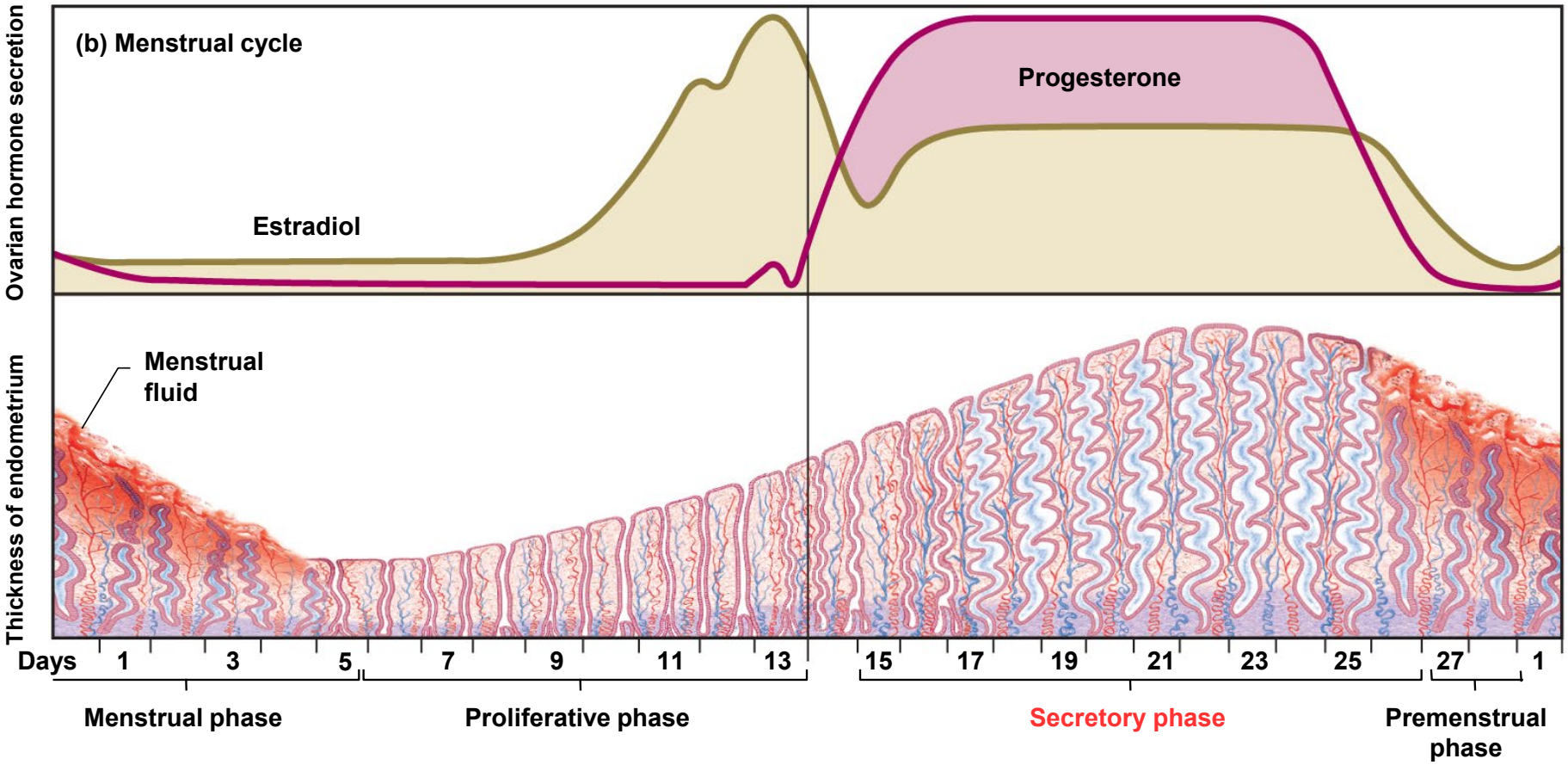
•Beginning of new cycle /// first discharge of endometrium from previous cycle

Second Phase = Proliferative Phase



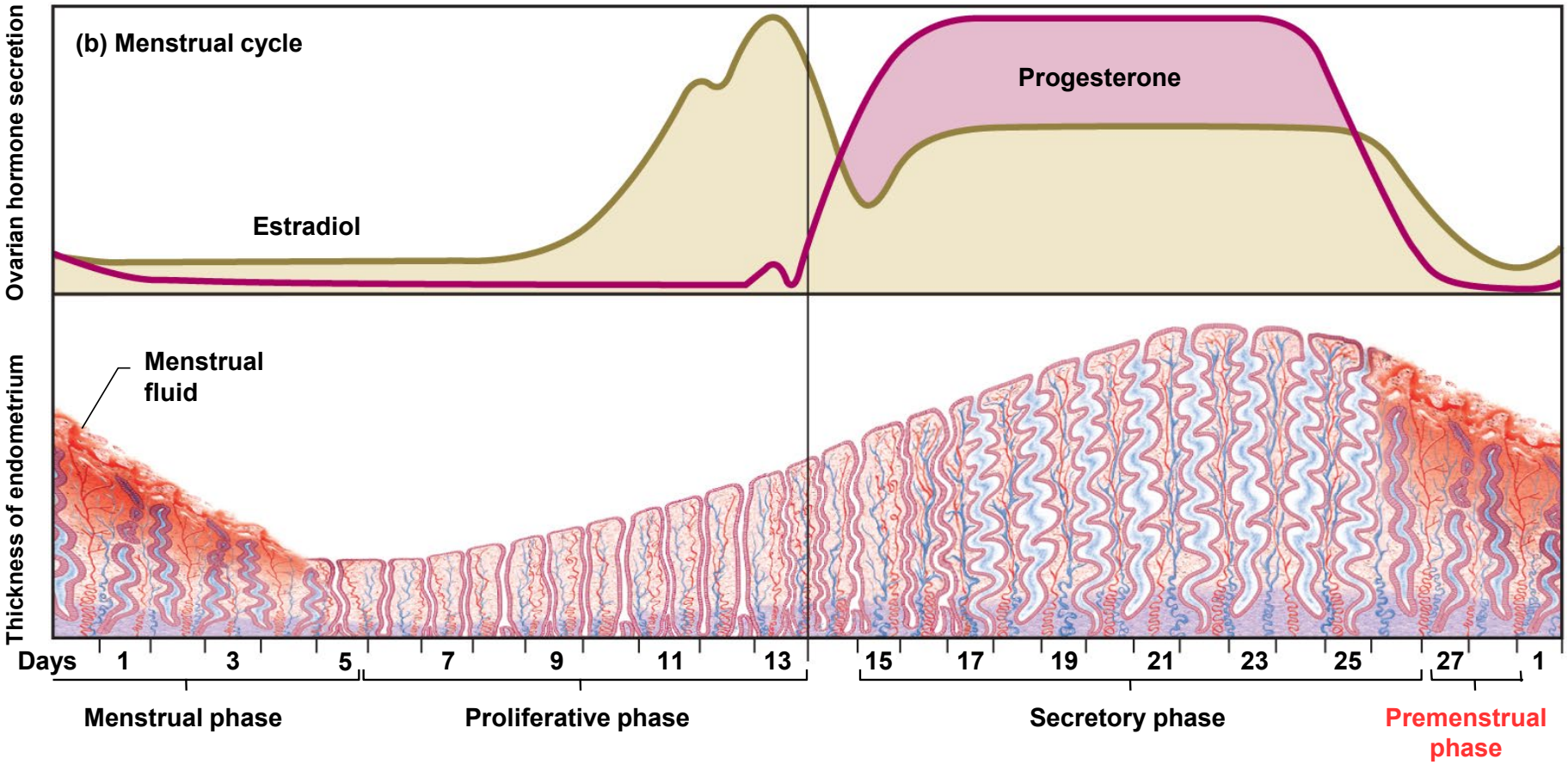
- Hyperplasia of endometrium // under control of estrogen
- Estrogen now also up-regulates endometrium with progesterone receptors

Third Phase = Secretory Phase



- Follows release of ovum from ovary
- Corpus luteum secretes progesterone
- Progesterone stimulates endometrium secretions (uterine milk)
- Endometrium maintained as long as progesterone present

Fourth Phase = Premenstrual Phase



- Corpus luteum stops producing progesterone, conceptus not viable
- Spiral arteries constrict // infarction with loss of endometrium

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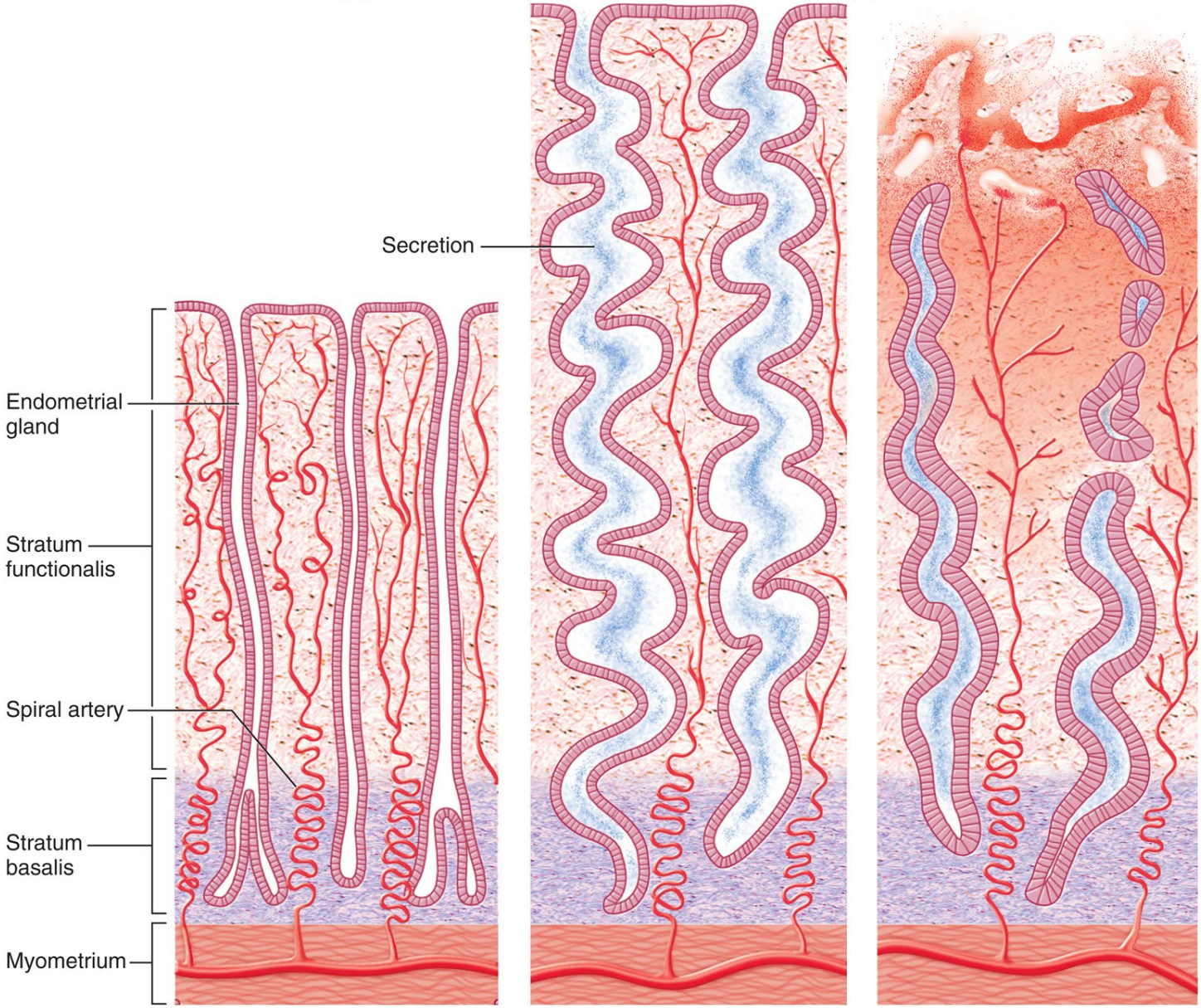
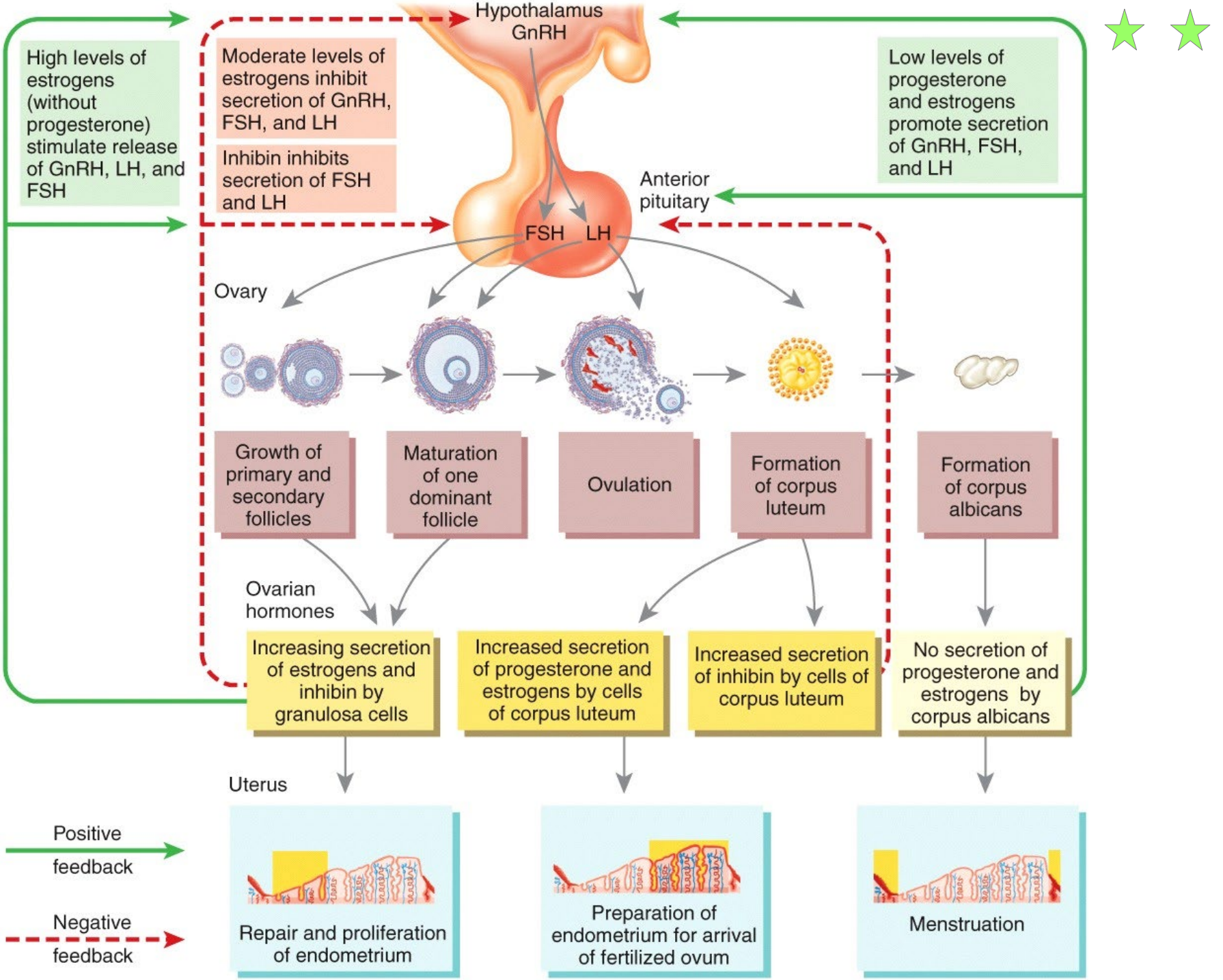
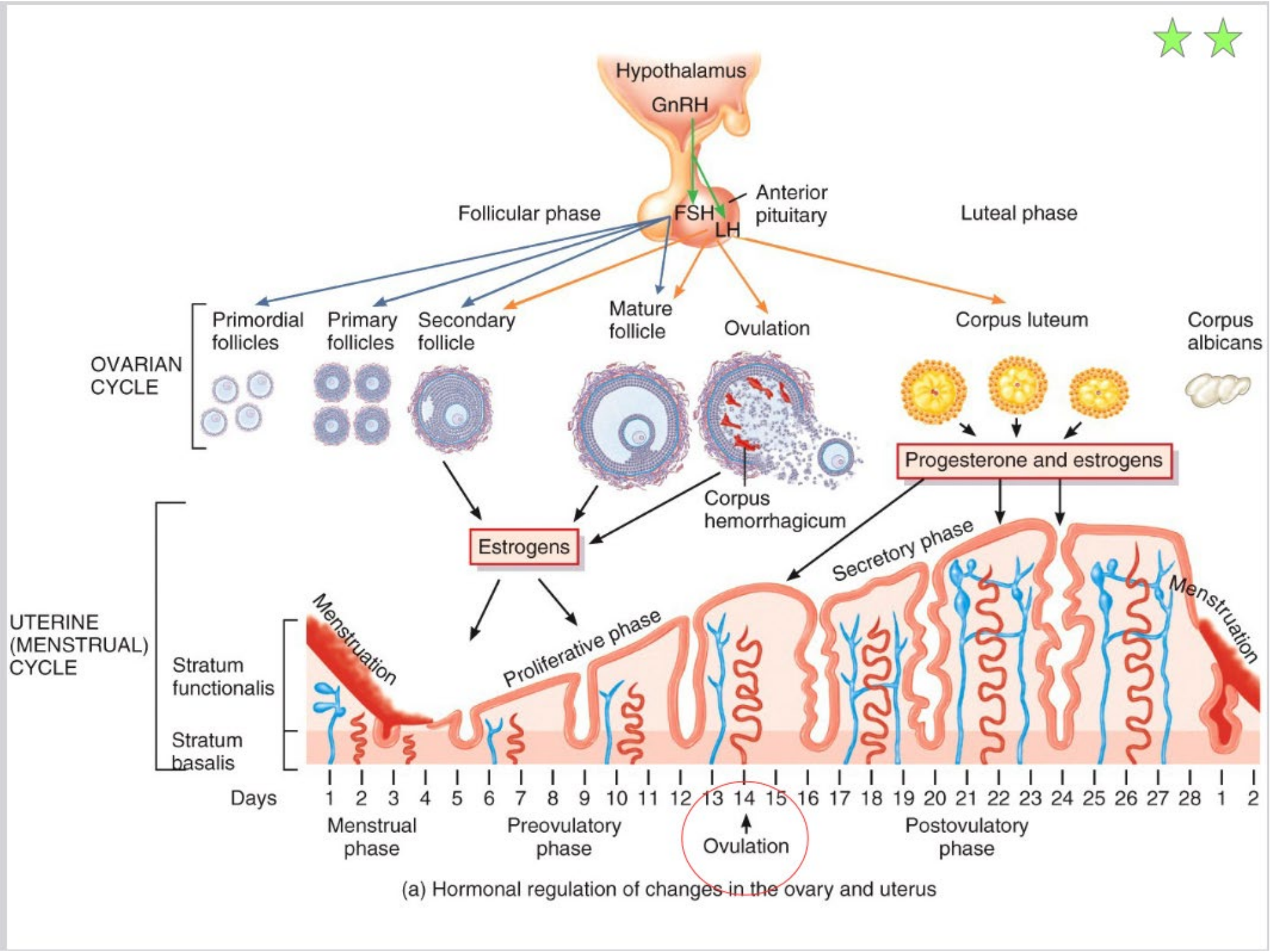



Hypothalamus
GnRH
High levels of estrogens (without progesterone) stimulate release of GnRH, LH, and FSH
Moderate levels of estrogens inhibit secretion of GnRH, FSH, and LH
Inhibin inhibits secretion of FSH and LH
Low levels of progesterone and estrogens promote secretion of GnRH, FSH, and LH
Anterior pituitary
FSH
LH
Ovary
Growth of primary and secondary follicles
Maturation of one dominant follicle
Ovulation
Formation of corpus luteum
Formation of corpus albicans
Ovarian hormones
Increasing secretion of estrogens and inhibin by granulosa cells
Increased secretion of progesterone and estrogens by cells of corpus luteum
Increased secretion of inhibin by cells of corpus luteum
No secretion of progesterone and estrogens by corpus albicans
Uterus
Positive feedback
Negative feedback
Repair and proliferation of endometrium
Preparation of endometrium for arrival of fertilized ovum
Menstruation



(a) Hormonal regulation of changes in the ovary and uterus

When Is Pregnancy Most Likely to Occur?

200 million sperm enter the vagina

Fewer than two million enter cervix

Only about 200 reach the secondary oocyte

Fertilization most likely to occur 12 to 24 hours after ovulation

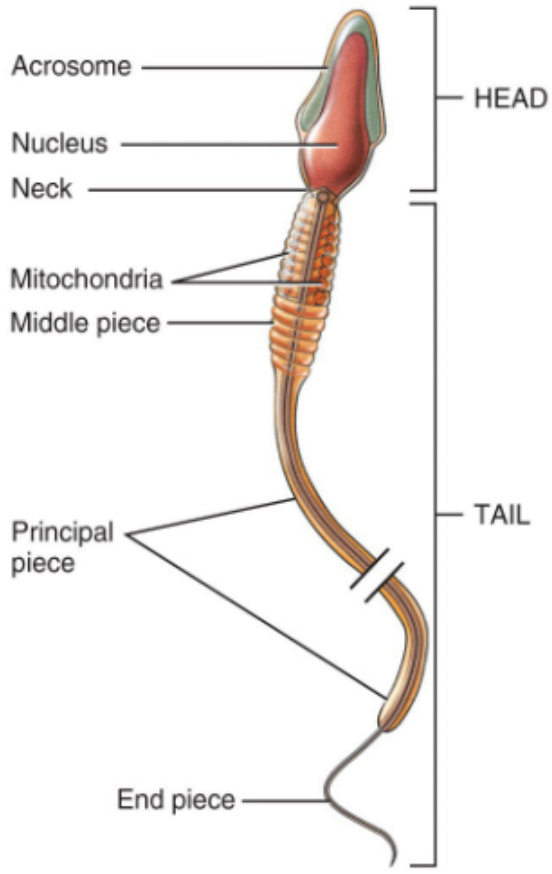
Egg is only viable for 24 hours

Sperm can not fertilize egg for first 10 hours after deposit in female (i.e. period of capacitation)

Sperm most viable 48 hours after they enter vagina /// may last for up to five days

According to the American College of Obstetricians and Gynecologists (ACOG), a woman can become pregnant if they have sex anywhere from 5 days before until 1 day after ovulation.

(Test Answer: 5 days before ovulation and 1 day after)



Combined Oral Contraceptive Pill (COCP)
Mechanism of action (Wiki)

Combined oral contraceptive pills were developed to prevent ovulation by suppressing the release of gonadotropins. Combined hormonal contraceptives, including COCPs, inhibit follicular development and prevent ovulation as a primary mechanism of action.

Progesterone negative feedback decreases the pulse frequency of gonadotropin-releasing hormone (GnRH) release by the hypothalamus, which decreases the secretion of follicle-stimulating hormone (FSH) and greatly decreases the secretion of luteinizing hormone (LH) by the anterior pituitary.

Decreased levels of FSH inhibit follicular development, preventing an increase in estradiol levels.

Progesterone negative feedback and the lack of estrogen positive feedback on LH secretion prevent a mid-cycle LH surge. Inhibition of follicular development and the absence of an LH surge prevent ovulation.

Estrogen was originally included in oral contraceptives for better cycle control (to stabilize the endometrium and thereby reduce the incidence of breakthrough bleeding), but was **also found to inhibit follicular development and help prevent ovulation.**

Estrogen negative feedback on the anterior pituitary greatly decreases the secretion of FSH, which inhibits follicular development and helps prevent ovulation.

Combined Oral Contraceptive Pill (COCP)
Mechanism of action (Wiki)

Another primary mechanism of action of all progestogen-containing contraceptives is **inhibition of sperm penetration through the cervix** into the upper genital tract (uterus and fallopian tubes) by decreasing the water content and increasing the viscosity of the cervical mucus.

The estrogen and progestogen in COCPs have other effects on the reproductive system, but these have not been shown to contribute to their contraceptive efficacy:

Slowing tubal motility and ova transport, which may interfere with fertilization.

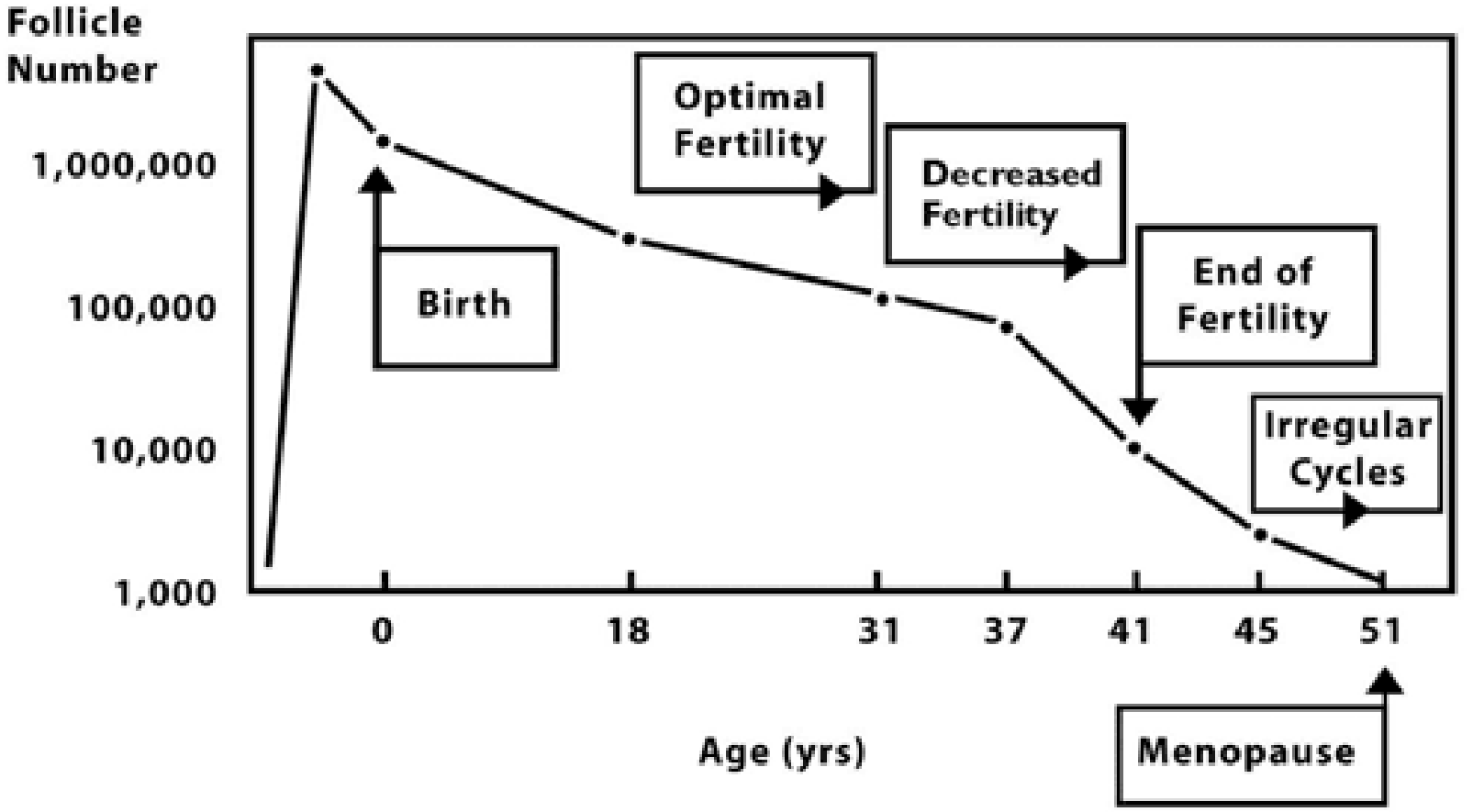
Endometrial atrophy and alteration of metalloproteinase content, which may impede sperm motility and viability, or theoretically inhibit implantation.

Endometrial edema, which may affect implantation.

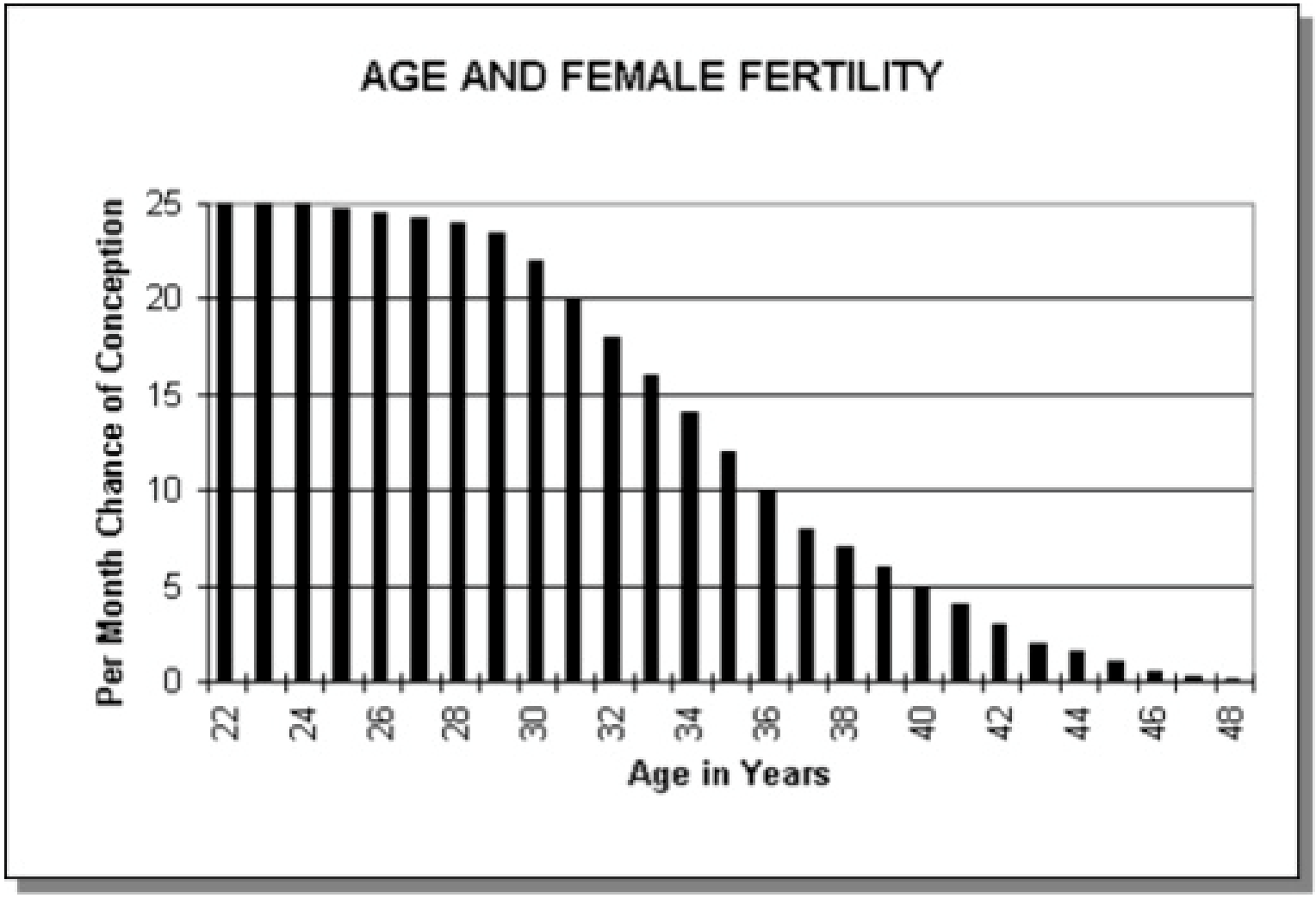
Insufficient evidence exists on whether changes in the endometrium could actually prevent implantation.

The primary mechanisms of action are so effective that the possibility of fertilization during COCP use is very small. Since pregnancy occurs despite endometrial changes when the primary mechanisms of action fail, endometrial changes are unlikely to play a significant role, if any, in the observed effectiveness of COCPs.

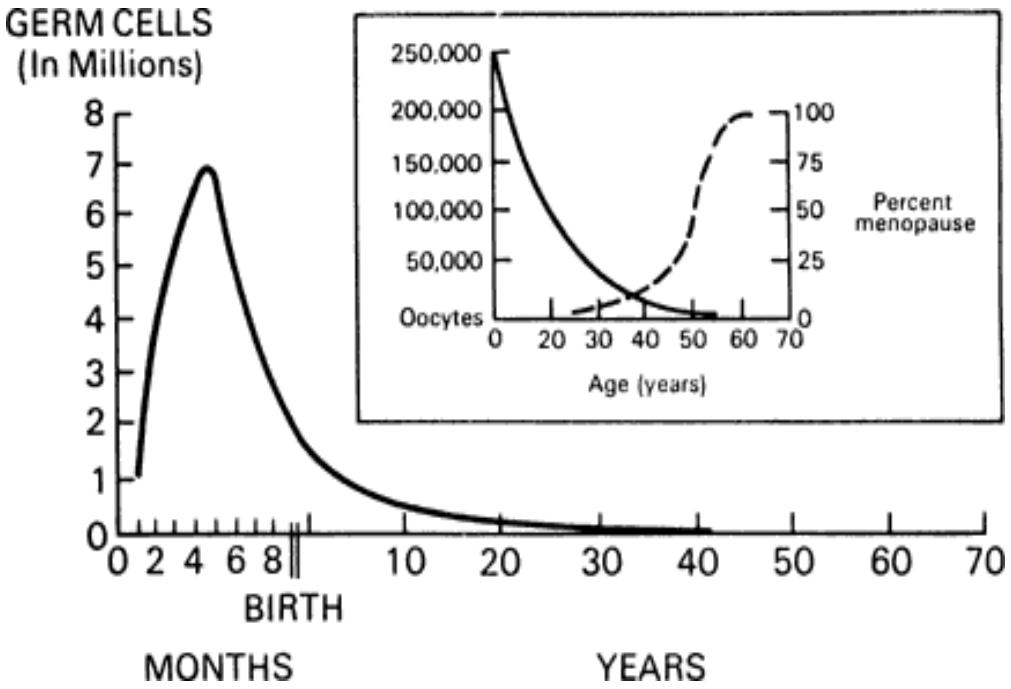
Female Fertility



E.R. TE VELDE ET AL., 1998


AGE AND FEMALE FERTILITY
Per Month Chance of Conception
25
20
15
10
5
0
22
24
26
28
30
32
34
36
38
40
42
44
46
48
Age in Years

Female Oogenesis



First sign of gamete development seen during first five weeks of embyonic development.

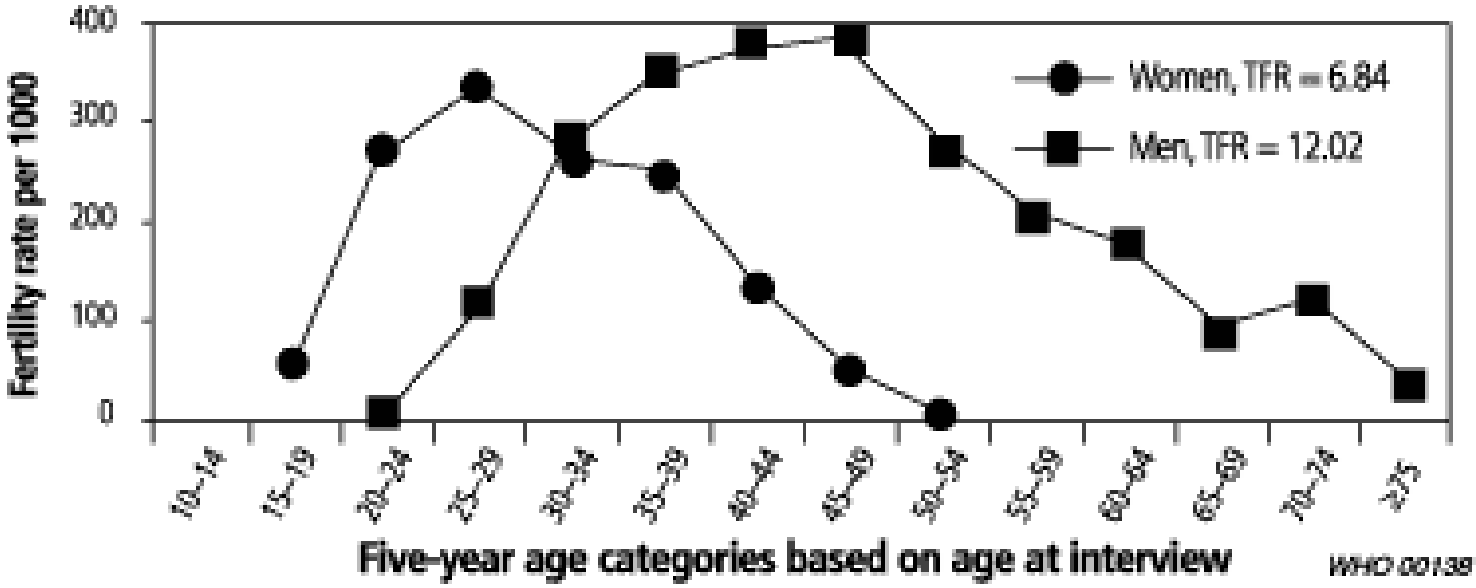
Called oogonia and continue to develop until fifth month.

By fifth month, female fetus has developed 6 to 7 million oogonia. They now enter state of arrested development until shortly before birth. Oogonia now referred to as primary oocytes.

Primary oocytes undergo atresia before birth and only about 2 million eggs remain at time of birth.

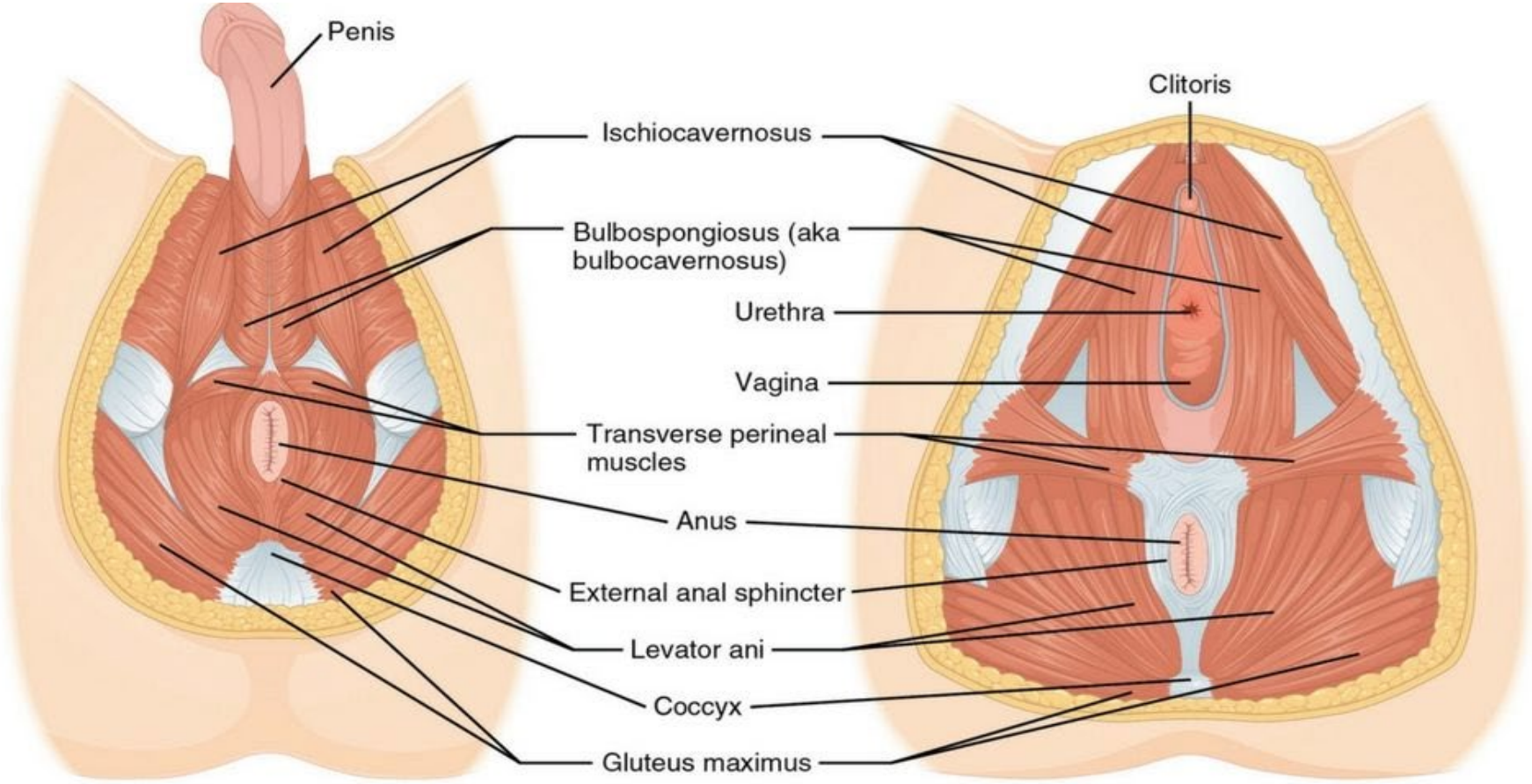
During childhood, most eggs undergo atresia and by puberty only 200,000 eggs remain. If woman ovulates between 14 and 50 on a 28 day cycle then she would only need 480 eggs!

Fig. 2. **Men's and women's age-specific fertility rates, 1993–97**
(TFR = total fertility rate)



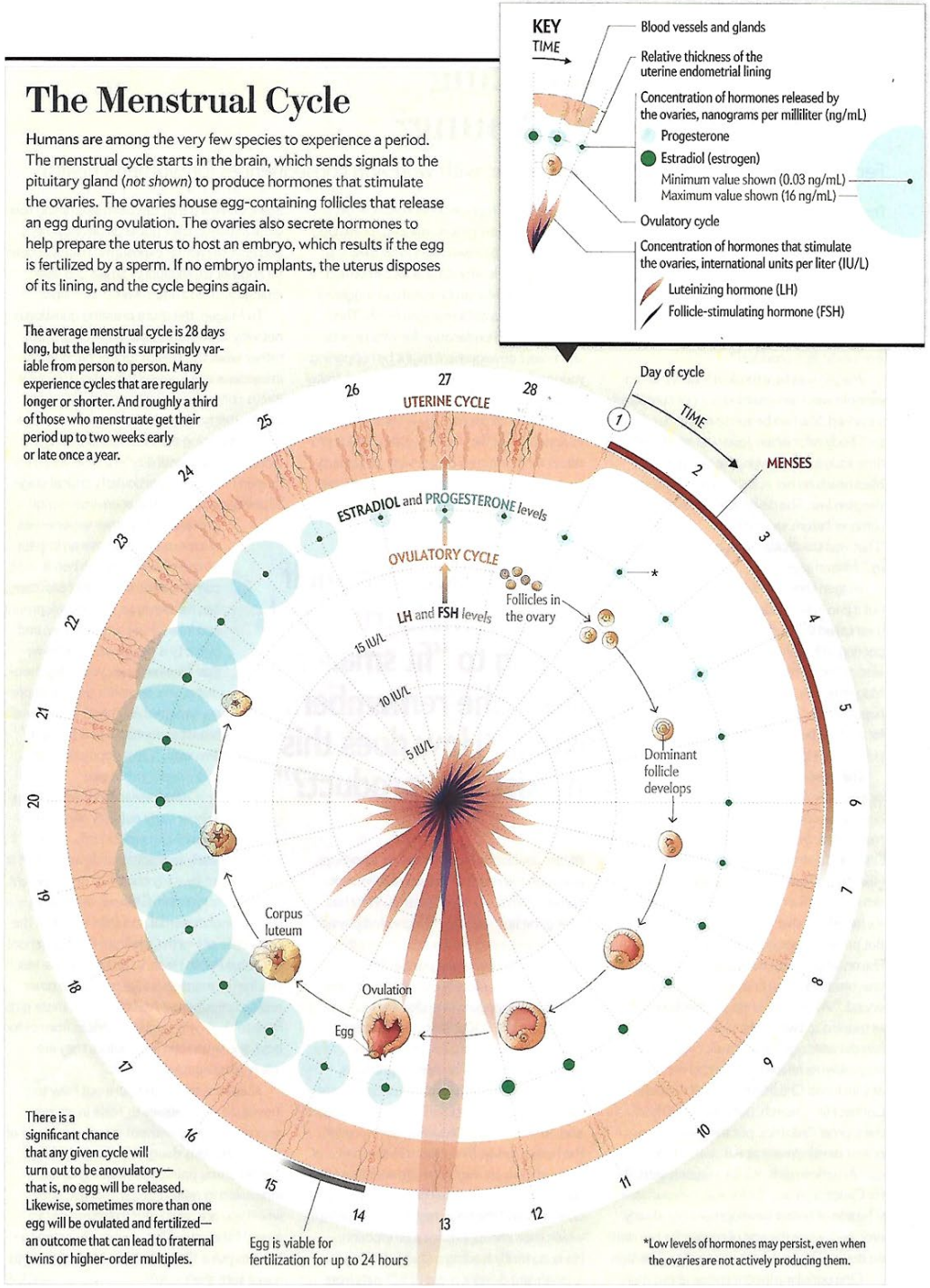
Perineum Location & Perineal Muscles

The perineum is the space between the anus and scrotum in the male and between the anus and



Male perineal muscles: inferior view

Female perineal muscles: inferior view



See review article posted on Web site Unit 4 – C27-28 under Articles of Interest:

A Review of Female Reproductive Health published in Scientific American

The science of women's reproductive health has been a history driven by myth, misinformation and neglect of knowledge Take the time to learn some of the history and how female reproductive services are being improved. // These are the articles included in the SA review.

The point of the period

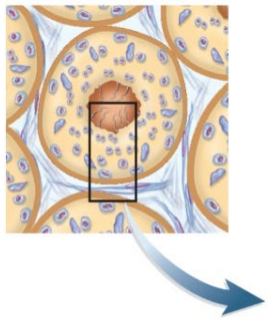
Set it and forget it.

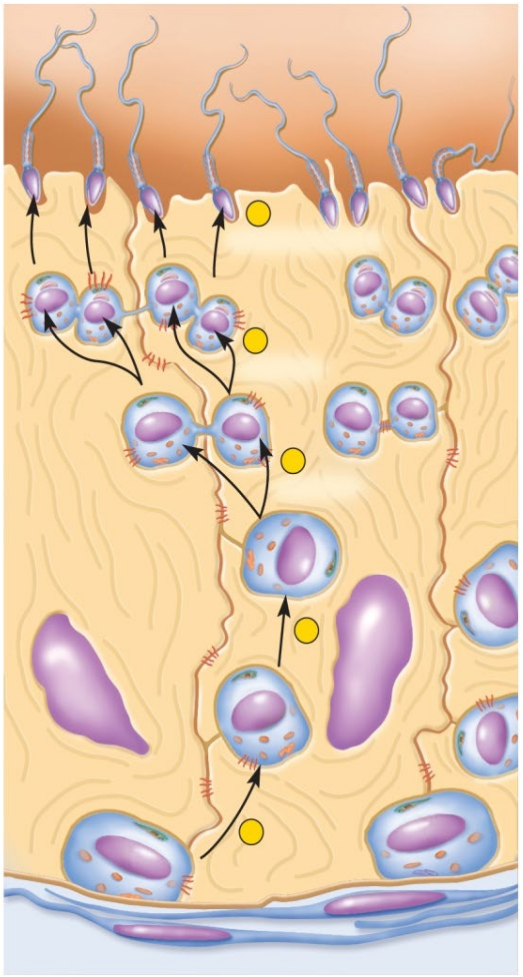
Maternal Mortality

Eggs on Ice

Menstrual Cycle Composit Graphic

Male Reproductive Physiology





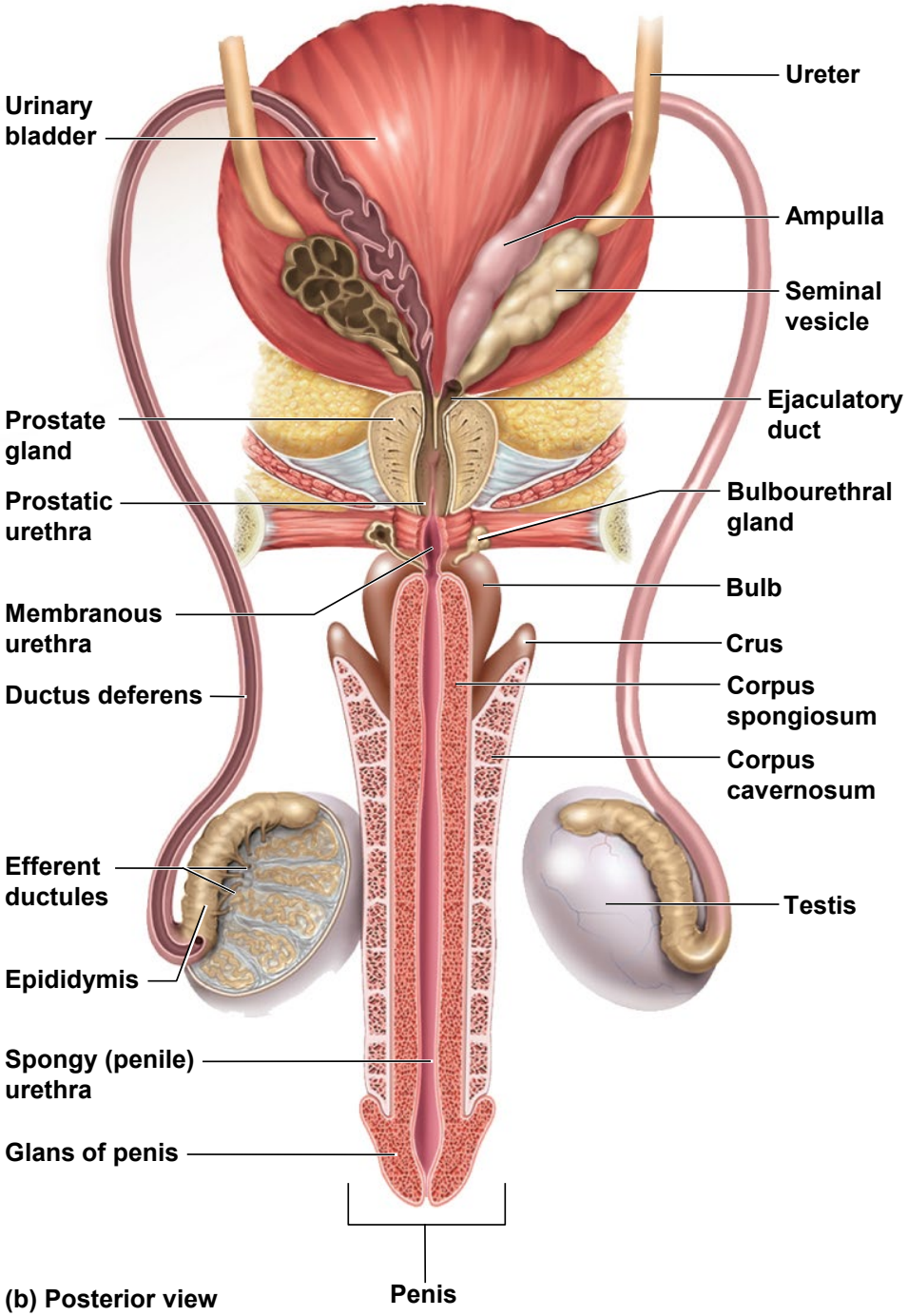
Overview of Male Reproductive System

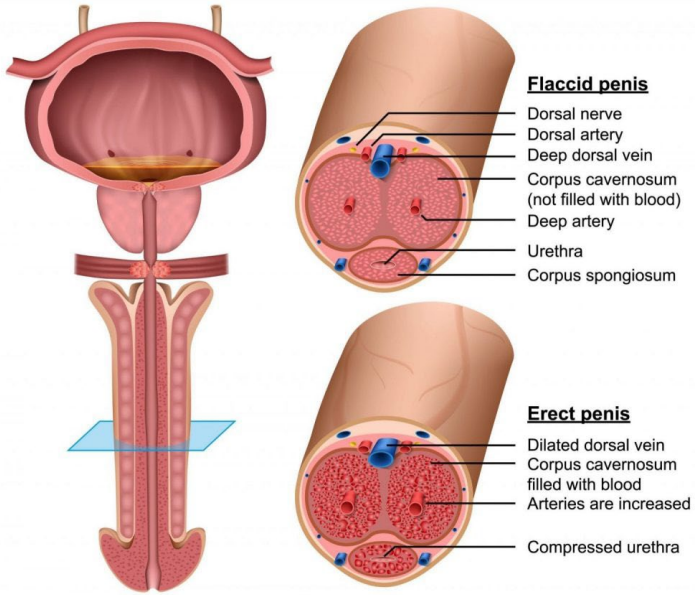
Reproductive system consists of primary and secondary sex organs

Primary sex organs (the gonads / testes) // produce gametes (sperm)

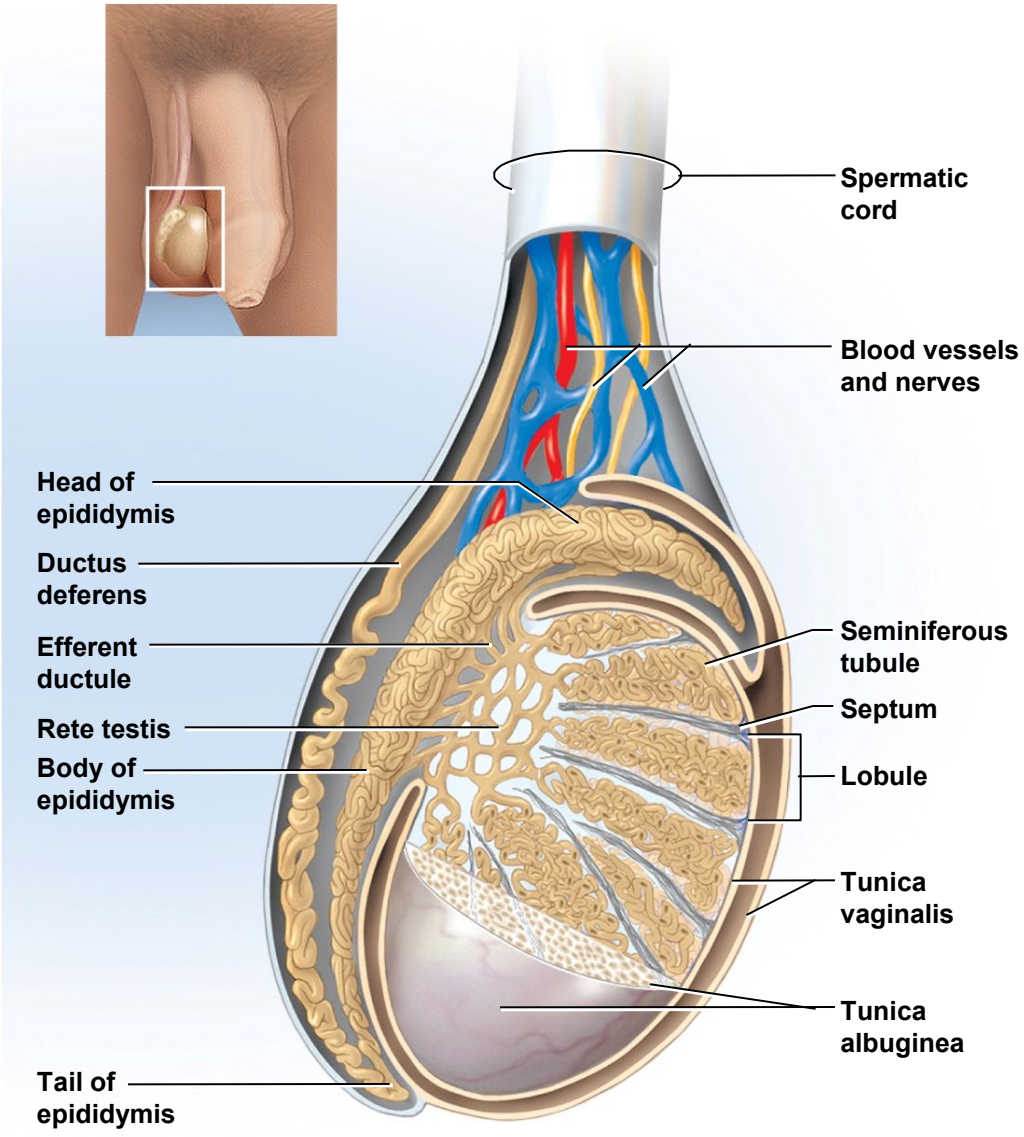
Secondary sex organs // organs other than the gonads necessary for reproduction = <u>system of ducts, glands, and penis</u>

Male Reproductive System



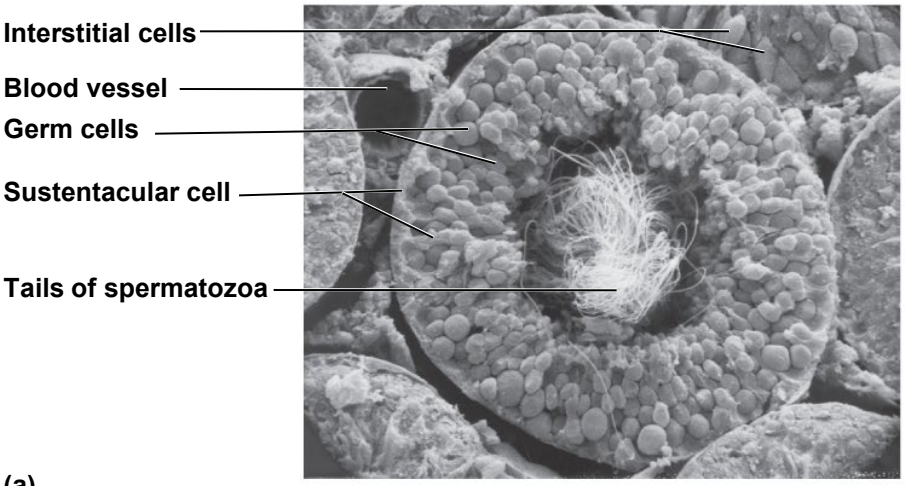


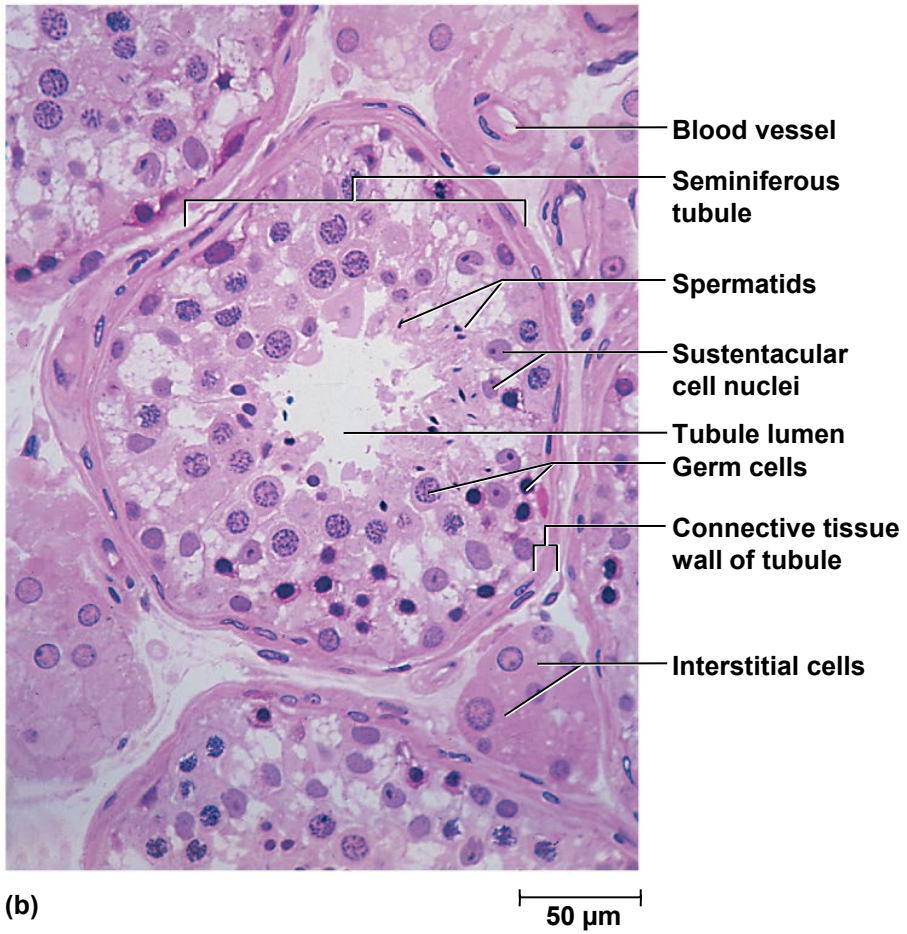
Testis and Associated Structures



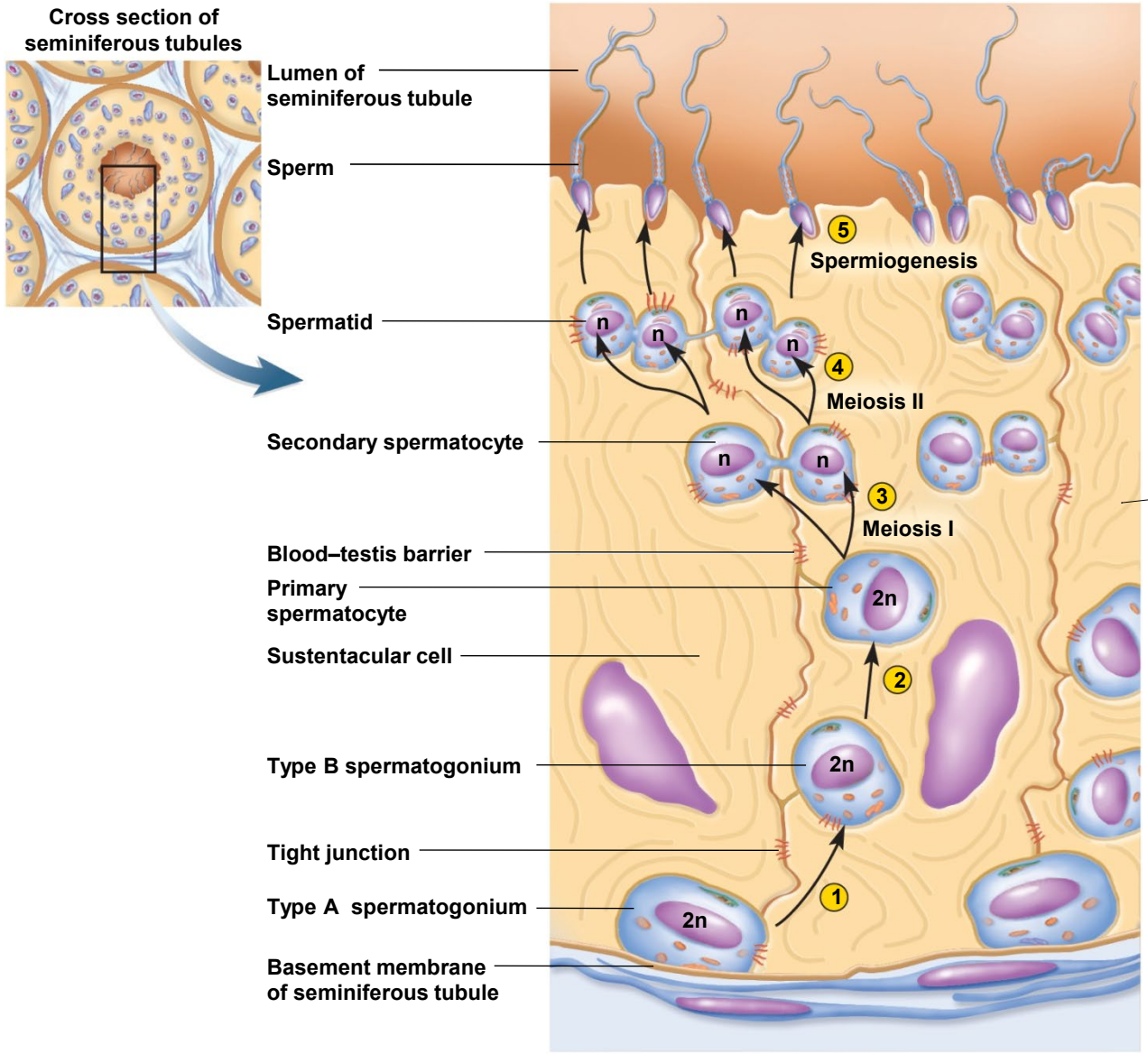
Cross Section of the Seminiferous Tubule

Histology of Testis





Spermatogenesis



Sustentacular cells form the wall of the seminifierous tubule

Follicle Stimulating Hormone (FSH) - Male

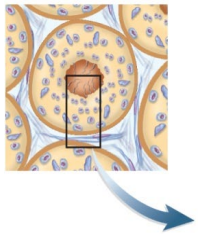
FSH produced by anterior pituitary

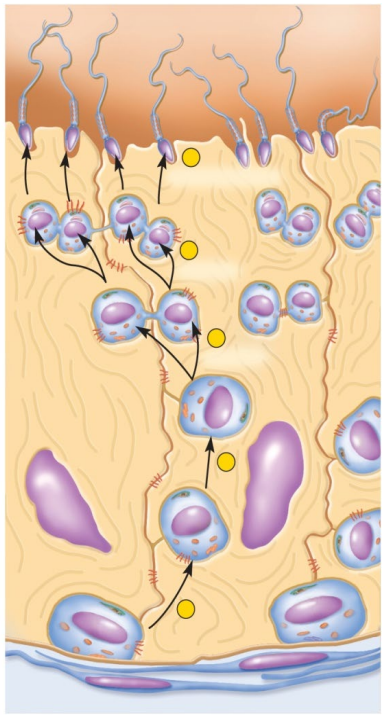
Target tissue = sustentacular cells (SC) in the seminiferous tubules (located in testis)

SC secrete androgen binding protein

ABP required to concentrate testosterone inside seminiferous tubules

Note: LH stimulates interstitial cells to produce testosterone outside of the tubules





Sustentacular cells will secrete inhibin if sperm are not ejaculated for extended period

Inhibin stops release of FSH resulting in no ABP produced by sustentacular cells.

Without ABP the testosterone is not concentrated in testes and spermatogenesis stops // note: testosterone is still produced under influence of LH

Luteininzing hormone (LH)

(Also called interstitial cell stimulating hormone - ICSH)

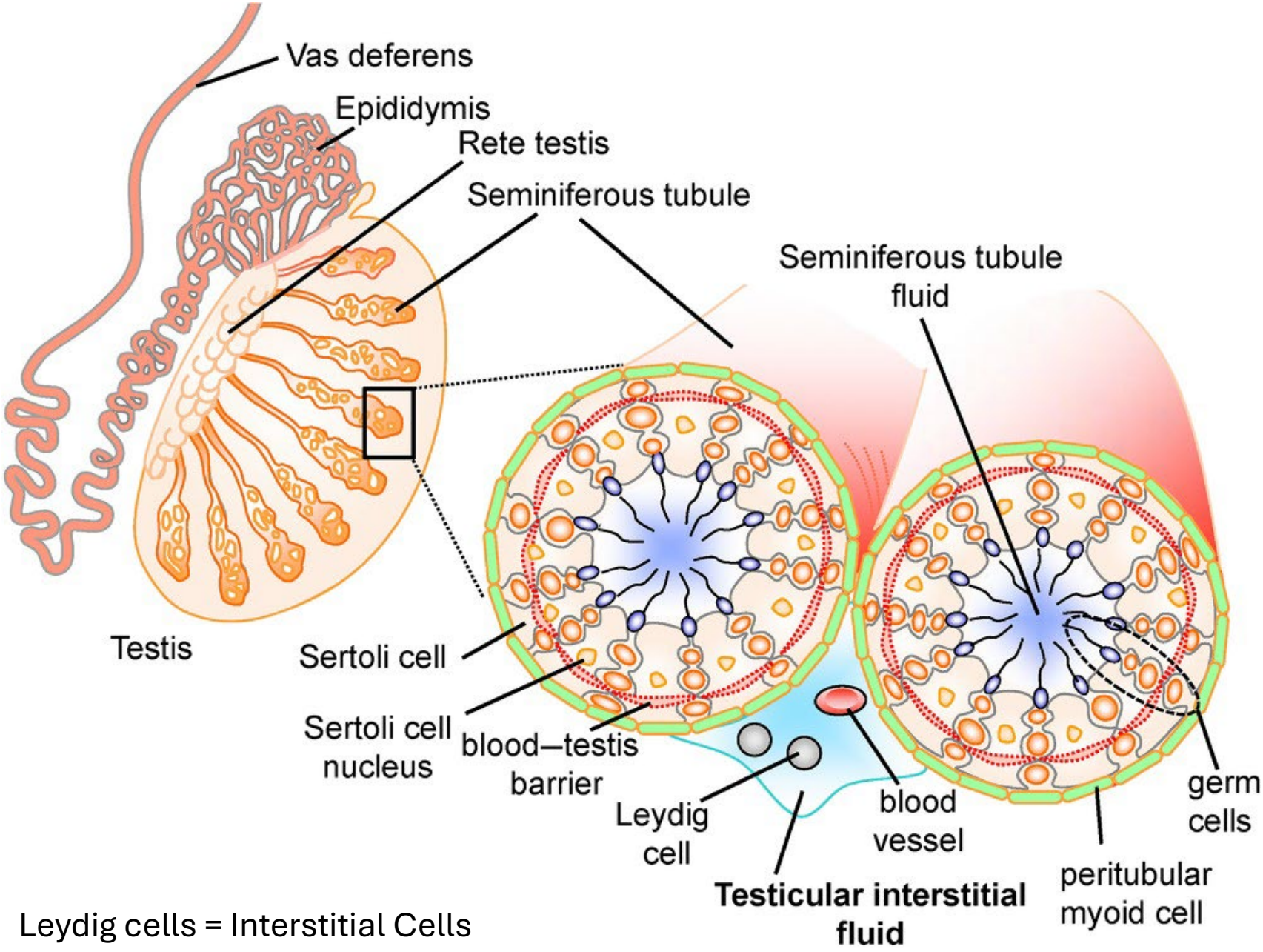
LH produced by anterior pituitary

Target tissue = interstitial cells in testes // located in spaces between seminiferous tubules // these cells produce testosterone

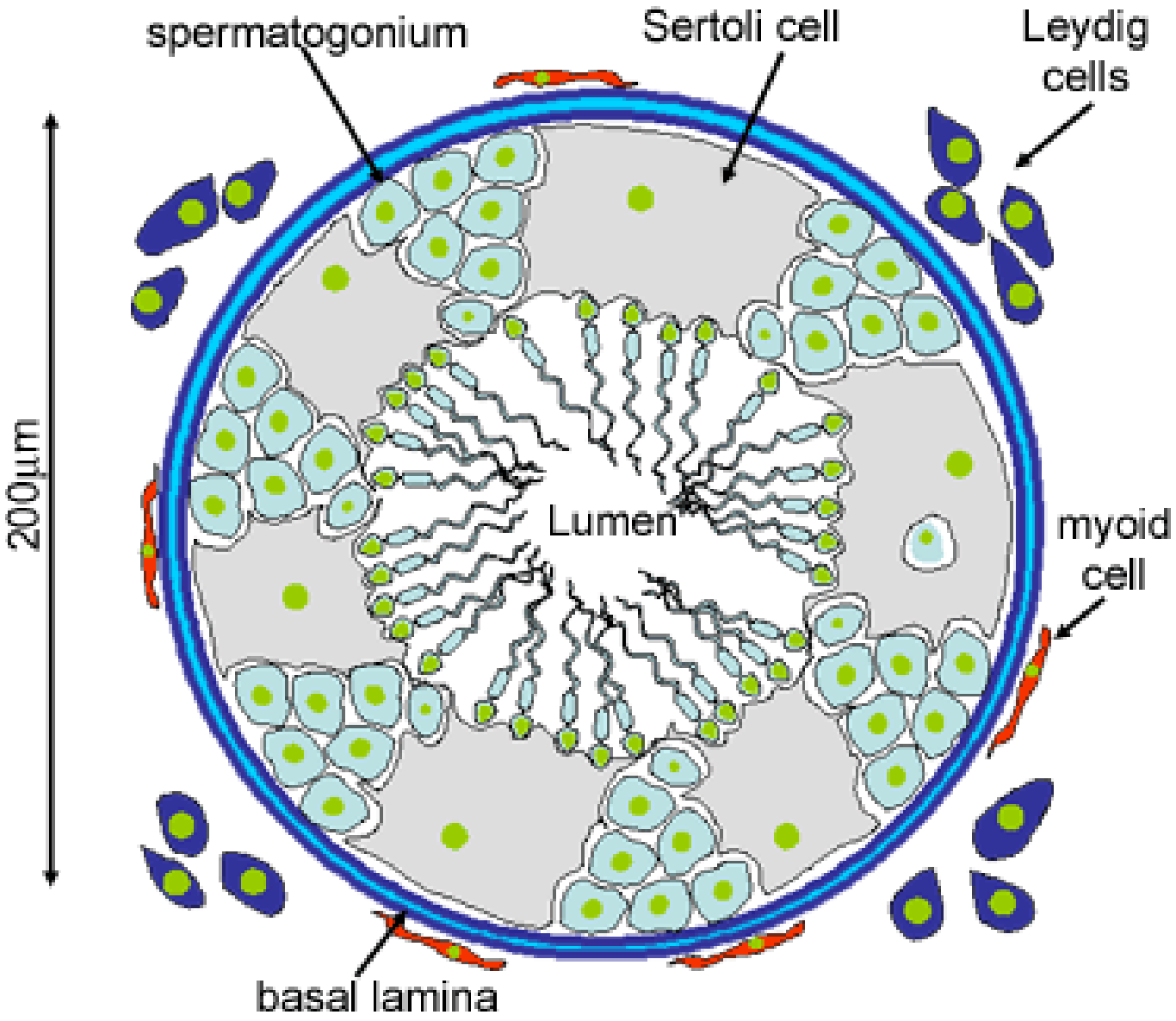
Testosterone must be concentrated inside seminiferous tubules for sperm production

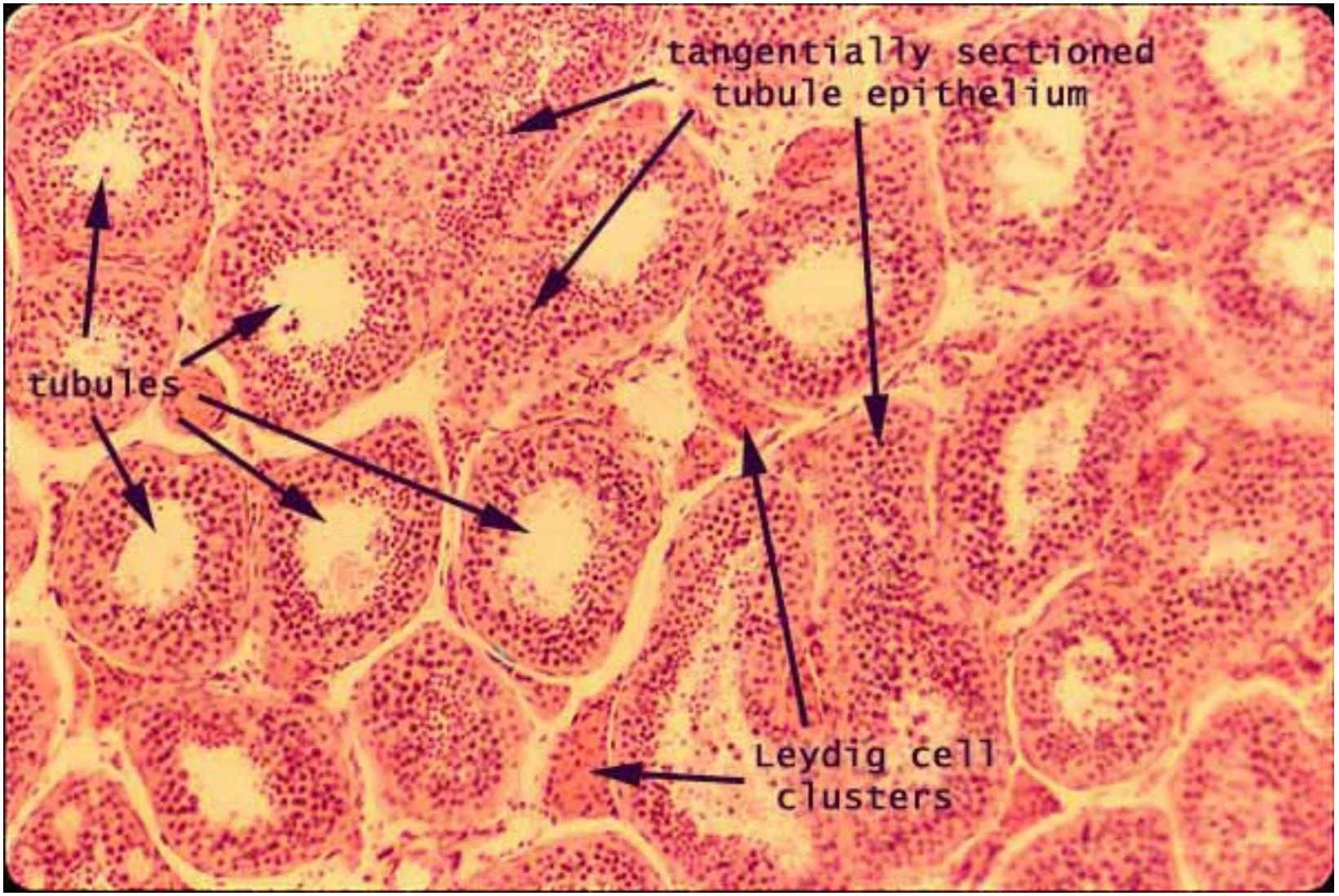
Androgen Binding Protein produced by Sertoli cells within semininferous tubules cause testosterone to diffuse into the seminiferous tubules

High concentration of testosterone inside semininerous tubules stimulates spermatogonium cells /// stimulates spermatogenesis



Leydig cells = Interstitial Cells
(interstitial cells of Leydig)


spermatogonium
Sertoli cell
Leydig cells
= Interstitial Cells
200µm
Lumen
myoid cell
basal lamina



Leydig cells = Interstitial Cells
(interstitial cells of Leydig)

Testosterone

Produced by interstitial cells of the testes

LH receptors on interstitial cells // Interstitial cells produce testosterone

Testosterone responsible for secondary sexual characteristics

Testosterone also required for spermatogenesis

Testosterone must be concentrated by ABP within seminiferous tubules for spermatogenisis

Inhibin

Released by sustentacular cells of testes

Inhibits FSH release

By stopping FSH - prevents SC from producing ABP // this results in testosterone not being concentrated in testes which stops spermatogenesis

LH secretions continues to stimulate interstitial cells /// production of testosterone continues so other functions like muscle growth, hair growth, behavior, and other secondary sexual characteristics occurs

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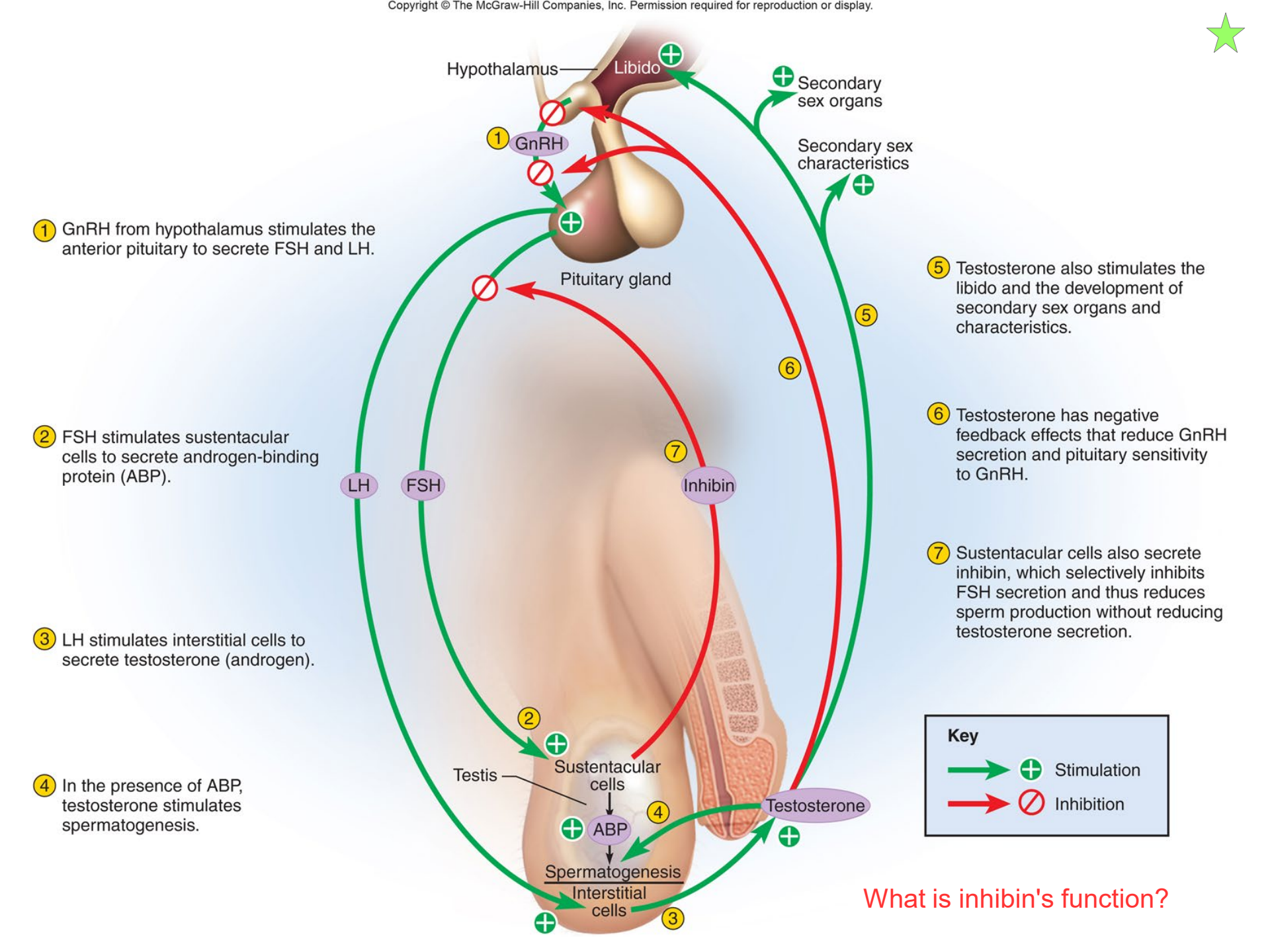
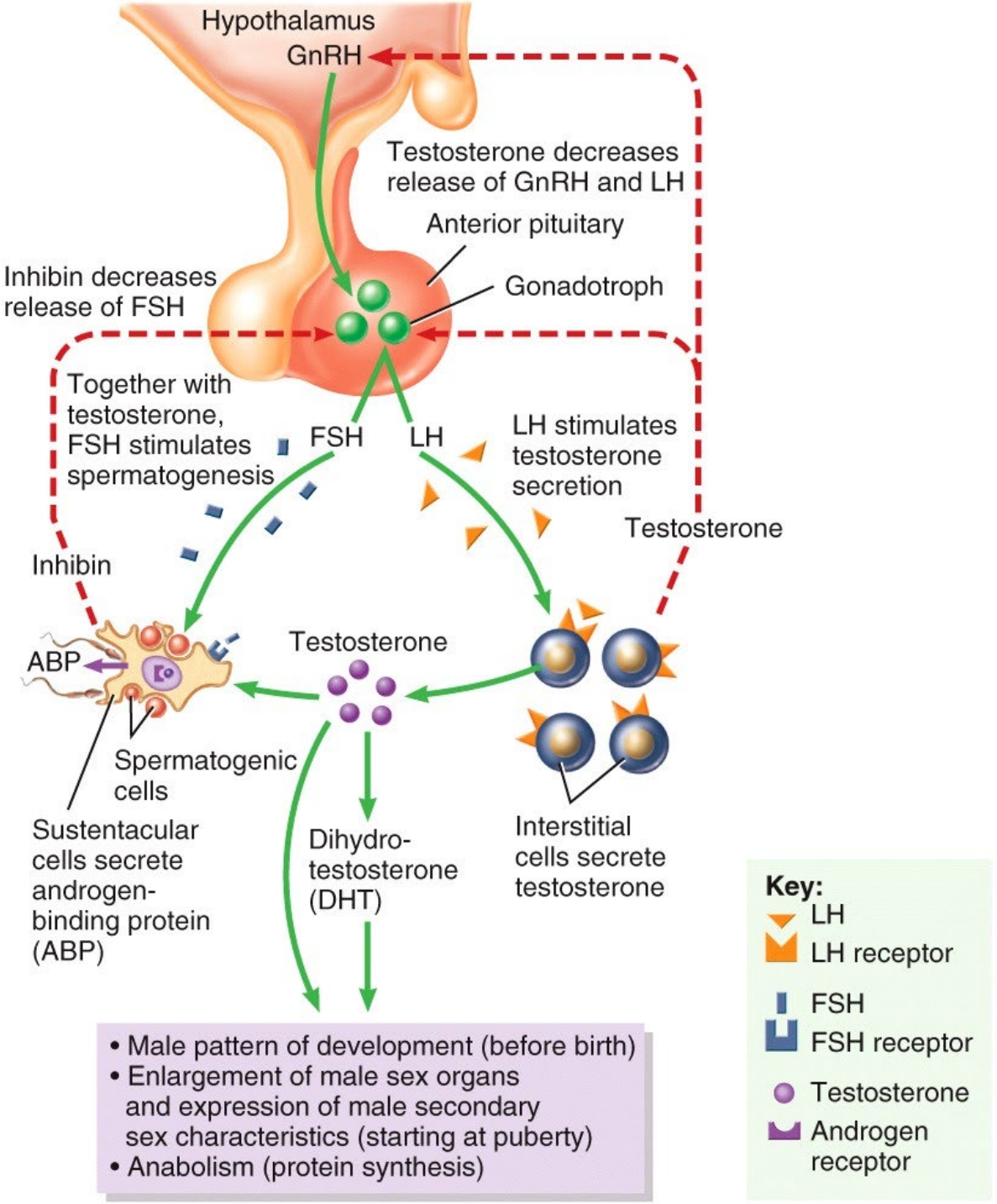
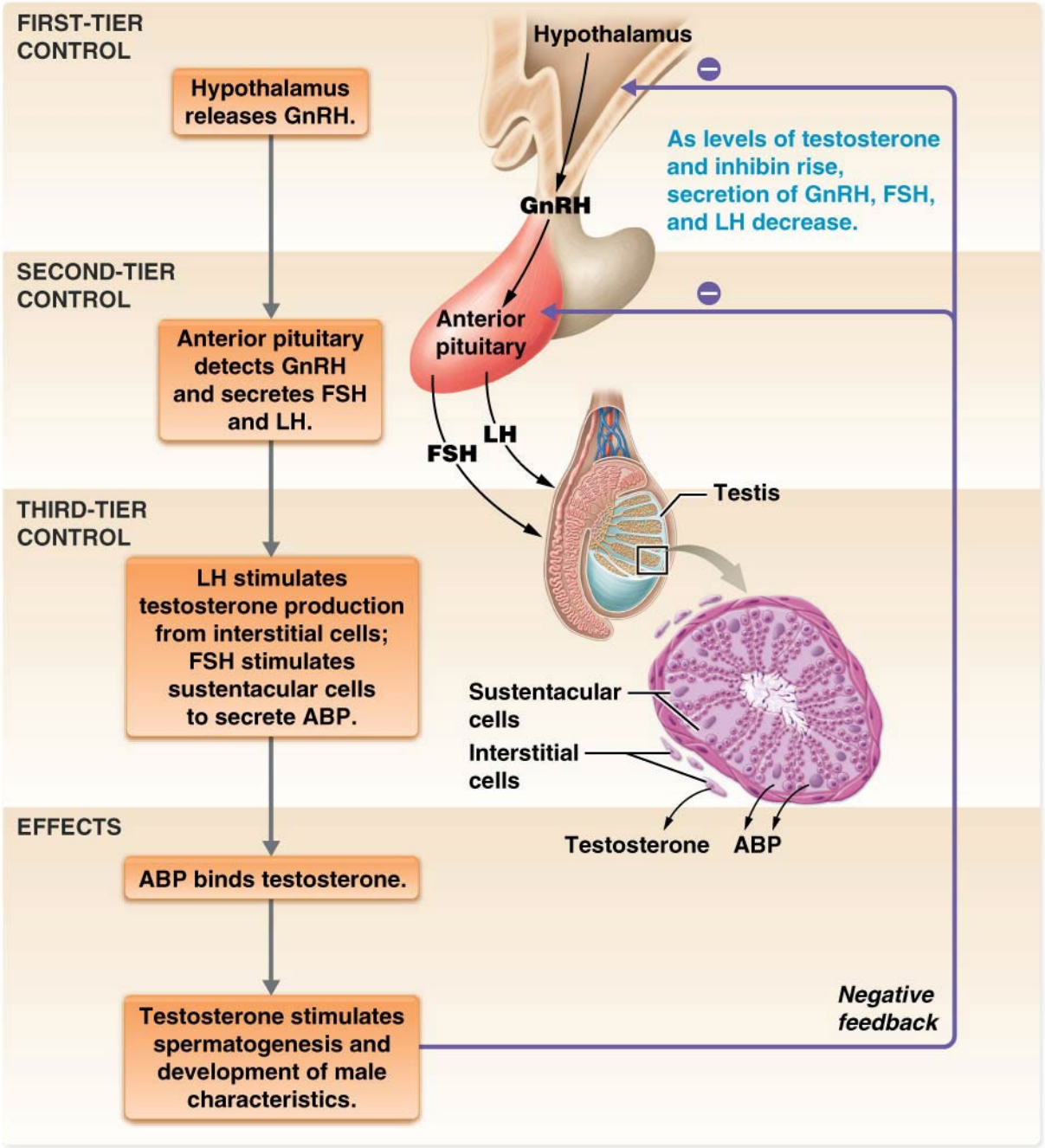


1. GnRH from hypothalamus stimulates the anterior pituitary to secrete FSH and LH.
2. FSH stimulates sustentacular cells to secrete androgen-binding protein (ABP).
3. LH stimulates interstitial cells to secrete testosterone (androgen).
4. In the presence of ABP, testosterone stimulates spermatogenesis.
5. Testosterone also stimulates the libido and the development of secondary sex organs and characteristics.
6. Testosterone has negative feedback effects that reduce GnRH secretion and pituitary sensitivity to GnRH.
7. Sustentacular cells also secrete inhibin, which selectively inhibits FSH secretion and thus reduces sperm production without reducing testosterone secretion.

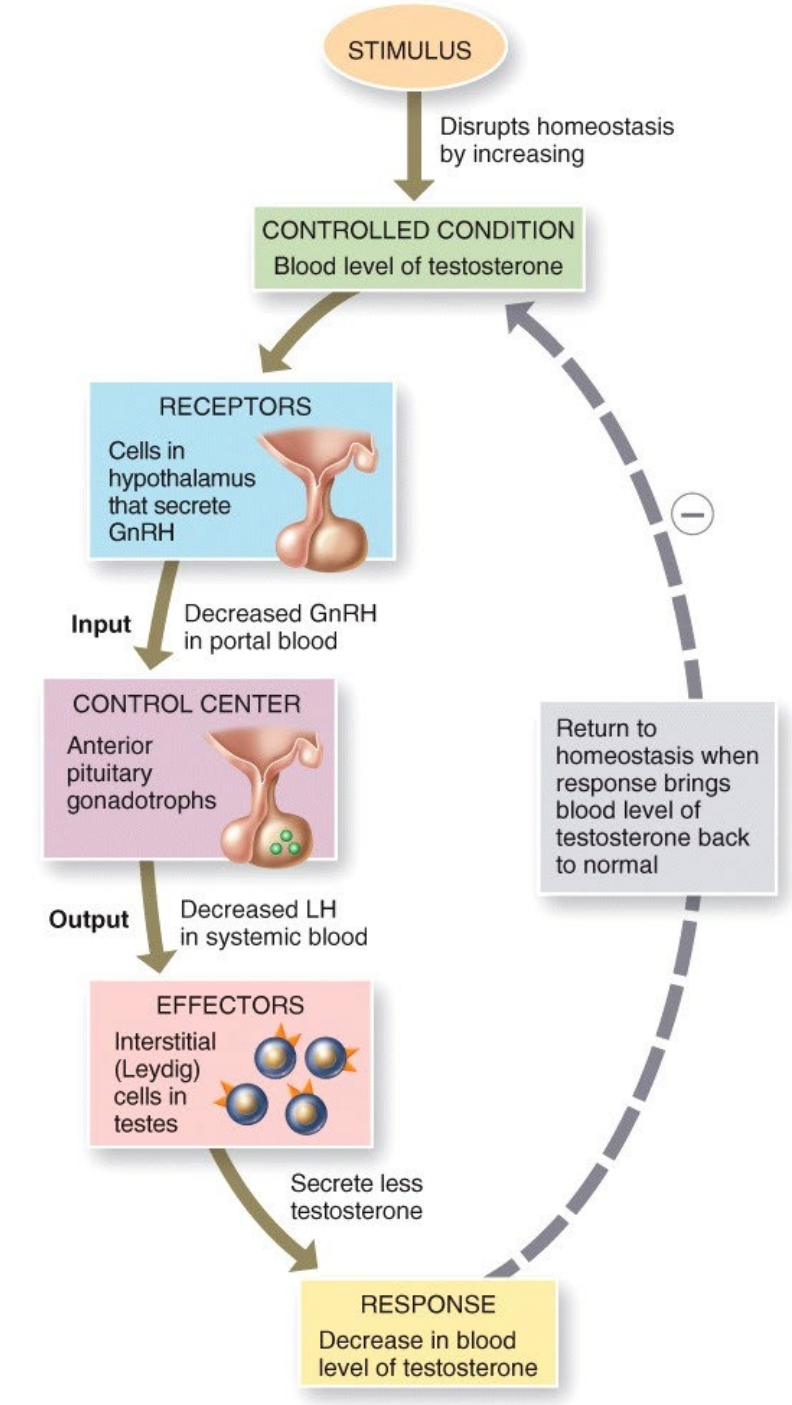
What is inhibin's function?

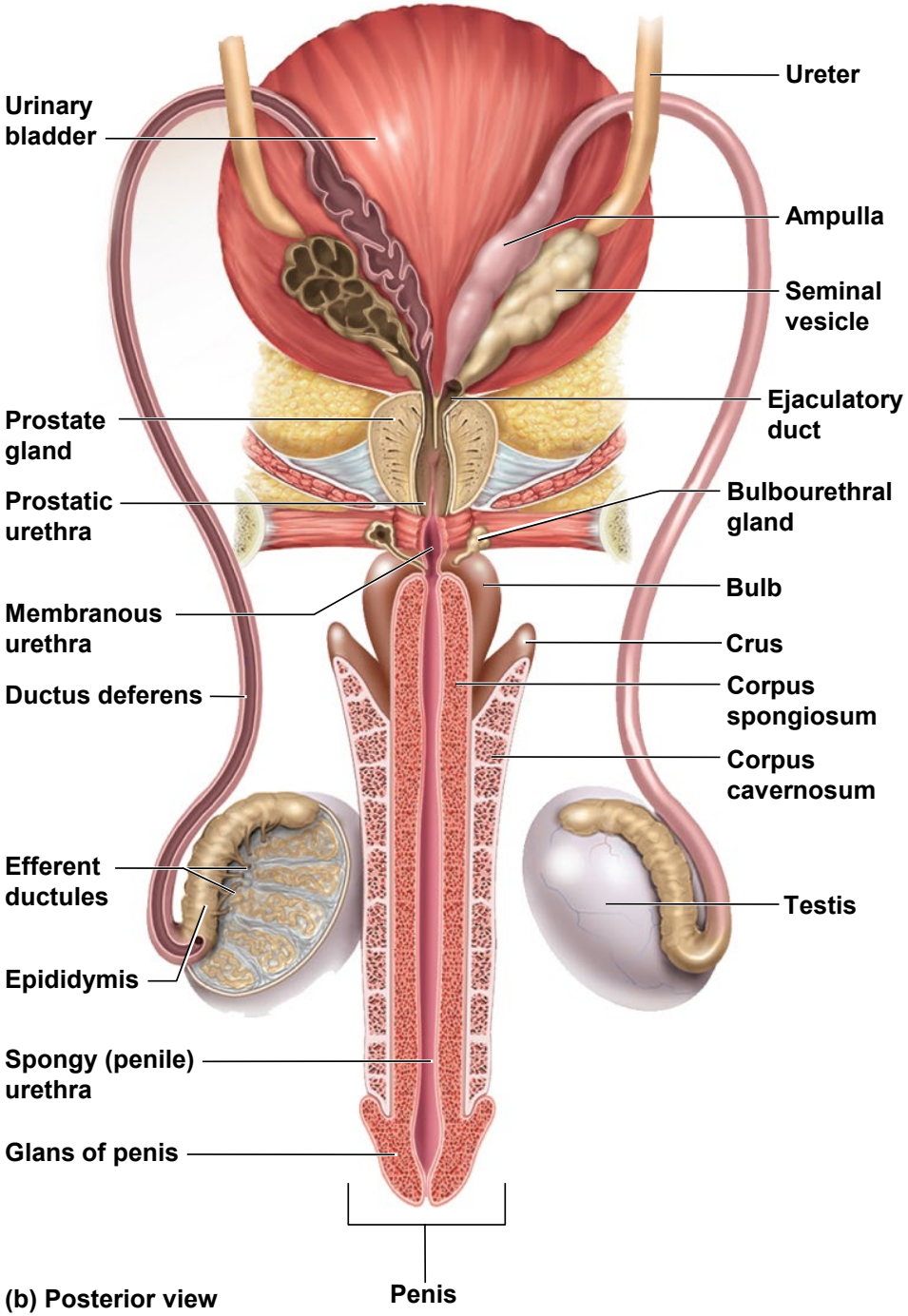

Hypothalamus
GnRH
Testosterone decreases release of GnRH and LH
Anterior pituitary
Gonadotroph
Inhibin decreases release of FSH
Together with testosterone, FSH stimulates spermatogenesis
FSH
LH
LH stimulates testosterone secretion
Testosterone
Inhibin
ABP
Testosterone
Spermatogenic cells
Sustentacular cells secrete androgen-binding protein (ABP)
Dihydro-testosterone (DHT)
Interstitial cells secrete testosterone
• Male pattern of development (before birth)
• Enlargement of male sex organs and expression of male secondary sex characteristics (starting at puberty)
• Anabolism (protein synthesis)
Key:
LH
LH receptor
FSH
FSH receptor
Testosterone
Androgen receptor

Hormonal regulation of testicular function via the hypothalamic-pituitary-gonadal (HPG) axis.



Response to Excess Testosterone





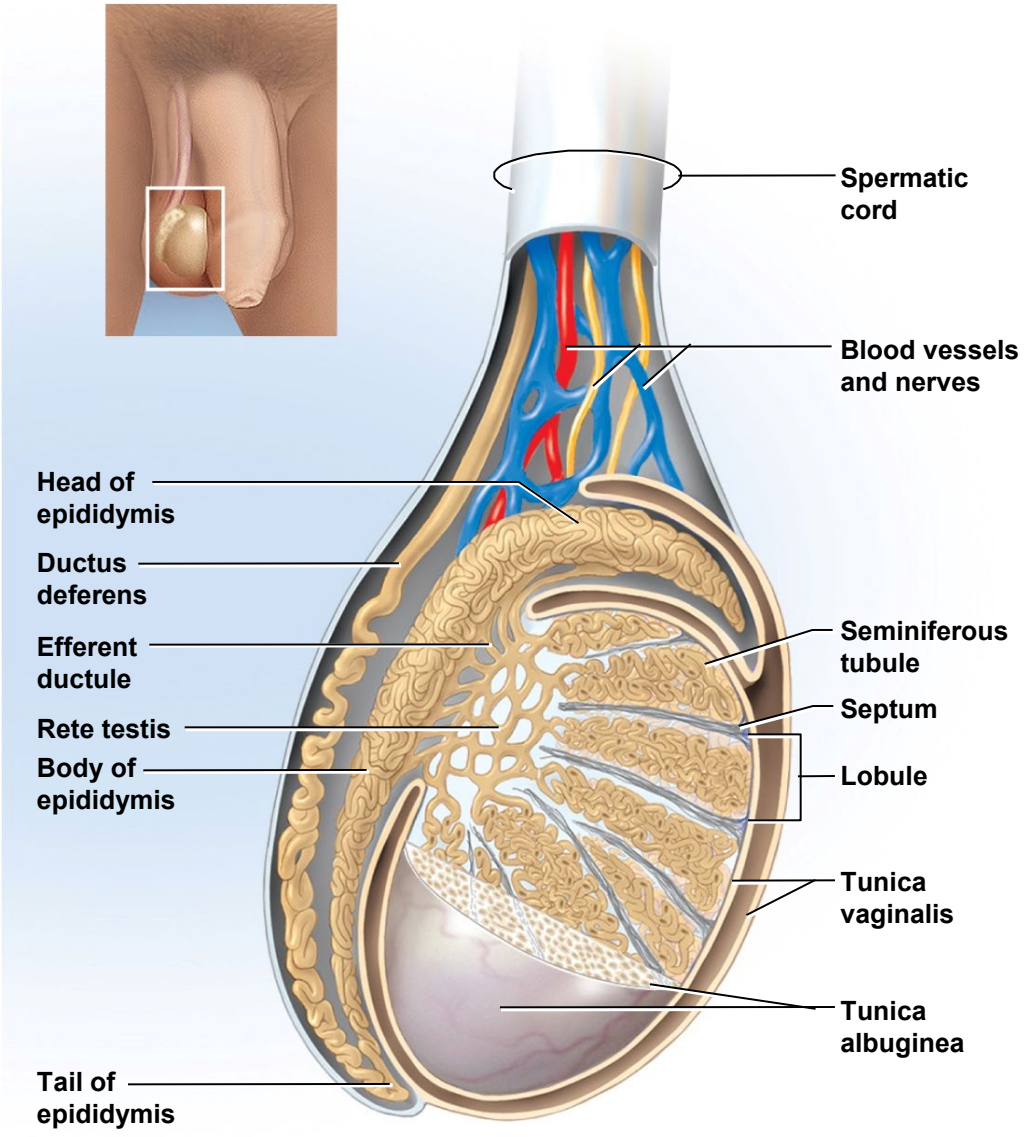
Why is male testes outside the abdominal cavity?

Testis must be outside abdominal cavity for spermatogenisis

Elevated temperature within the abdominal cavity will inhibit spermatogenisis.

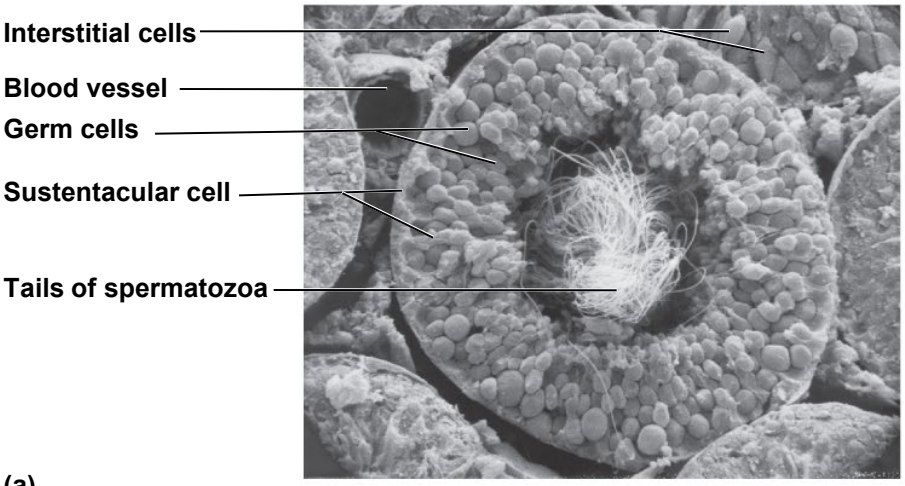
Testes must migrate from the abdominal cavity, through the spermatic cord, and into the scrotum.

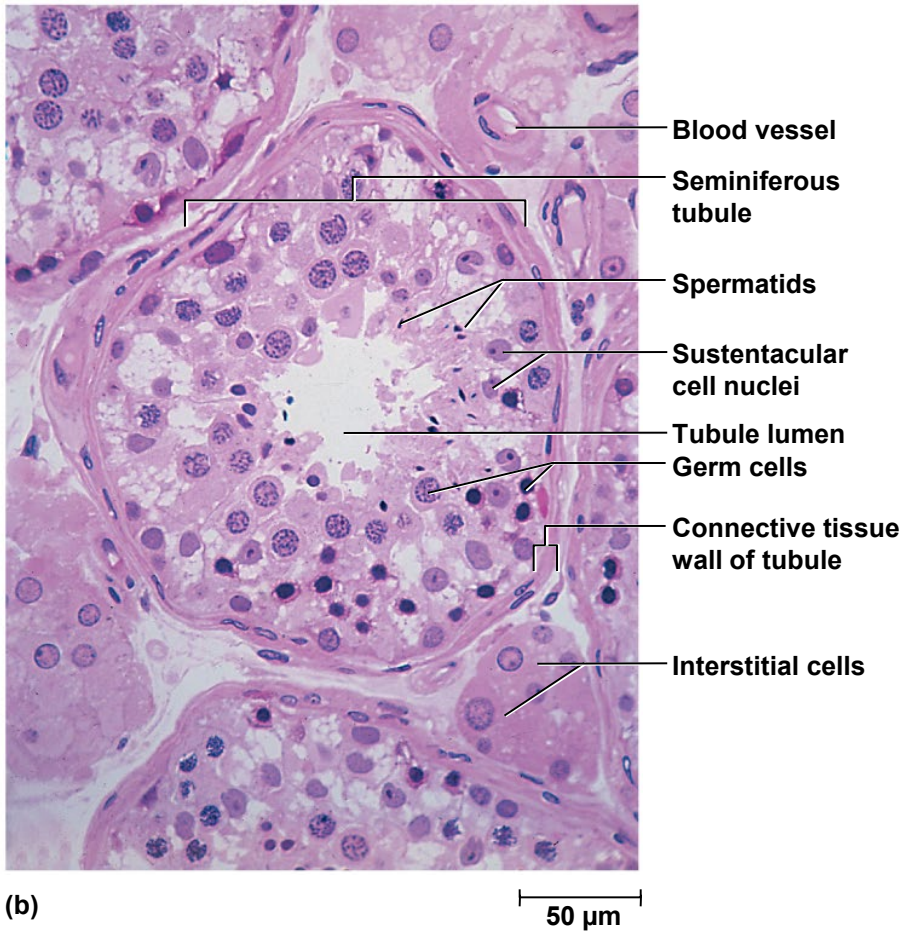
Testis and Associated Structures



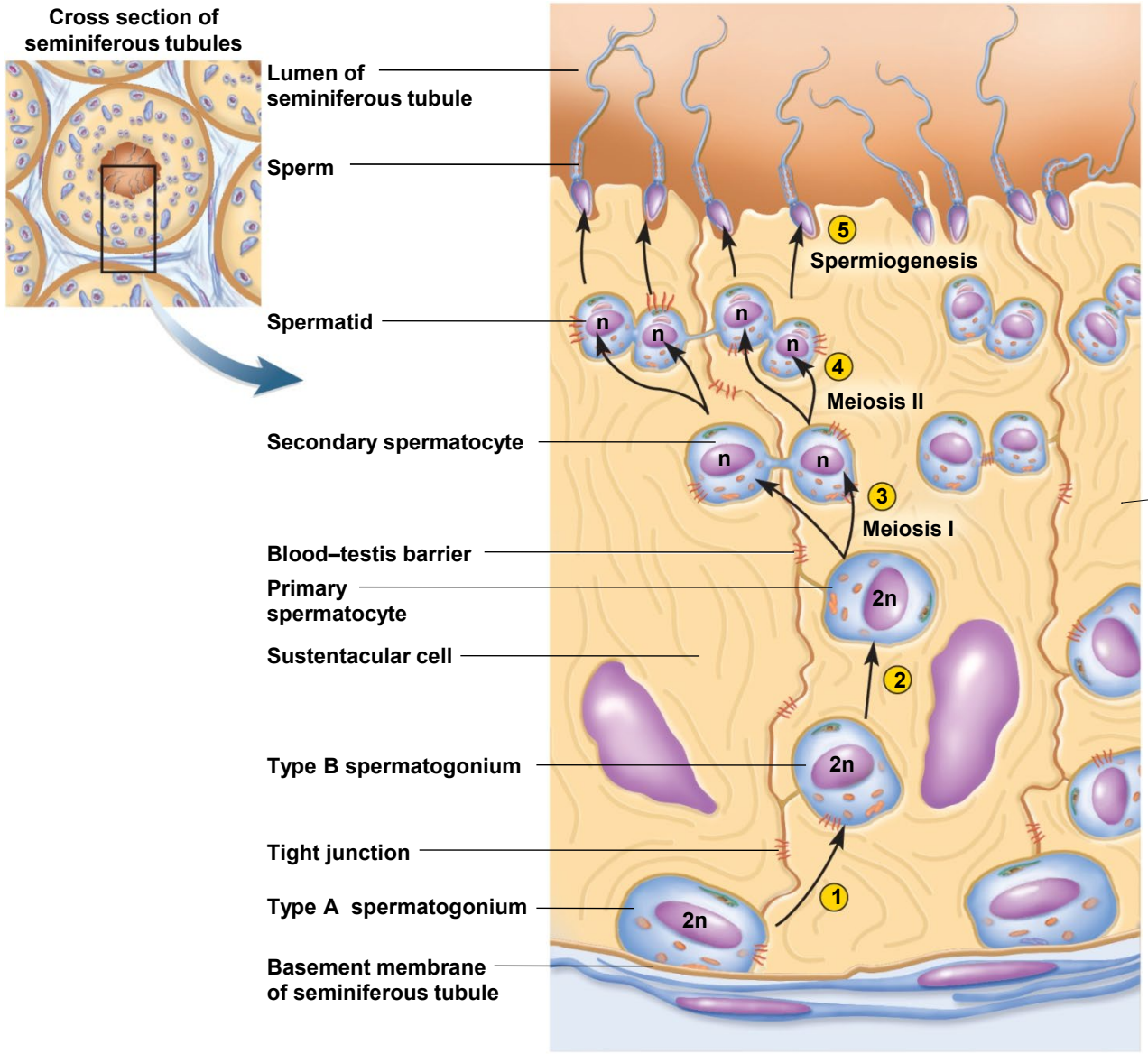
Cross Section of the Seminiferous Tubule

Histology of Testis





Spermatogenesis



Sustentacular cells form the wall of the seminifierous tubule

Spermatogenesis and Meiosis

Spermatogenesis - process of sperm production in seminiferous tubules

Involves three principal events:

- remodeling of large germ cells (stem cells) into small, mobile sperm cells with flagella
- reduction of chromosome number by one-half in sperm cells (unites with egg to return to 46)
- shuffling of genes so new combinations exist in the sperm that is different from the male

Ensures genetic variation in the offspring

Four sperm cells produced from one germ cell by meiosis (haploid cells)

Spermatogenesis and the Testes

Seminiferous Tubules

One to three in each lobule /// each tubule lined with a thick germinal epithelium for sperm generation /// these are the sustentaclar cells

Interstitial (Leydig) Cells

Located between tubules // these cells produce testosterone

Sustentacular Cells (also called Sertoli Cells or Nurse Cells)

SC located between germinal epithelium cells // protect the germ cells and promote their development

Germ cells depend on “nurse cells” for their nutrients, waste removal, growth factors, and other needs

Developing sperm connected to nurse cells by gap junctions

Spermatogenesis

Puberty brings on spermatogenesis

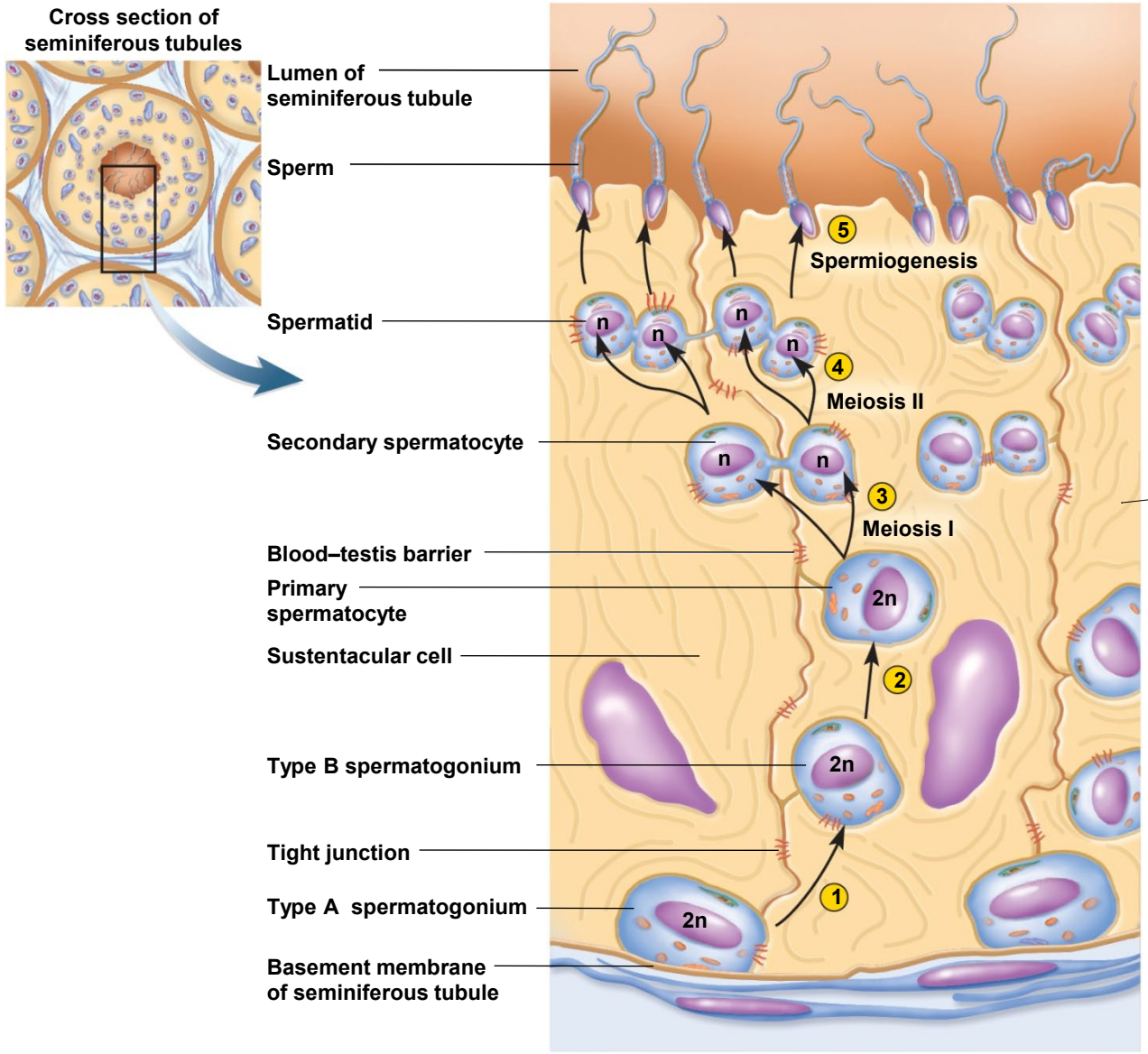
Spermatogonia lie along the periphery of the seminiferous tubules and divide by mitosis

One daughter cell of each division remains in the tubule wall as a stem cell - **type A spermatogonium**

Other daughter cell migrates slightly away from the wall to become a future sperm – the **type B spermatogonium**

Produce 400 million sperm per day

Spermatogenesis



Sustentacular cells form the wall of the seminifierous tubule

Spermatogenesis and the Blood-Testis Barrier (BTB)

BTB formed by tight junctions between **sustentacular cells**

Separating developing sperm from immune system // sperm are “haploid”

Prevents antibodies and other large molecules in the blood from getting to germ cells

Germ cells are immunologically different from body cells and would be attacked by immune system

Spermatogenesis and the Blood-Testis Barrier (BTB)

Once the primary spermatocyte undergoes meiosis, it becomes genetically different and needs to be protected from the host immune system

The primary spermatocyte moves towards the lumen of the seminiferous tubule.

A tight junction forms between sustentacular cells // blocking antibodies from reaching newly formed primary spermatocytes

Tight junctions create the blood-testis barrier

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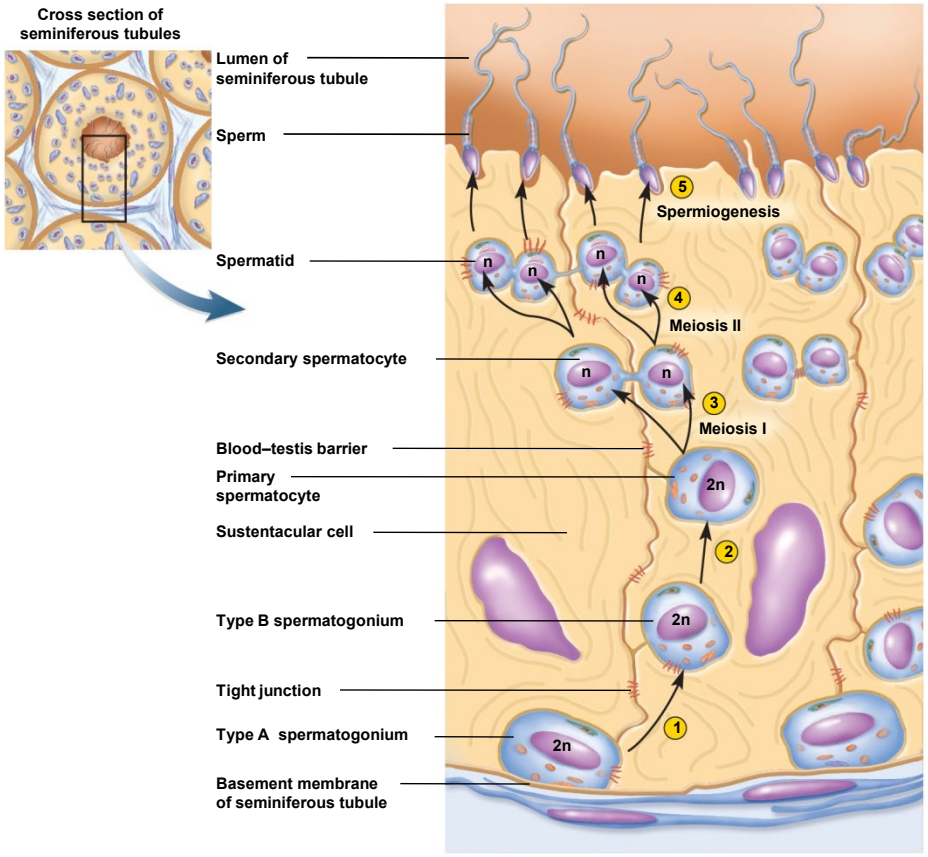


Contributors to Semen's Volume

Three sets of glands in the male reproductive system add to the volume to semen // normal volume 2.5 ml (range 2.5 – 5 ml) // test benchmark 2.5 ml

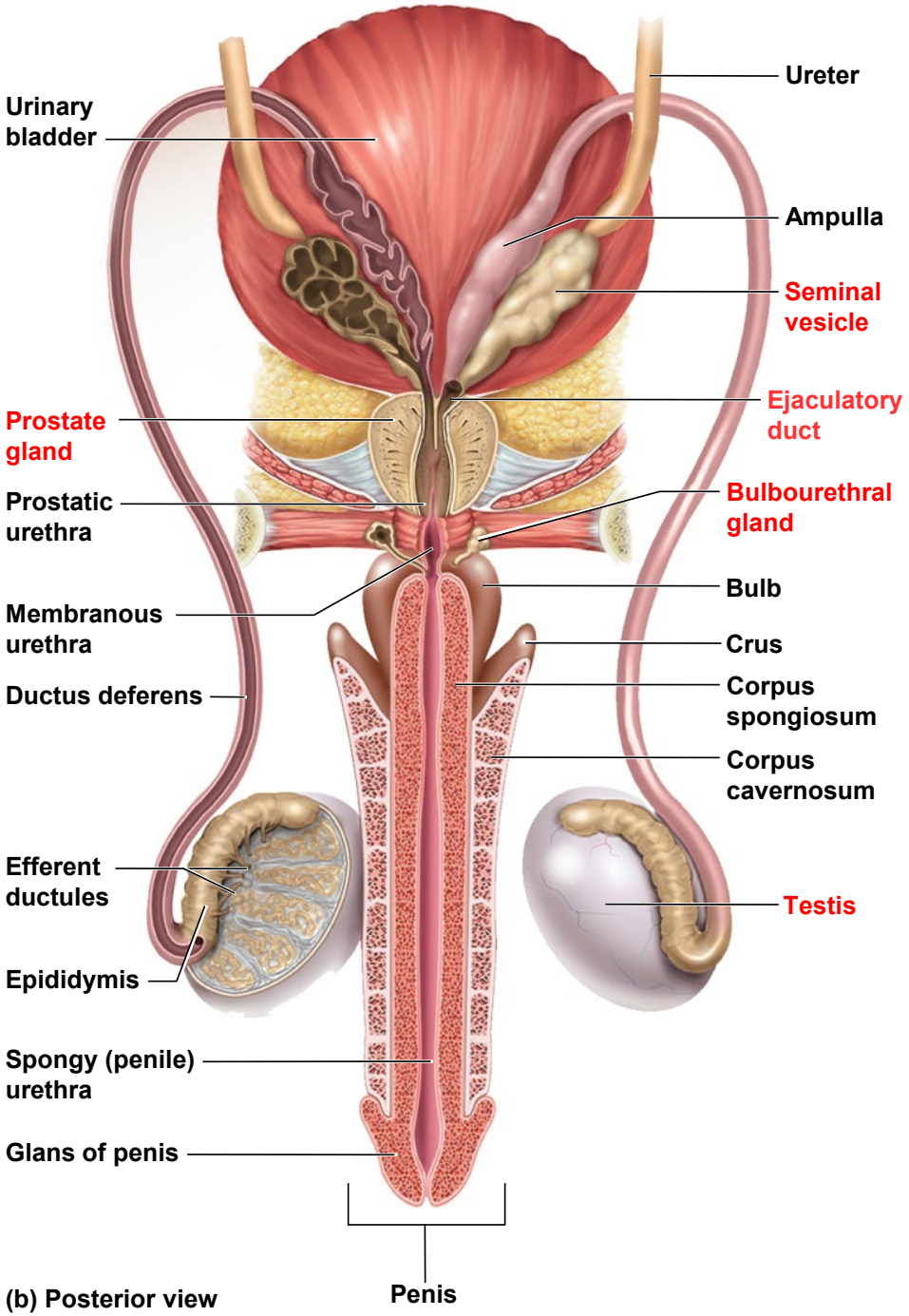
seminal vesicles // 60%

prostate gland // 30%

secretions from seminiferous tubules and sperm volume // 10%

bulbourethal gland (also called Cowper's gland) // < 0.1

Male Duct System & Accessory Glands



Seminal Vesicles

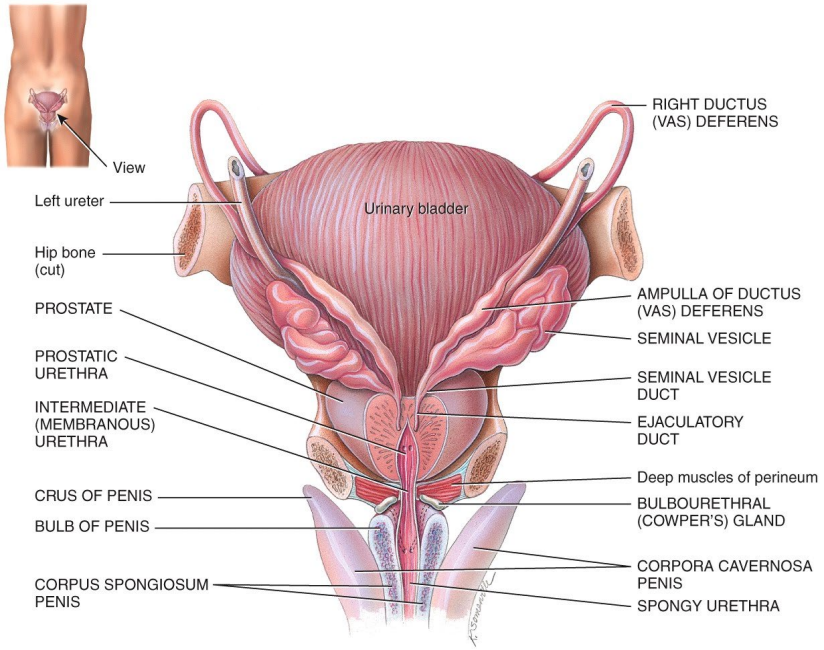
Pair of glands posterior to bladder

Seminal vesicle's secretions moves into ejaculatory duct during orgasm

Accounts for 60% of semen volume

Normal sperm count 30-400 million/mL

If lower than 20 to 25 million/mL = infertility



(a) Posterior view of male accessory organs of reproduction

Seminal Vesicles

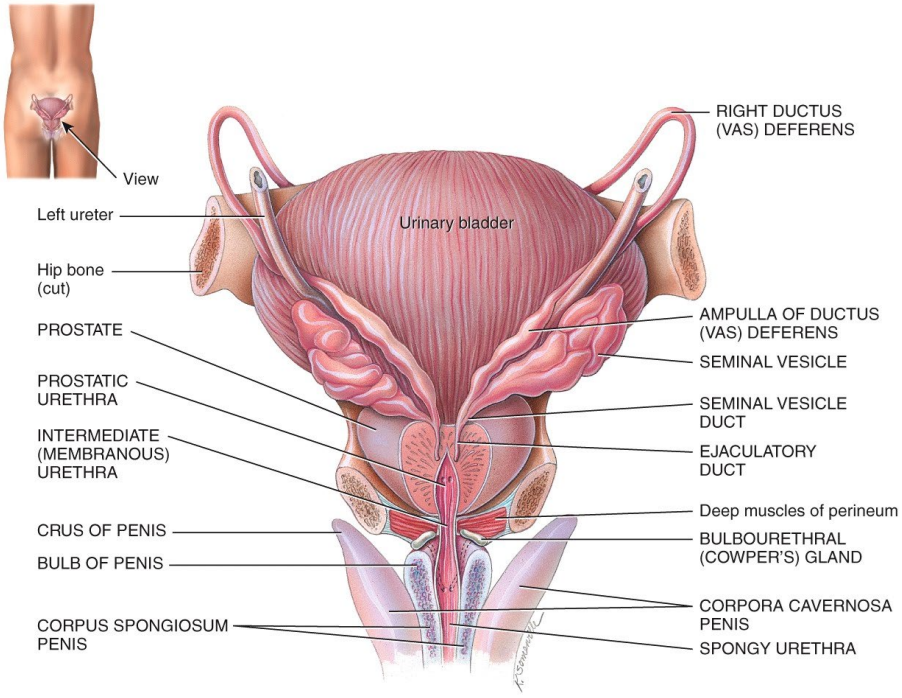
Seminal vesicles contribute viscous yellowish fluid

Contains fructose, other carbohydrates, citrate, prostaglandins, and pro-seminogelin.

Pro-seminogelin is a protein

Pro-seminogelin is converted to seminogelin by clotting enzyme secreted by prostate gland

Seminogelin is a viscous, sticky molecule // its function is to "stick" sperm near entrance of cervix



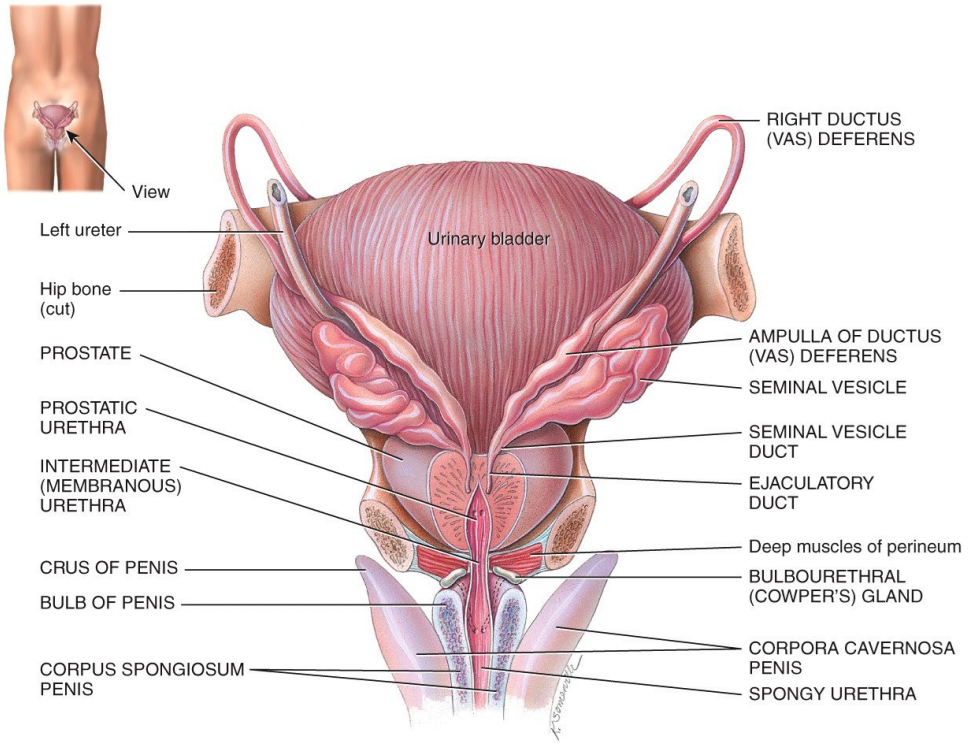
(a) Posterior view of male accessory organs of reproduction

Prostate Gland

Surrounds urethra and ejaculatory ducts /// located inferior to the urinary bladder

30 to 50 compound tubuloacinar glands

Empty through about 20 pores into the prostatic urethra



(a) Posterior view of male accessory organs of reproduction

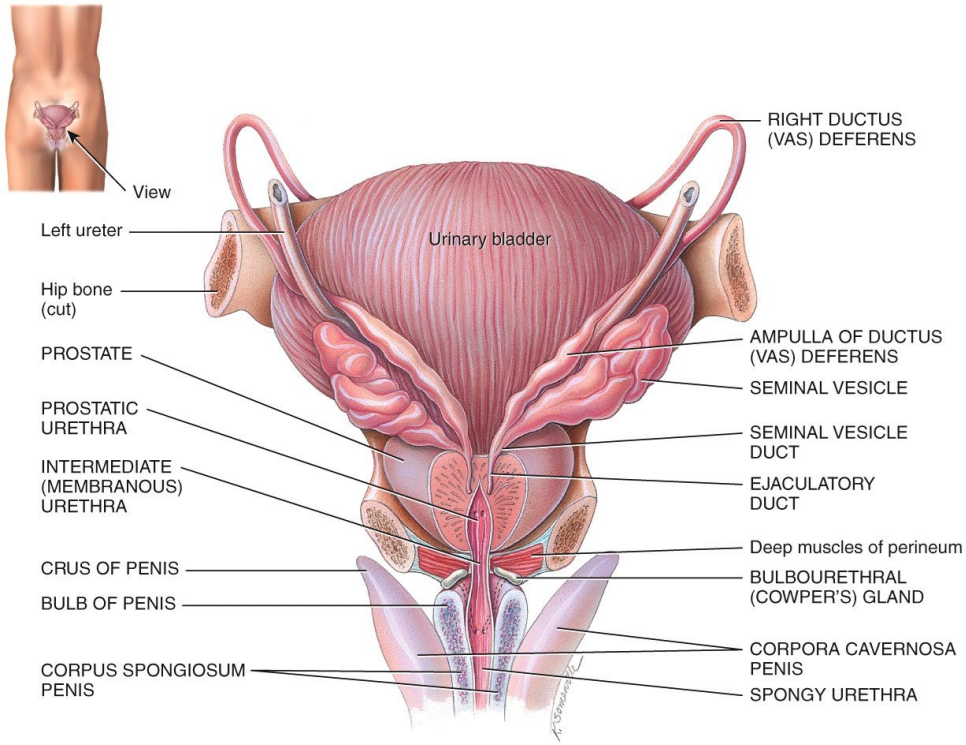
Prostate Gland

Secretes thin, milky white fluid (30% seminal fluid volume)

Contains calcium, citrate, phosphate ions, and two enzymes /// target is pro-seminogelin

First enzyme is the "clotting enzyme" – converts proseminogelin into seminogelin

Second enzyme is the hydrolyzing enzyme – serine protease /// breaks down the clot (this is the prostate-specific antigen)



(a) Posterior view of male accessory organs of reproduction

Role of Pro-seminogelin in Fertilization

“Stickiness” of semen promotes fertilization

Proseminogelin secreted from seminal vesicles

Prostate's clotting enzyme from prostate activates **proseminogelin**

Clotting enzyme converts proseminogelin to a sticky fibrin-like protein – **seminogelin**

Seminogelin entangles the sperm // sticks semen to the inner wall of the vagina and cervix

This ensures that the semen does not drain out of the vagina

Promotes uptake of sperm-laden “clott” near cervix into the uterus

20 to 30 minutes after ejaculation, serine protease from prostatic fluid breaks down seminogelin, and liquifies the semen

It is now when the sperm become motile

At same time, prostaglandins now thins the mucus of the cervix and initiates peristaltic waves in uterus and uterine tubes to promote movement of sperm towards ovum in fallopian tube

Bulbourethral Glands (Cowper's Gland)

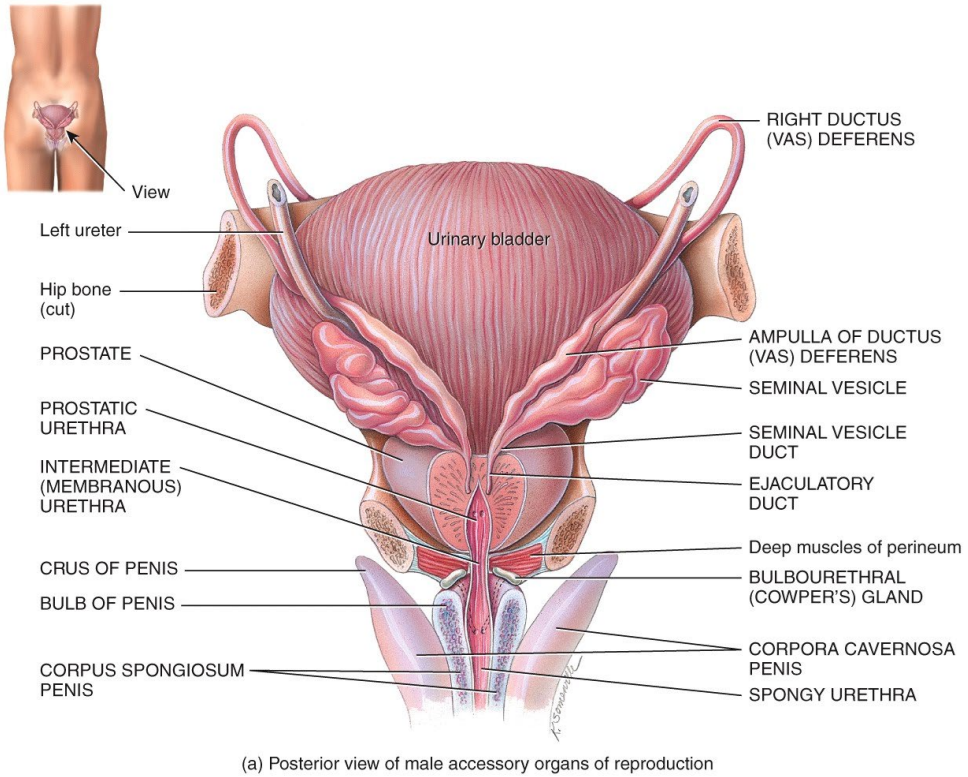
Located near bulb of penis

During sexual arousal, they produce a clear viscous lubricating fluid

Lubricates the head of the penis in preparation for intercourse

Secretion also protects the sperm by neutralizing the acidity of residual urine in the urethra

Less than 0.1%



(a) Posterior view of male accessory organs of reproduction

Sperm's Pathway in Male Duct System

Seminiferous tubules

Rete testes

Efferent ductules

Epididymis

Ductus deferens

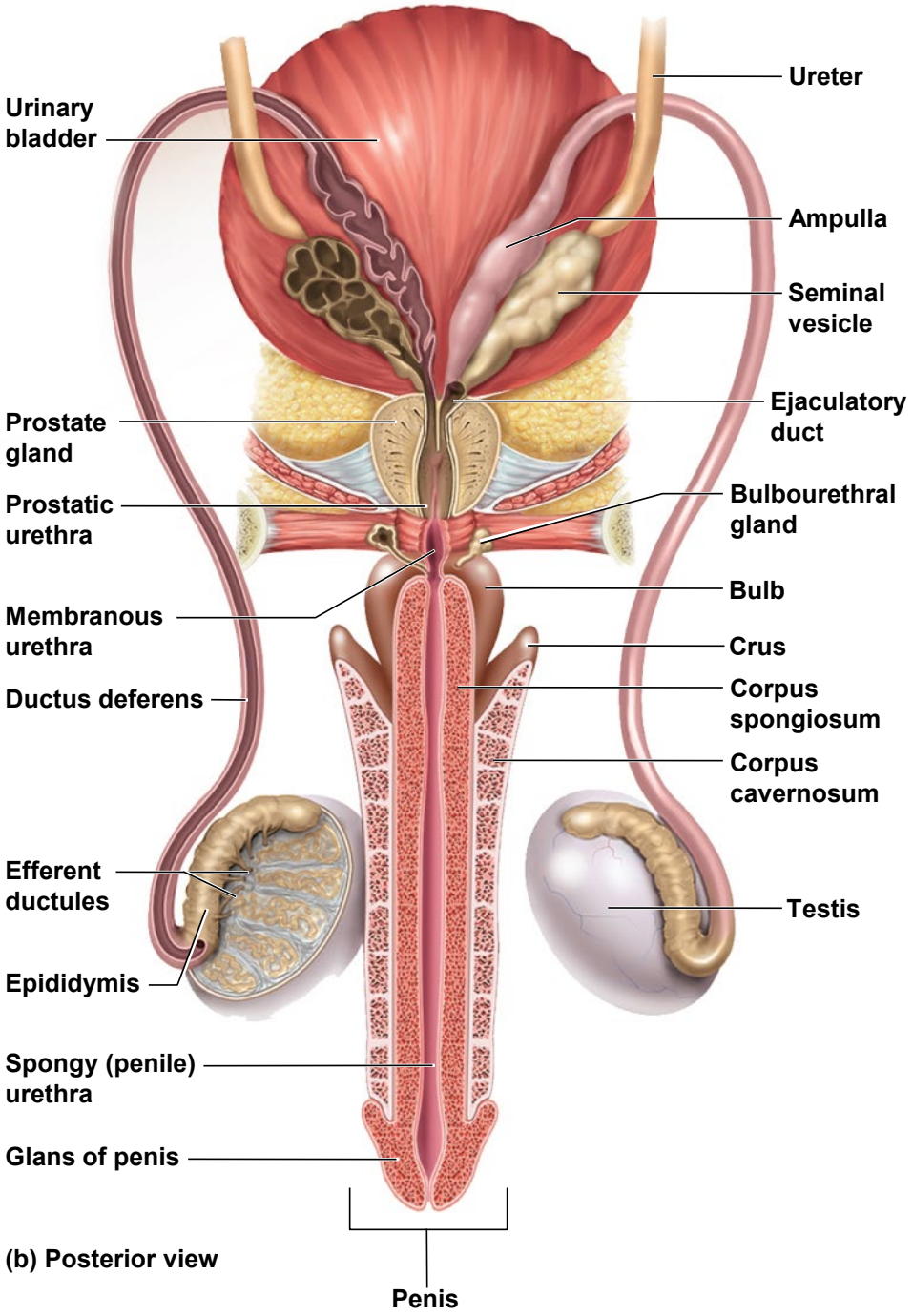
Ampulla of ductus deferens

Ejaculatory duct

Prostatic urethra

Membranous urethra

Spongy (penile) urethra

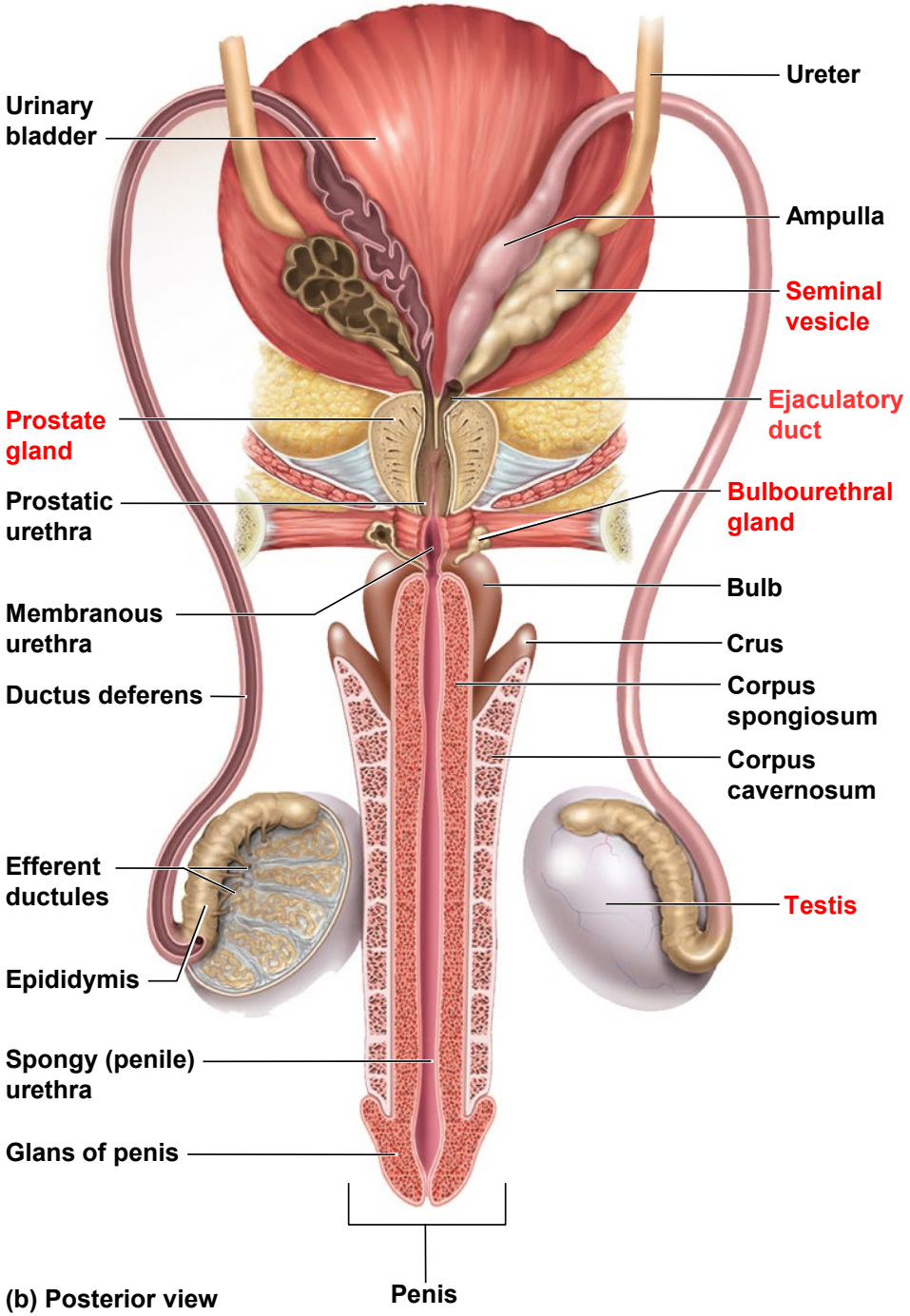


Where are sperm stored?

How long may sperm be stored?

Mature sperm is stored in the epididymis – the coil-like structure that runs across the top of each testicle.

Sperm can remain in the epididymis for about two weeks before ejaculation, after two weeks broken down and reabsorbed by the body.



When Is Pregnancy Most Likely to Occur?

200 million sperm enter the vagina

Fewer than two million enter cervix

Only about 200 reach the secondary oocyte

Fertilization most likely to occur 12 to 24 hours after ovulation

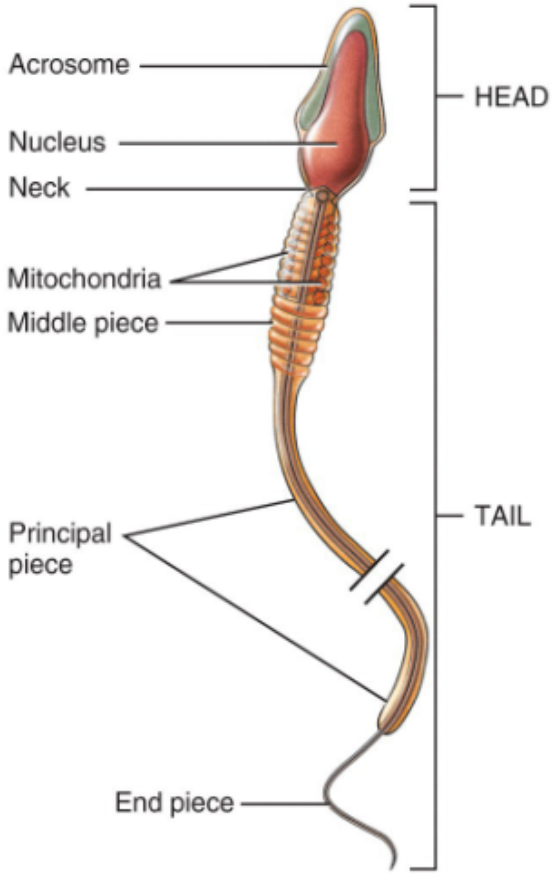
Egg is only viable for 24 hours

Sperm can not fertilize egg for first 10 hours after deposit in female (i.e. period of capacitation)

Sperm most viable 48 hours after they enter vagina /// may last for up to five days

According to the American College of Obstetricians and Gynecologists (ACOG), a woman can become pregnant if they have sex anywhere from 5 days before until 1 day after ovulation.

(Test Answer: 5 days before ovulation and 1 day after)



Male Sexual Response

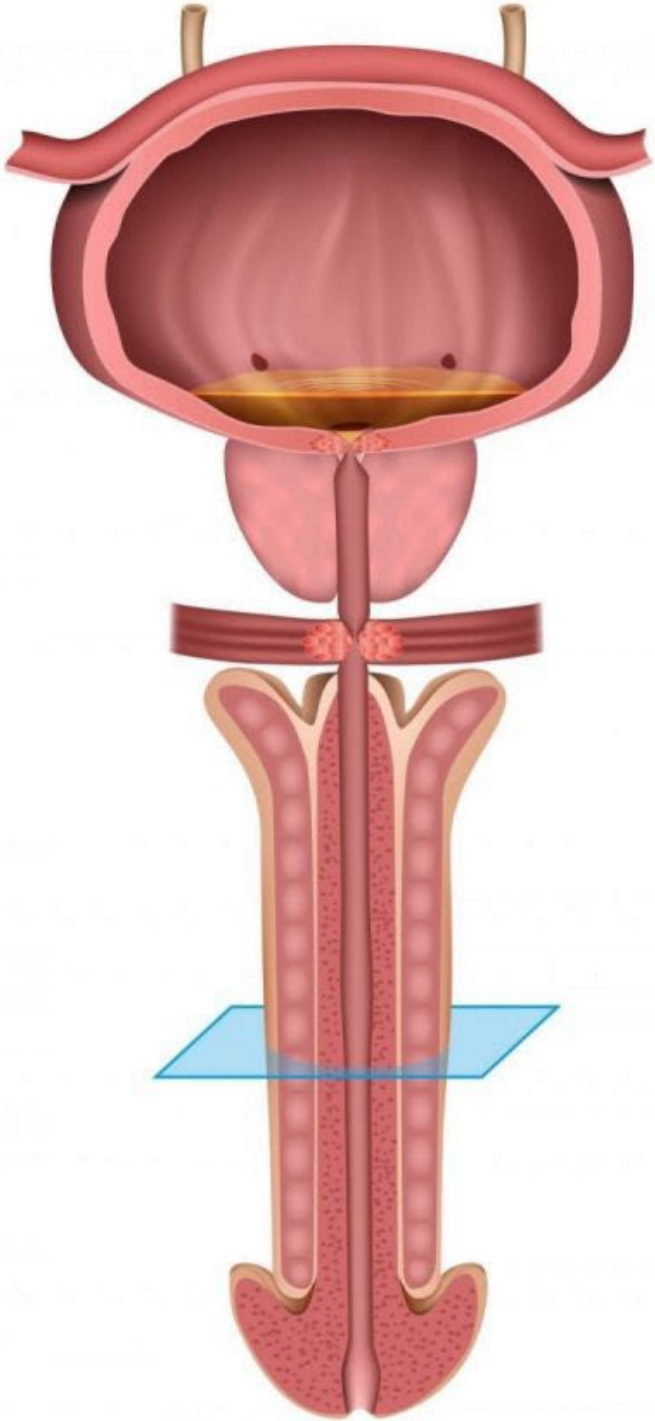
Brought to general public by groundbreaking publication of research papers by William Masters and Virginia Johnson (1966)

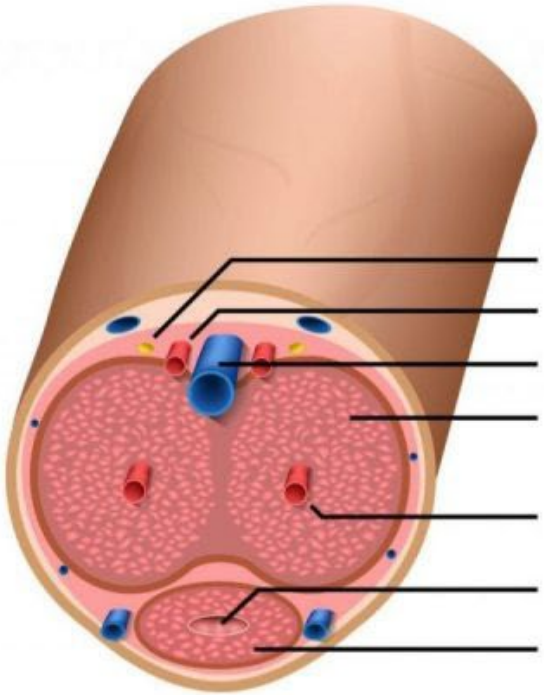
Sexual Response divided into four recognizable phases (see next slide)

- Excitement
- Orgasm (event 1) – emission stage (sperm moved into urethra)
- Orgasm (event 2) – ejaculation of sperm or expulsion stage
- Resolution

Similar phases occur in male and female sexual response // Masters & Johnson's work led to therapy for sexual dysfunction

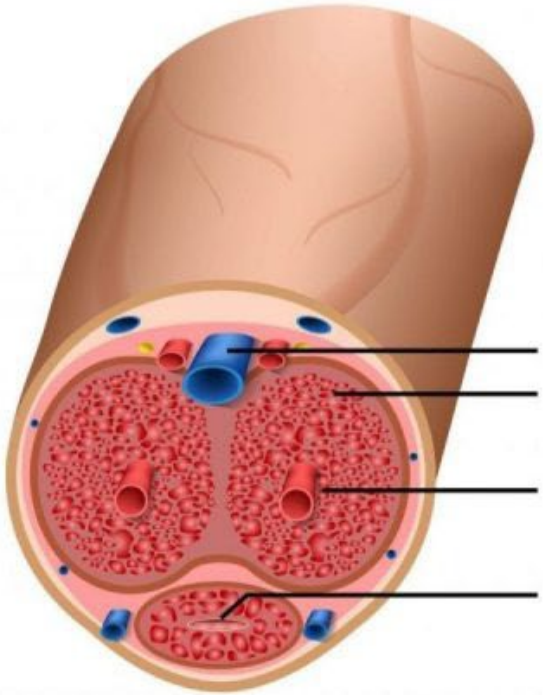
Sexual intercourse is also known as coitus, coition, or copulation





Flaccid penis

Dorsal nerve
Dorsal artery
Deep dorsal vein
Corpus cavernosum (not filled with blood)
Deep artery
Urethra
Corpus spongiosum



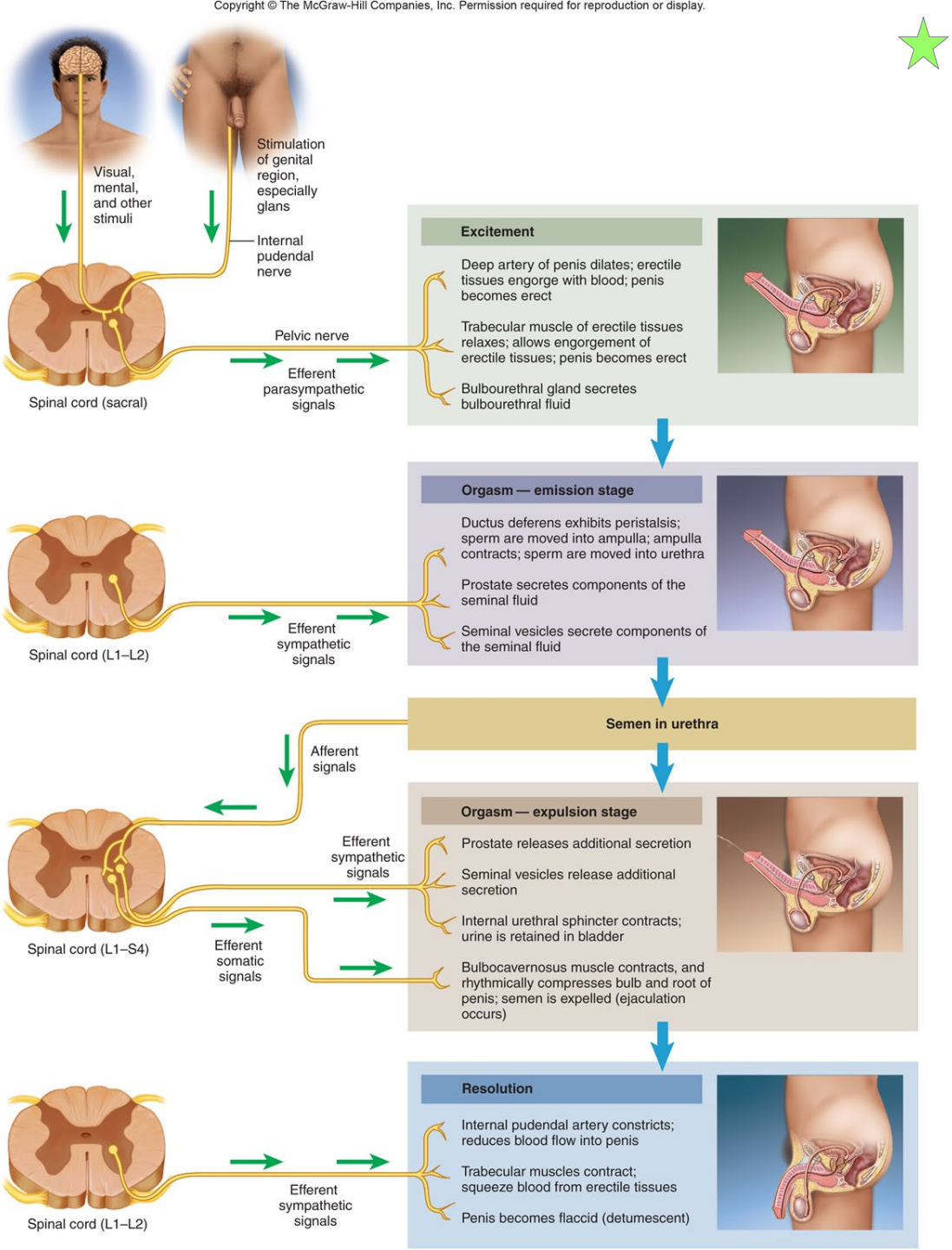
Erect penis

Dilated dorsal vein
Corpus cavernosum filled with blood
Arteries are increased
Compressed urethra

Male Sexual Response

Occurs in Four Stages

- Excitement (engorgement of penile erectile tissue)
- Emission Stage of orgasm (peristalsis moves sperm from epididymis into penile urethra
- Secretions enter urethra from prostate and seminal vesicles)
- Expulsion stage of orgasm (rhythmic contraction of bulbocavernosus muscle causes ejaculation // semen is expelled)
- Resolution (penis becomes flaccid)



Male Sexual Response and Innervation of the Penis

The glans penis has abundance of tactile, pressure, and temperature receptors.

Dorsal nerve and internal pudendal nerve of penis lead to integrating centers in sacral spinal cord.

Autonomic nerves and somatic motor fibers carry impluses from integrating center to penis.

Sympathetic NS induce an erection in resonse to input from special senses and to sexual thoughts

Parasympathetic NS induce an erection in response to direct stimulation to the penis.

Orgasm and Ejaculation

Orgasm or **climax** – a short but intense reaction that is associated *usually with the discharge of semen*

–lasts 3 to 15 seconds

–heart rate, blood pressure, and breathing greatly elevate with orgasm

•**male sperm ejaculation occurs in two stages:**

–**Emission**

•sympathetic nervous system stimulates peristalsis which propels sperm through ducts as glandular secretions are added // fluids enter spongy urethra

–**Expulsion**

•semen fills and expand urethra to activate somatic and sympathetic reflexes /// this stimulates muscular contractions that lead to expulsion

•sympathetic reflex also constricts internal urethral sphincter so urine cannot enter the urethra and semen can not enter the bladder

•ejaculation and orgasm are not the same // orgasm can occur without ejaculation

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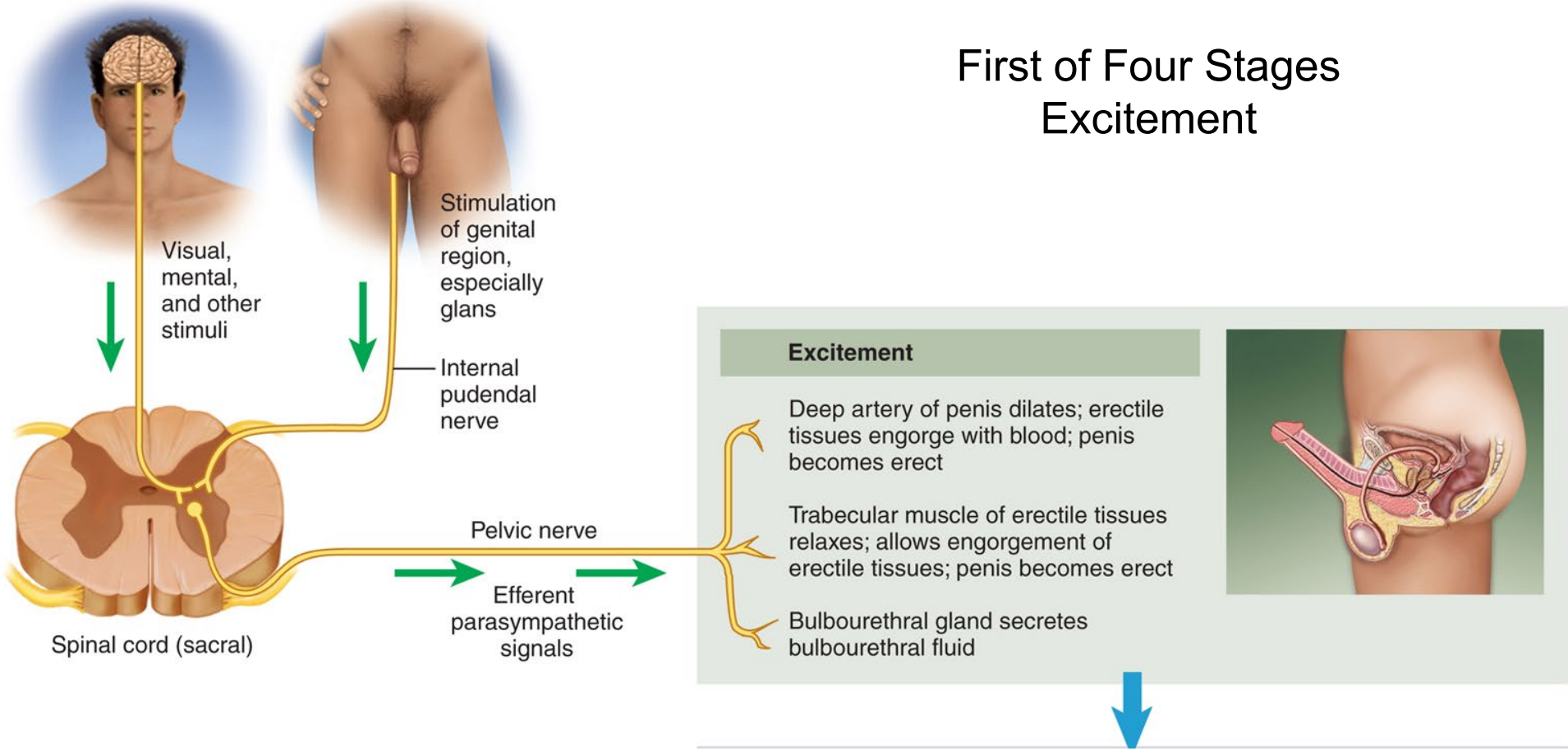
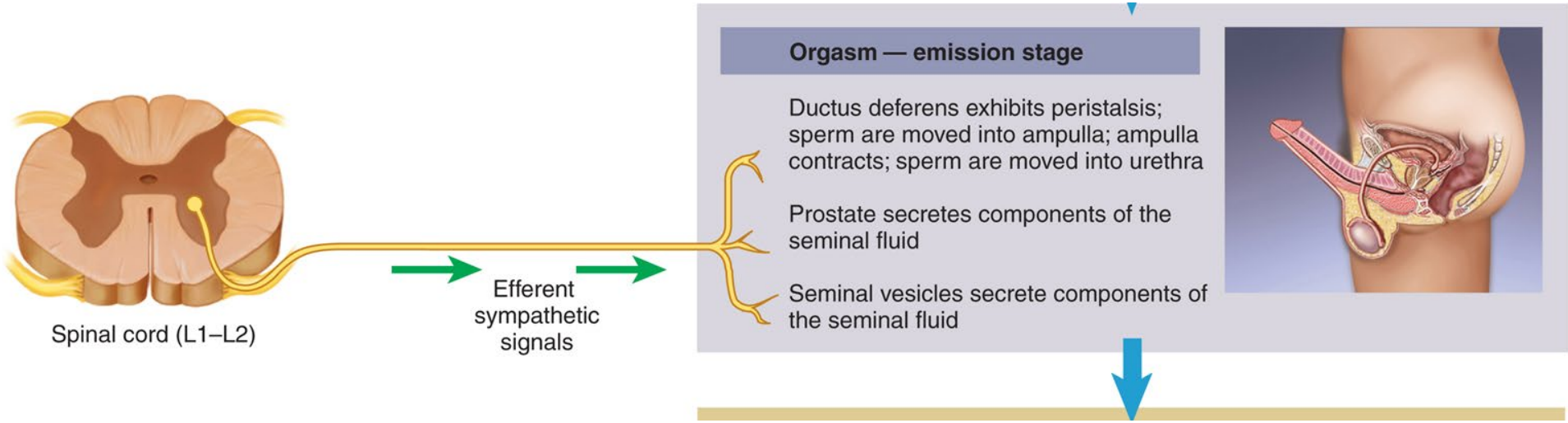
First of Four Stages
Excitement



Sympathetic NS induce an erection in resonse to input from special senses and to sexual thoughts

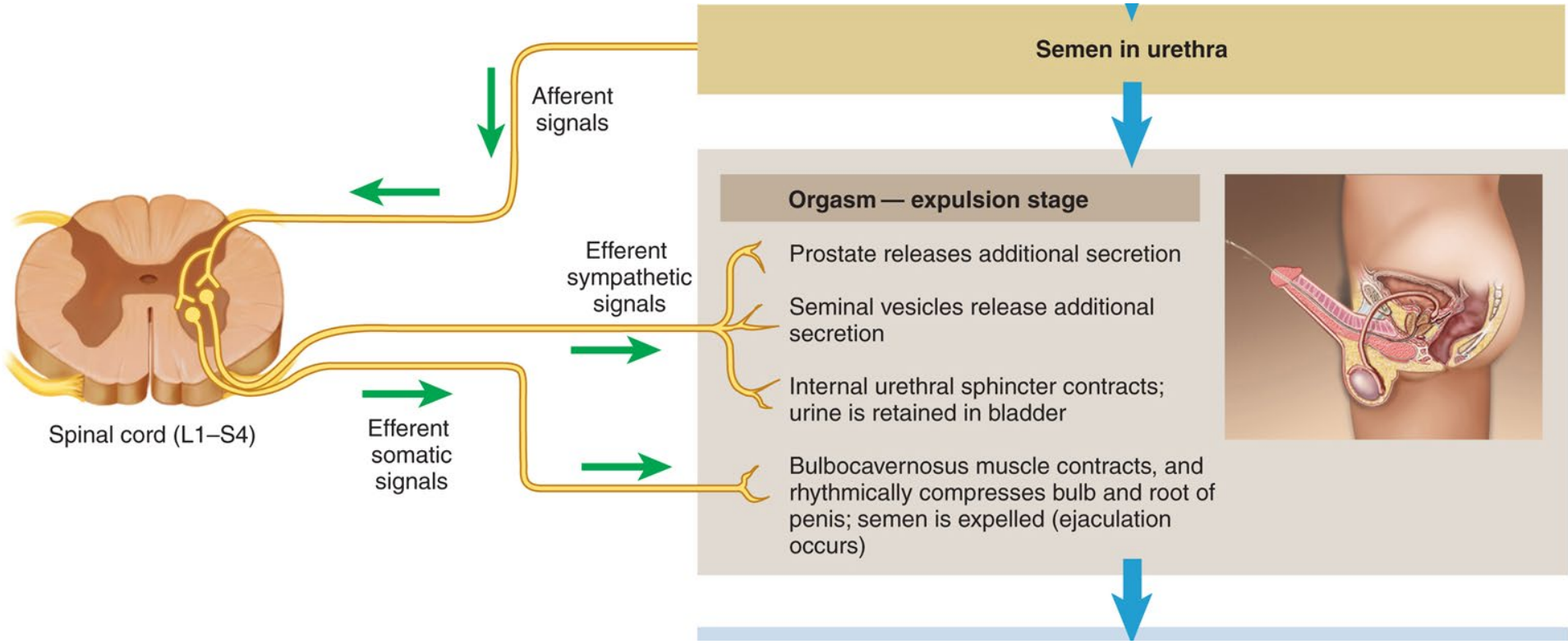
Parasympathetic NS induce an erection in response to direct stimulation to the penis.

Second of Four Stages
Emmission



Note: semen moves into urethra / this initiates an afferent nerve signal / see next slide

Third of Four Stages
Expulsion



Third of Four Stages
Resolution

