Marta Bałajewicz-Nowak, MD, PhD
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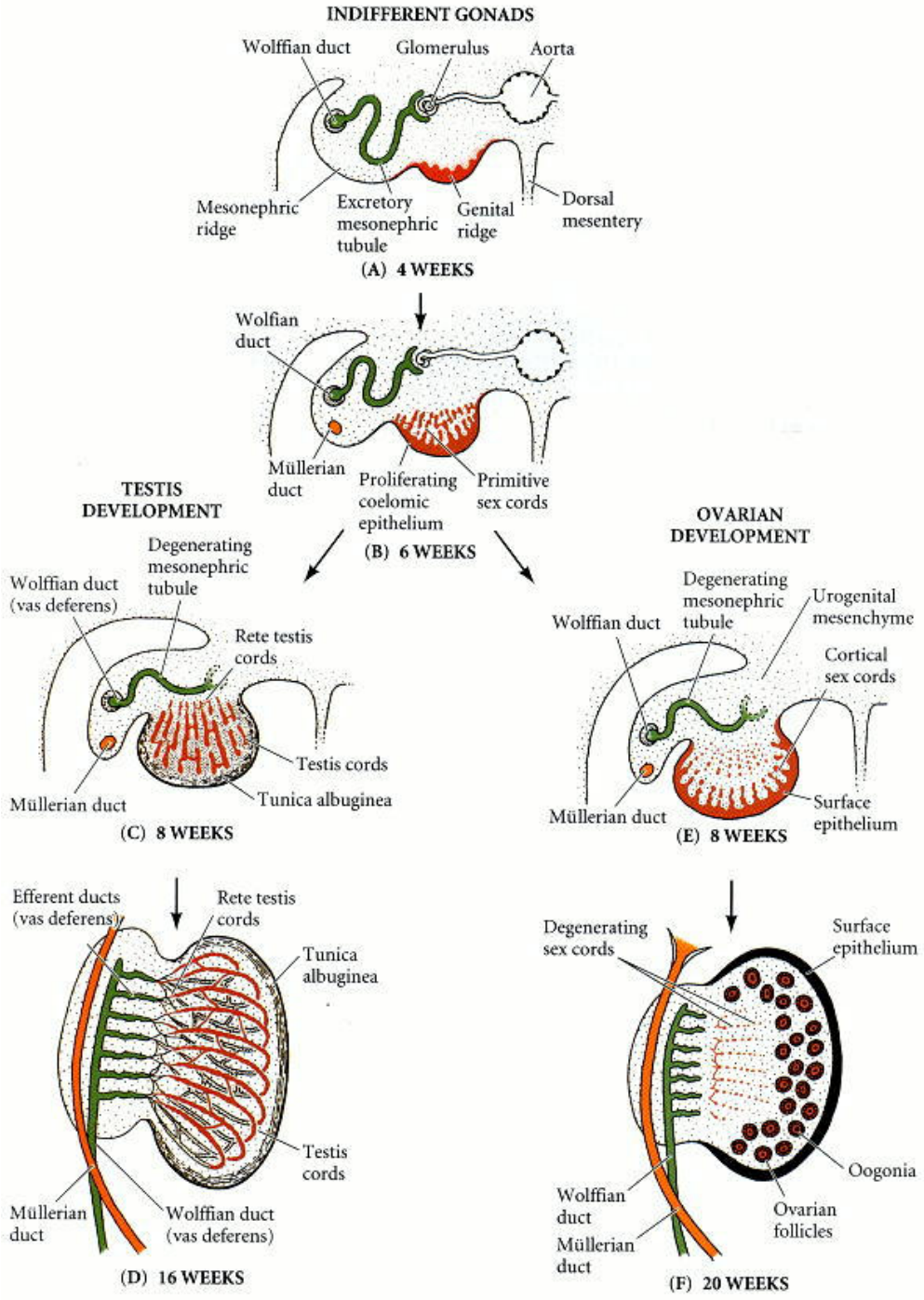


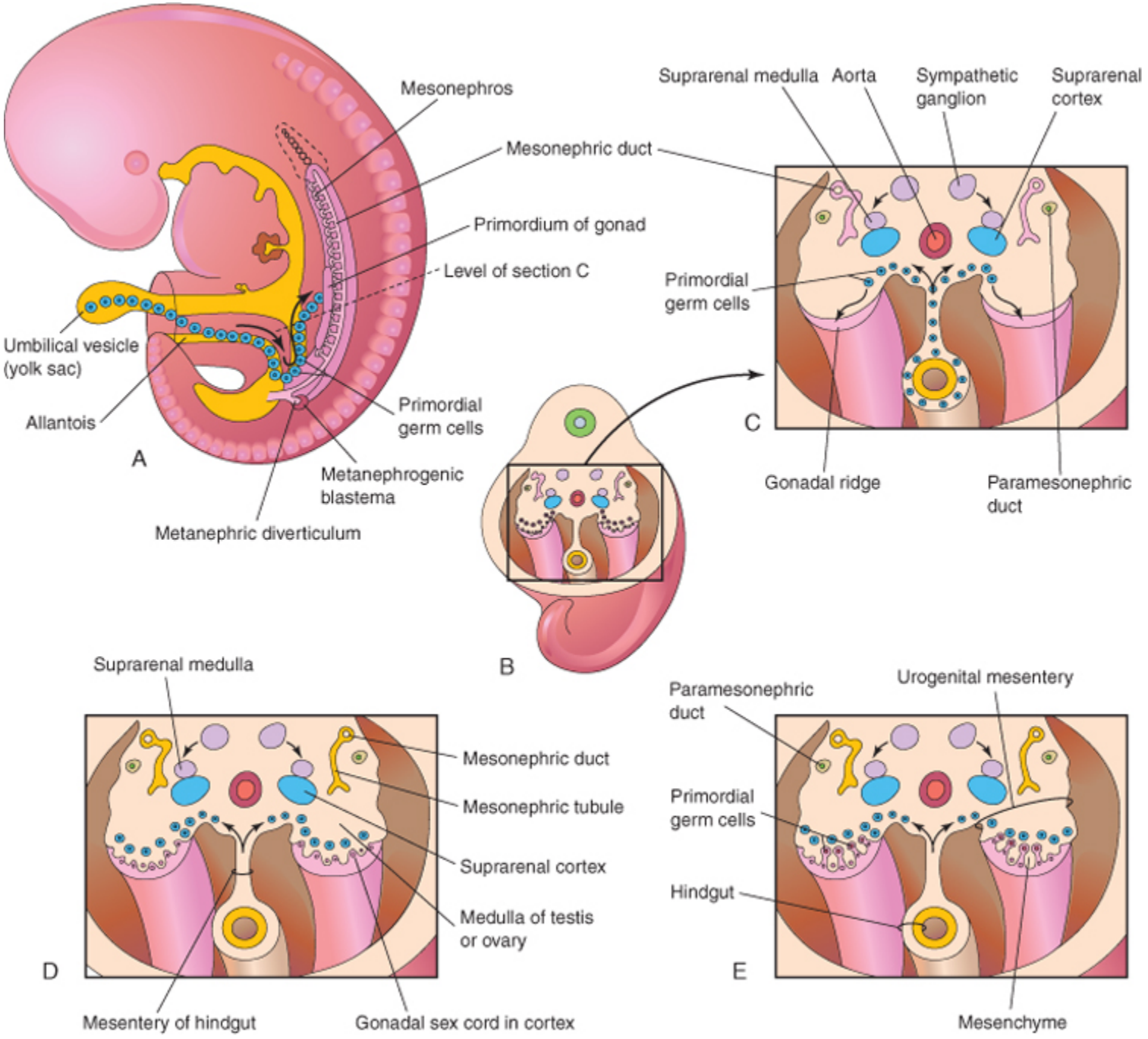
The gonads do not acquire male or female morphological characteristics until the **seventh week of development.**

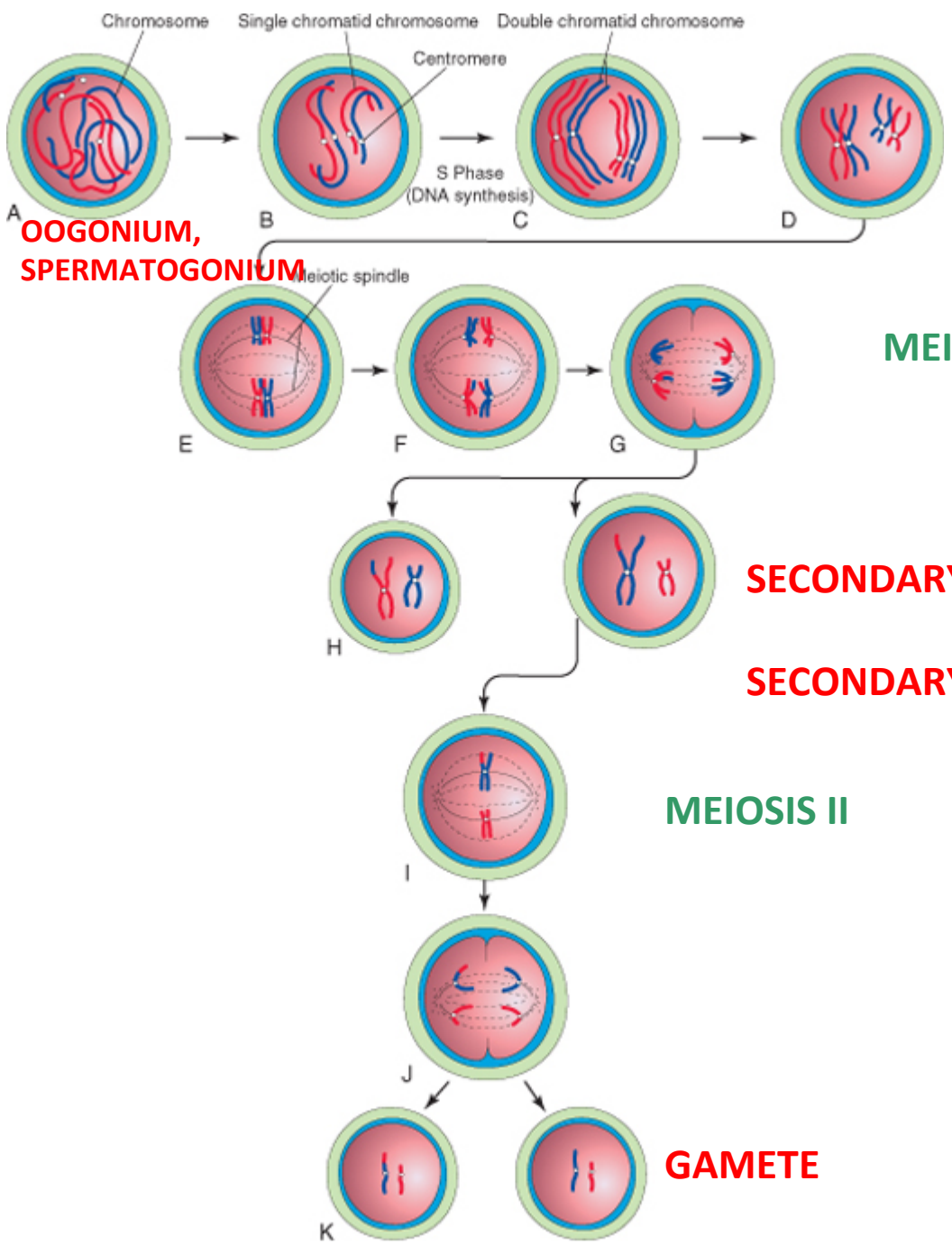
- Gonads appears initially as a pair of longitudinal ridges – genital/gonadal ridges.

- Primordial germ cells **(they're formed in the epiblast during the second week and than move to the wall of the yolk sac)** invade the genital ridges – 6th week.

- PGCs have inductive influence on development of gonads.

- Epithelial cells proliferate and penetrate the underlying mesenchyme – form **primitive sex cords = indifferent gonad**





OOGONIUM,
SPERMATOGONIUM

PRIMARY OOCYTE

PRIMARY SPERMATOCYTE

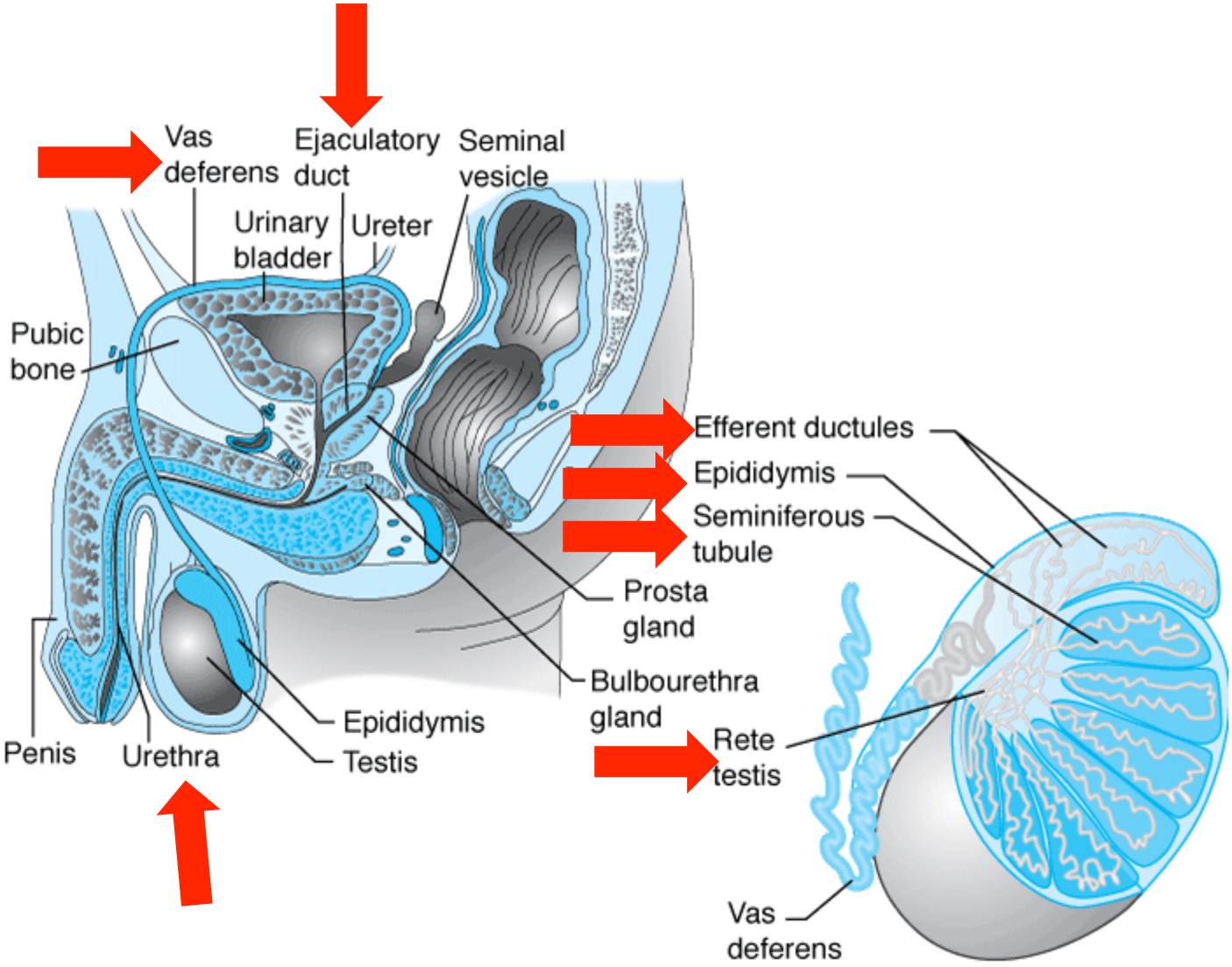
MEIOSIS I

SECONDARY OOCYTE

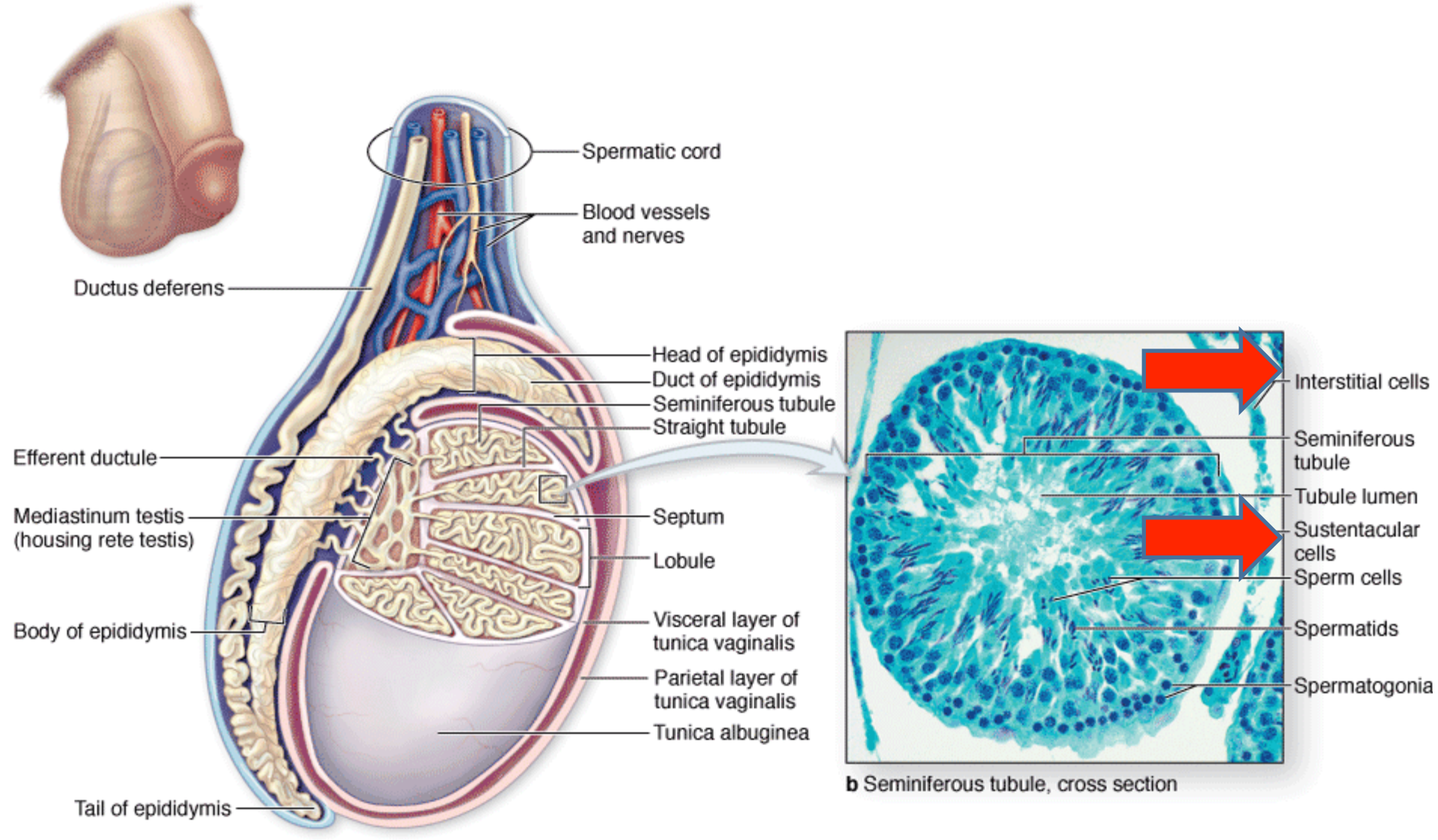
SECONDARY SPERMATOCYTE

MEIOSIS II

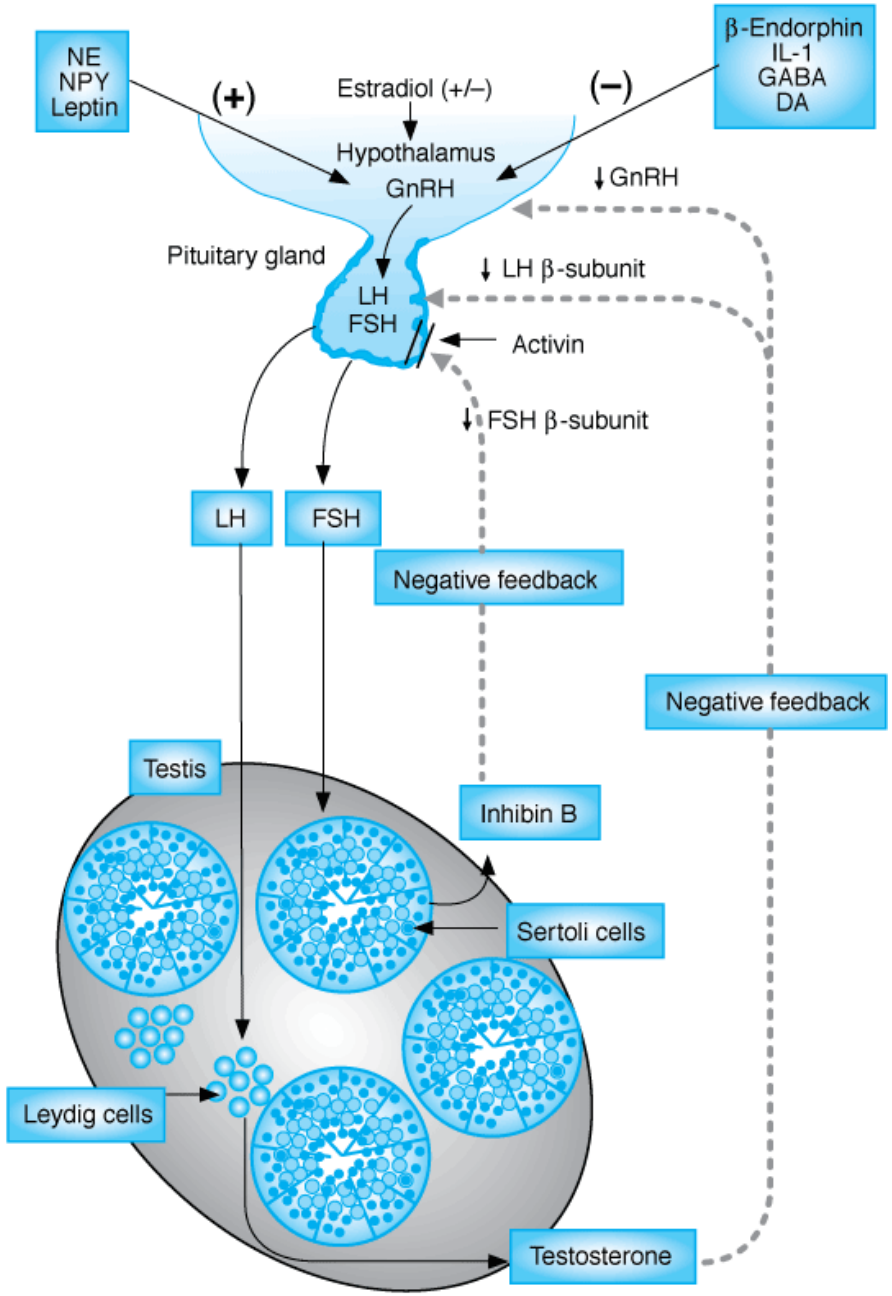
GAMETE



Source: Molina PE: *Endocrine Physiology, 3rd Edition:*
http://www.accessmedicine.com



Source: Mescher AL: *Junqueira's Basic Histology: Text and Atlas, 12th Edition:* http://www.accessmedicine.com



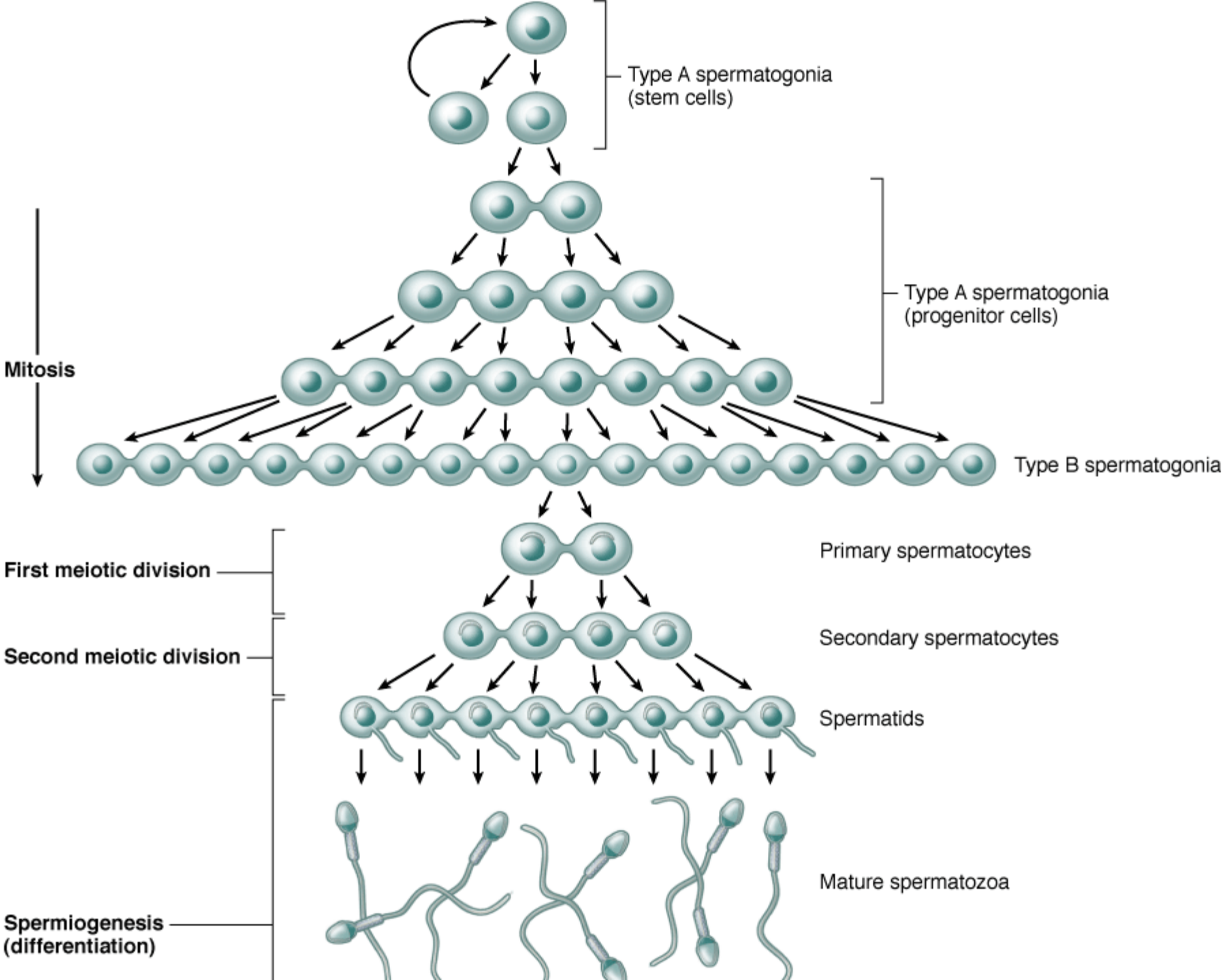
Source: Molina PE: *Endocrine Physiology, 3rd Edition:* http://www.accessmedicine.com

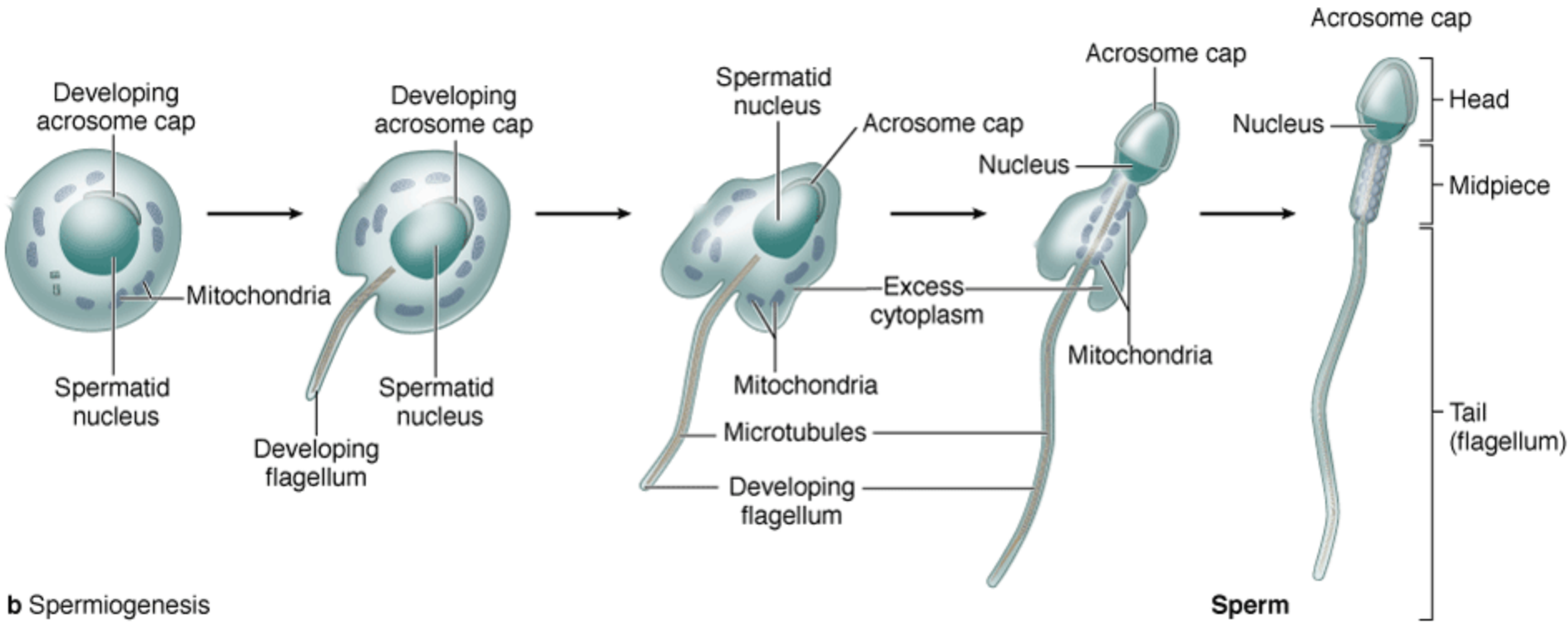
SERTTOLI CELLS

- **Support, protection, and nutrition of the developing spermatogenic cells -** spermatocytes, spermatids, and sperm are isolated from plasma proteins and nutrients by the blood-testis barrier,
- **Exocrine and endocrine secretion.** a fluid used for sperm transport in the direction of the genital ducts.
- **Phagocytosis.** During spermiogenesis, excess cytoplasm shed as residual bodies is phagocytosed and digested by **Sertoli cell** lysosomes. No proteins from sperm normally pass back across the **blood-testis barrier.**

LEYDIG CELLS

Leydig cells are responsible for the production of 95% of adult male testosterone.


Type A spermatogonia
(stem cells)
Type A spermatogonia
(progenitor cells)
Mitosis
Type B spermatogonia
First meiotic division
Primary spermatocytes
Second meiotic division
Secondary spermatocytes
Spermatids
Mature spermatozoa
Spermiogenesis
(differentiation)



WHO laboratory manual for the

Examination and processing of human semen

FIFTH EDITION

Table A1.1 Lower reference limits (5th centiles and their 95% confidence intervals) for semen characteristics

Parameter	Lower reference limit
Semen volume (ml)	1.5 (1.4–1.7)
Total sperm number (10^6 per ejaculate)	39 (33–46)
Sperm concentration (10^6 per ml)	15 (12–16)
Total motility (PR + NP, %)	40 (38–42)
Progressive motility (PR, %)	32 (31–34)
Vitality (live spermatozoa, %)	58 (55–63)
Sperm morphology (normal forms, %)	4 (3.0–4.0)
Other consensus threshold values	
pH	≥7.2
Peroxidase-positive leukocytes (10^6 per ml)	<1.0
MAR test (motile spermatozoa with bound particles, %)	<50
Immunobead test (motile spermatozoa with bound beads, %)	<50
Seminal zinc (μmol/ejaculate)	≥2.4
Seminal fructose (μmol/ejaculate)	≥13
Seminal neutral glucosidase (mU/ejaculate)	≥20

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Table A1.3 Nomenclature related to semen quality

aspermia	no semen (no or retrograde ejaculation)
asthenozoospermia	percentage of progressively motile (PR) spermatozoa below the lower reference limit
asthenoteratozoospermia	percentages of both progressively motile (PR) and morphologically normal spermatozoa below the lower reference limits
azoospermia	no spermatozoa in the ejaculate (given as the limit of quantification for the assessment method employed)
cryptozoospermia	spermatozoa absent from fresh preparations but observed in a centrifuged pellet
haemospermia (haematospermia)	presence of erythrocytes in the ejaculate
leukospermia (leukocytospermia, pyospermia)	presence of leukocytes in the ejaculate above the threshold value
necrozoospermia	low percentage of live, and high percentage of immotile, spermatozoa in the ejaculate
normozoospermia	total number (or concentration, depending on outcome reported)* of spermatozoa, and percentages of progressively motile (PR) and morphologically normal spermatozoa, equal to or above the lower reference limits
oligoasthenozoospermia	total number (or concentration, depending on outcome reported)* of spermatozoa, and percentage of progressively motile (PR) spermatozoa, below the lower reference limits
oligoasthenoteratozoospermia	total number (or concentration, depending on outcome reported)* of spermatozoa, and percentages of both progressively motile (PR) and morphologically normal spermatozoa, below the lower reference limits
oligoteratozoospermia	total number (or concentration, depending on outcome reported)* of spermatozoa, and percentage of morphologically normal spermatozoa, below the lower reference limits
oligozoospermia	total number (or concentration, depending on outcome reported)* of spermatozoa below the lower reference limit
teratozoospermia	percentage of morphologically normal spermatozoa below the lower reference limit

*Preference should always be given to total number, as this parameter takes precedence over concentration.

Semen Analysis

- Sperm count (number of sperm per cc)
- Motility (percentage of sperm moving)
- Sperm morphology

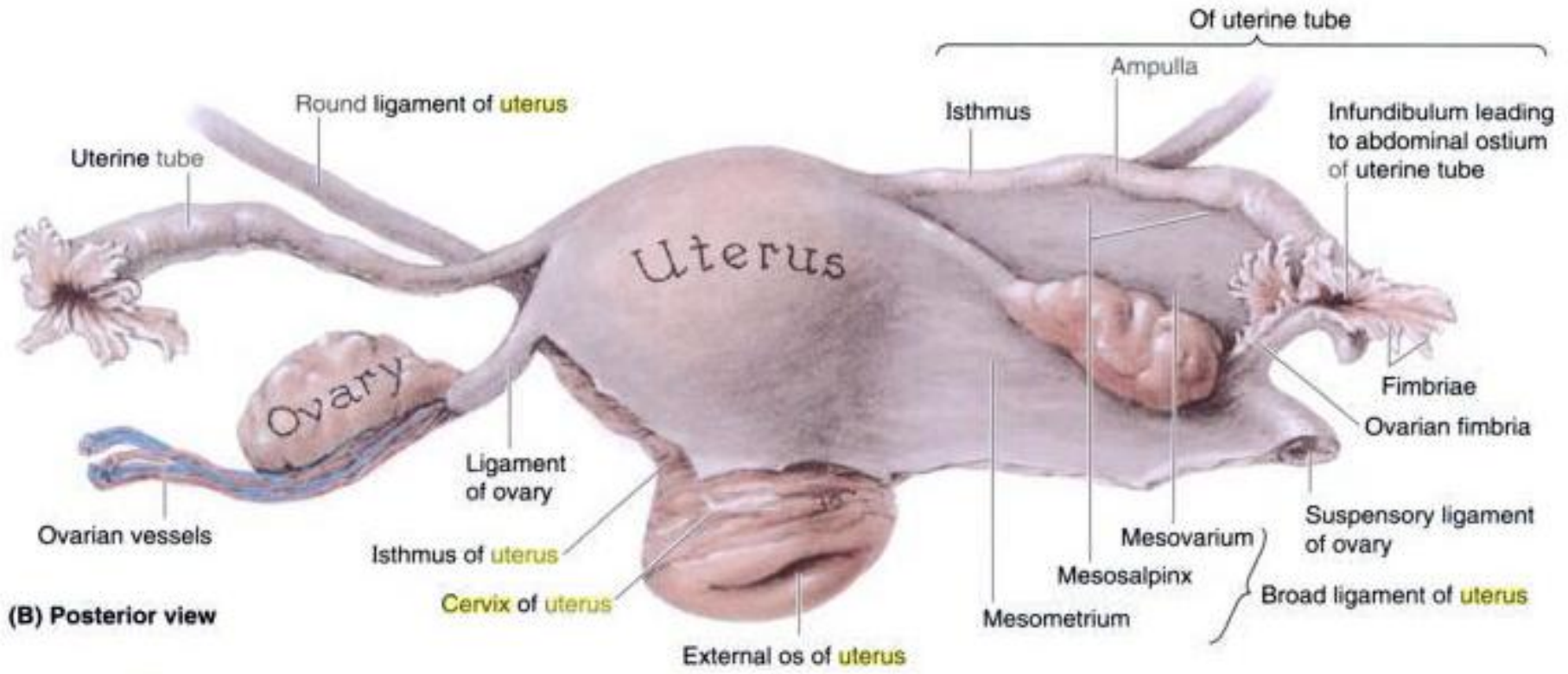
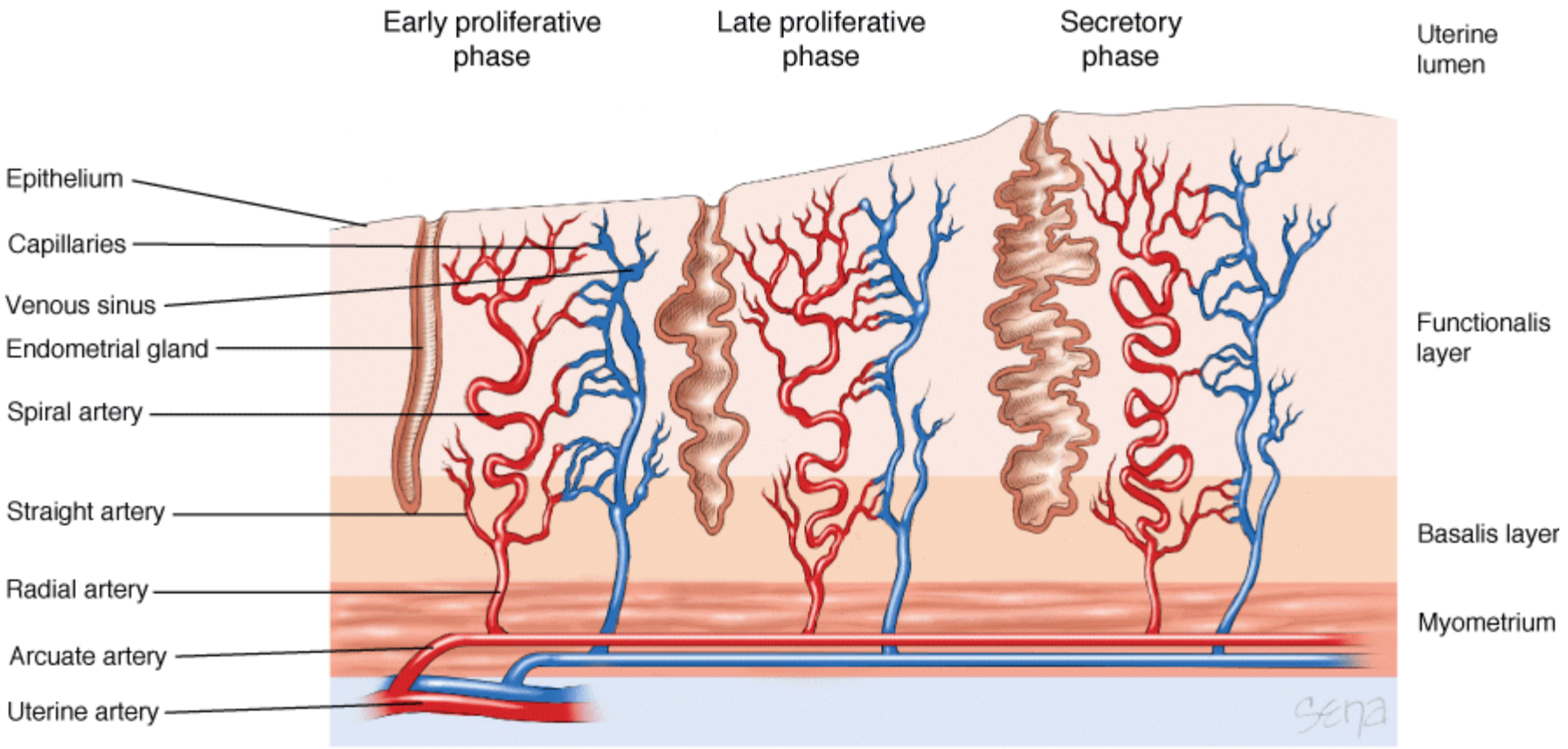
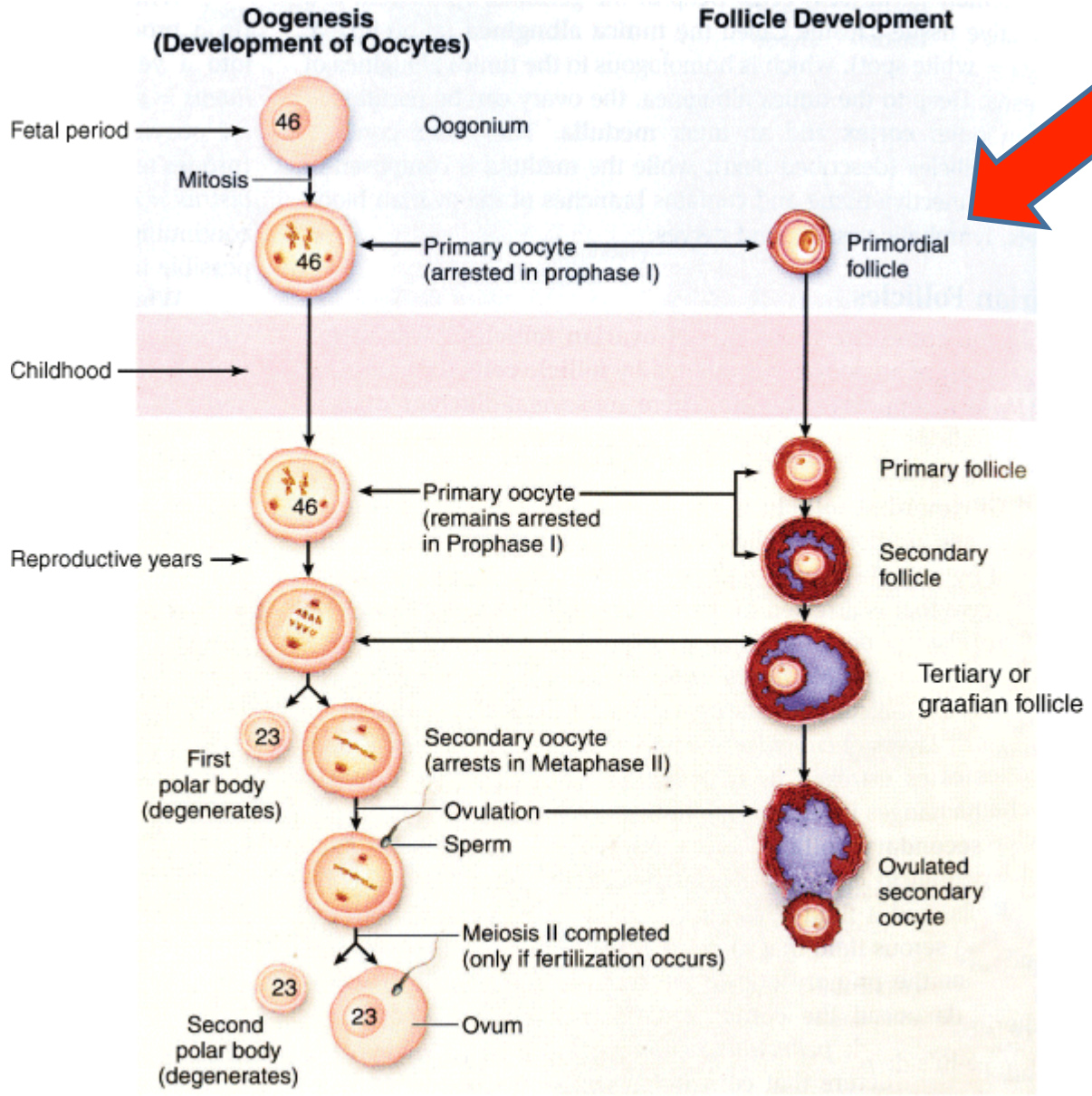


Figure 3.31. Female pelvic viscera. A. In this dissection of the female genital organs, the bladder and adjacent anterior pelvis (superior ramus and bodies of pubic bones) have been coronally sectioned and the anterior segment has been removed. On the right side, the uterine tube, ovary, broad ligament, and peritoneum covering the lateral wall of the pelvis have been removed to display the ureter and branches of the internal iliac artery. **B.** This dissection reveals the uterus, ovaries, uterine tubes, and related structures. The broad ligament is removed on the right side.



Source: Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY: *Williams Obstetrics, 23rd Edition:* http://www.accessmedicine.com



OOGENESIS

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

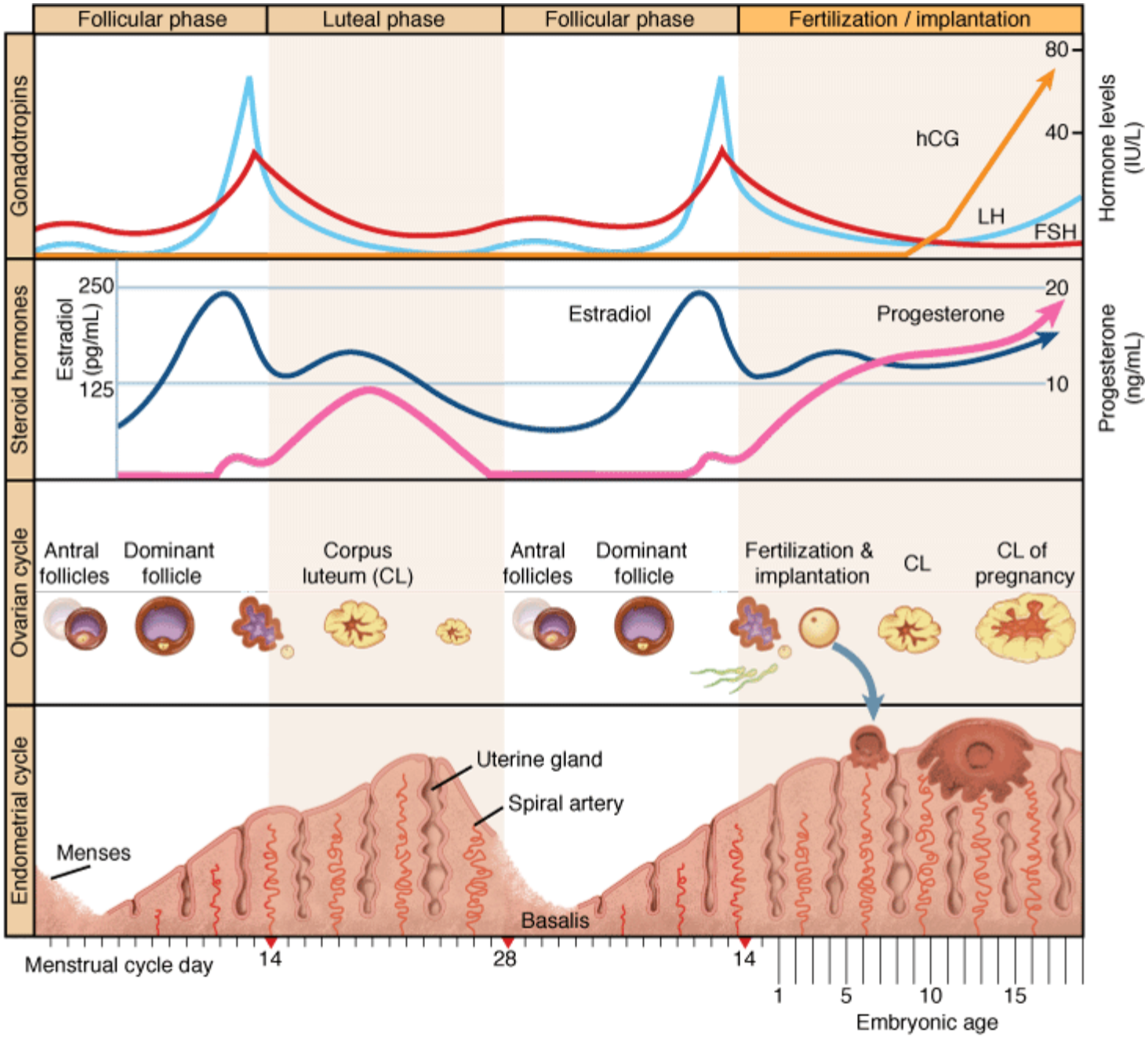
<u>Maturation of oocytes continues at puberty.</u> Until then they stay in the

DIPLOTEN STAGE = resting stage during **prophase MEIOSIS I.**

Maturation is stopped by OMI - oocyte maturation inhibitor producing by follicle cells.

Numbers

- In 5th month the number of germ cells reach max. 7 mln.
- The maximal number of oogonia is achieved at the 20th week of gestation, at which time **six to seven million oogonia** are present in the ovary
- Approximately one to two million oogonia are present at birth with less than **400,000** present at the initiation of puberty, of which less than **500** are destined to ovulate
- Therefore, most female germ cells are lost through atresia

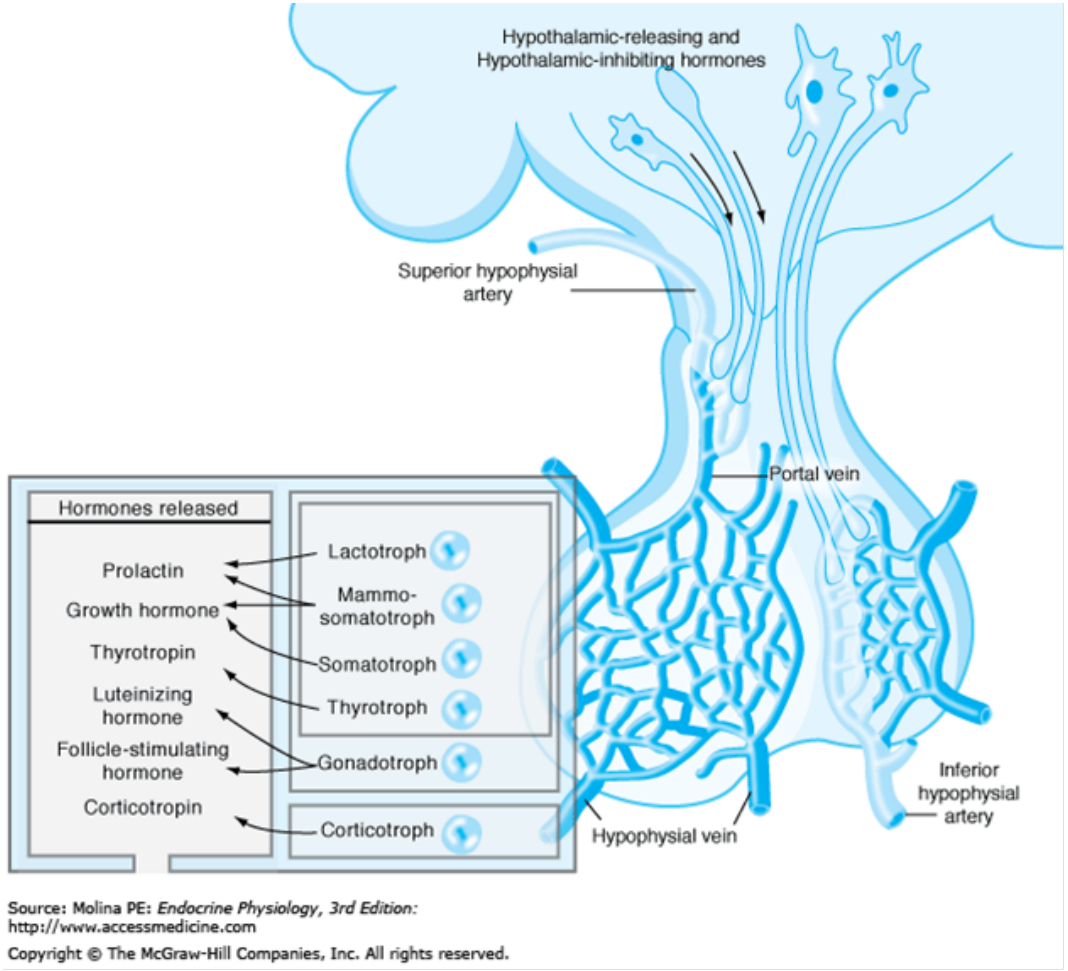

Follicular phase
Luteal phase
Follicular phase
Fertilization / implantation
Gonadotropins
80
40
hCG
LH
FSH
Hormone levels (IU/L)
Steroid hormones
250
125
Estradiol (pg/mL)
Estradiol
Progesterone
20
10
Progesterone (ng/mL)
Ovarian cycle
Antral follicles
Dominant follicle
Corpus luteum (CL)
Antral follicles
Dominant follicle
Fertilization & implantation
CL
CL of pregnancy
Endometrial cycle
Uterine gland
Spiral artery
Menses
Basalis
Menstrual cycle day
14
28
14
1
5
10
15
Embryonic age

BRAIN CONTROL

What's the role of hypothalamus?

ULTRA SHORT FEEDBACK LOOP

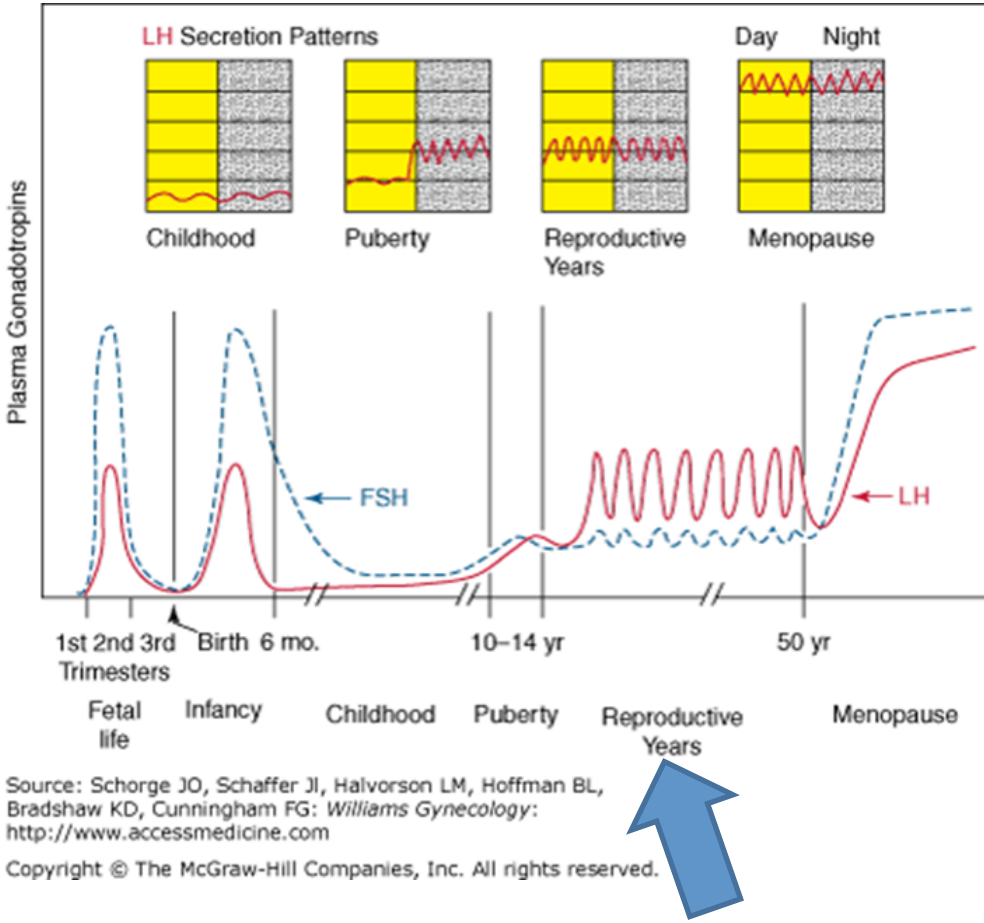
ARCUATE NUCLEUS (Gonadotropin Releasing Hormone)



Source: Molina PE: *Endocrine Physiology, 3rd Edition:* http://www.accessmedicine.com

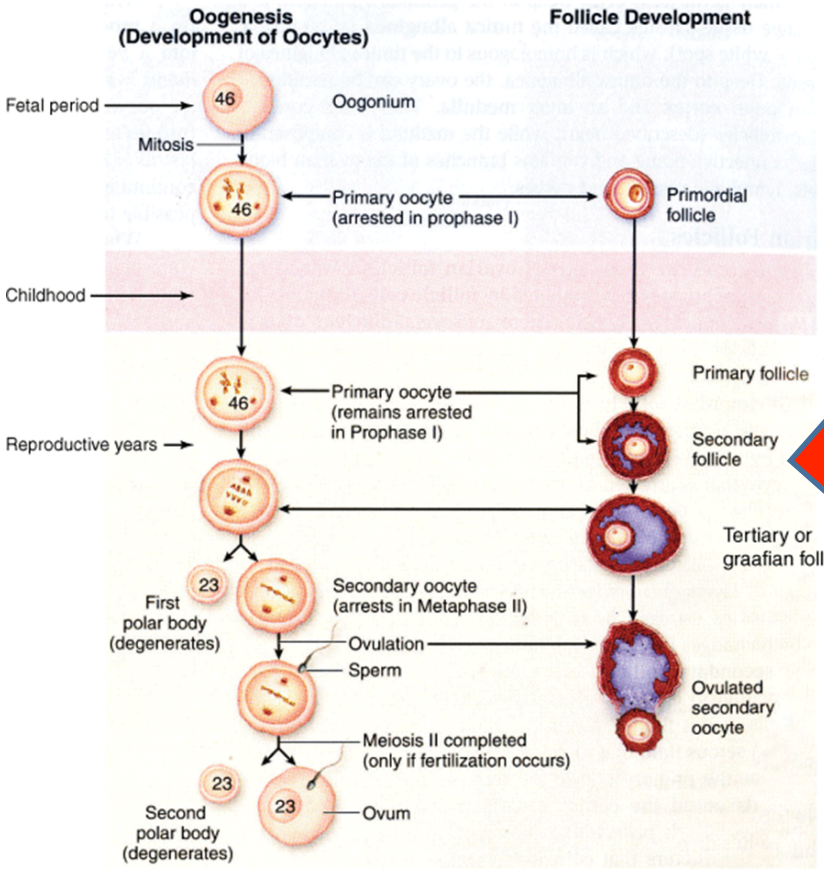
GnRH

- **Pulsatile release of gonadotropin-releasing hormone (GnRH)** from the hypothalamus stimulates pulsatile pituitary release of **luteinizing hormone (LH)** and **follicle-stimulating hormone (FSH).**
- GnRH secretion is regulated by dopamine, serotonin, -endorphin, and norepinephrine.
- Hypothalamus is responsive to light, stress, steroids, glucose level, autonimic outputs…



60-90 min.
GnRH

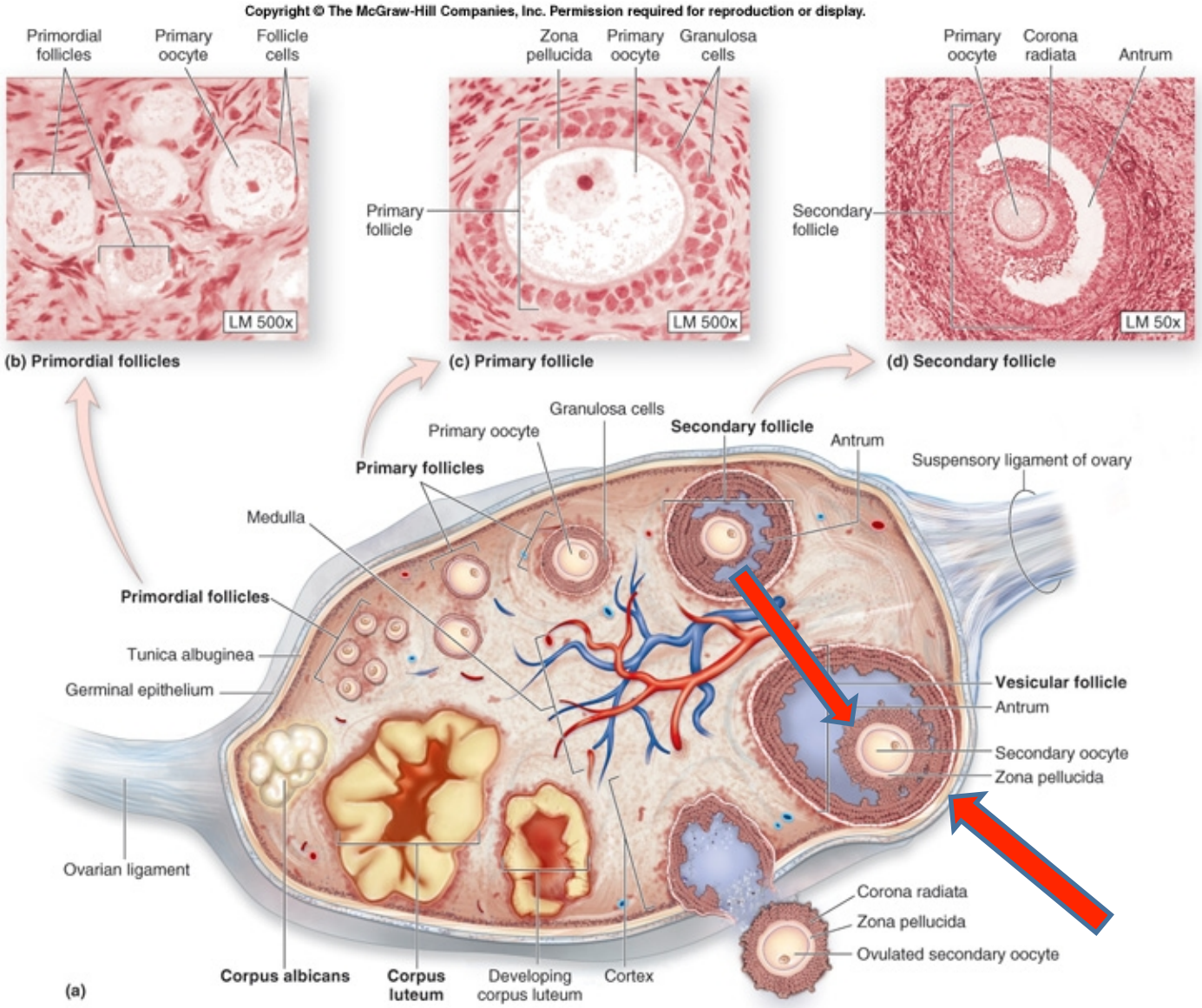
Proliferating/Follicular Phase

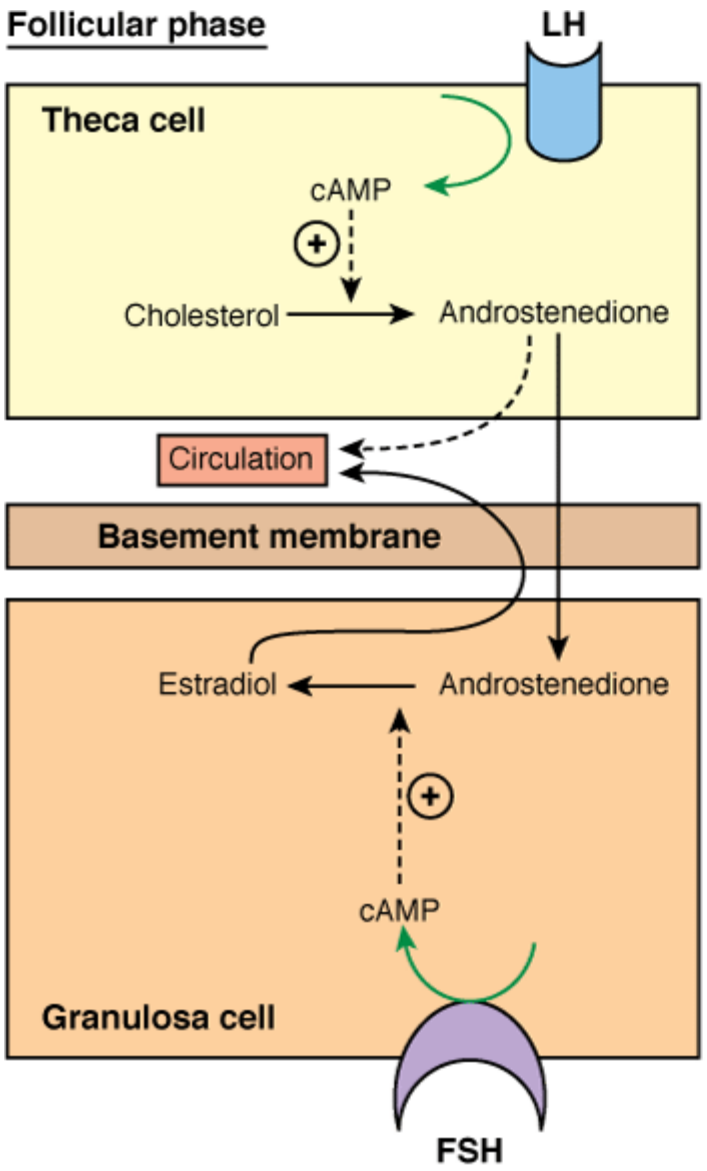


Source: Schorge JO, Schaffer JI, Halvorson LM, Hoffman BL, Bradshaw KD, Cunningham FG: *Williams Gynecology*: http://www.accessmedicine.com

- FSH is responsible for follicular recruitment and growth
- SELECTION WINDOW – FSH rise leading to the development of follicles: a group of **antral follicles** a *cohort* begins a phase of semisynchronous growth

Preovulatory Follicle





Source: Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY: *Williams Obstetrics, 23rd Edition:* http://www.accessmedicine.com

↑FSH

↑Granulosa cells ↑LH receptors

↑Estradiol

↑FSH receptors ↑LH

Recruitment
and
Growth

Ovulation requirements

- Estradiol ⇧⇧⇧⇧
- Progesteron⇧
- LH surge ⇧⇧⇧⇧

Collagenase activity

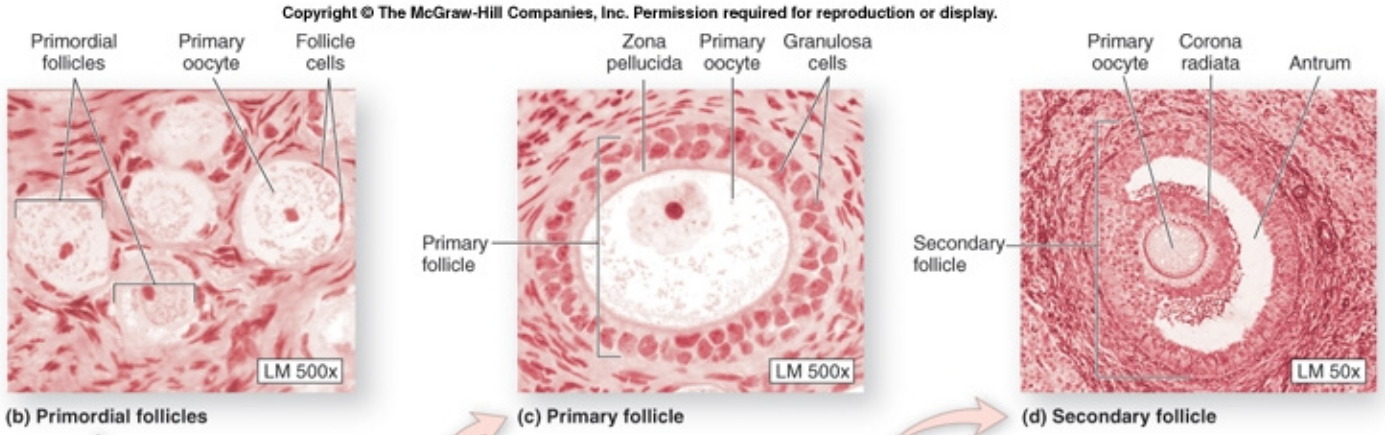
Prostaglandin level

Metalloproteinase level

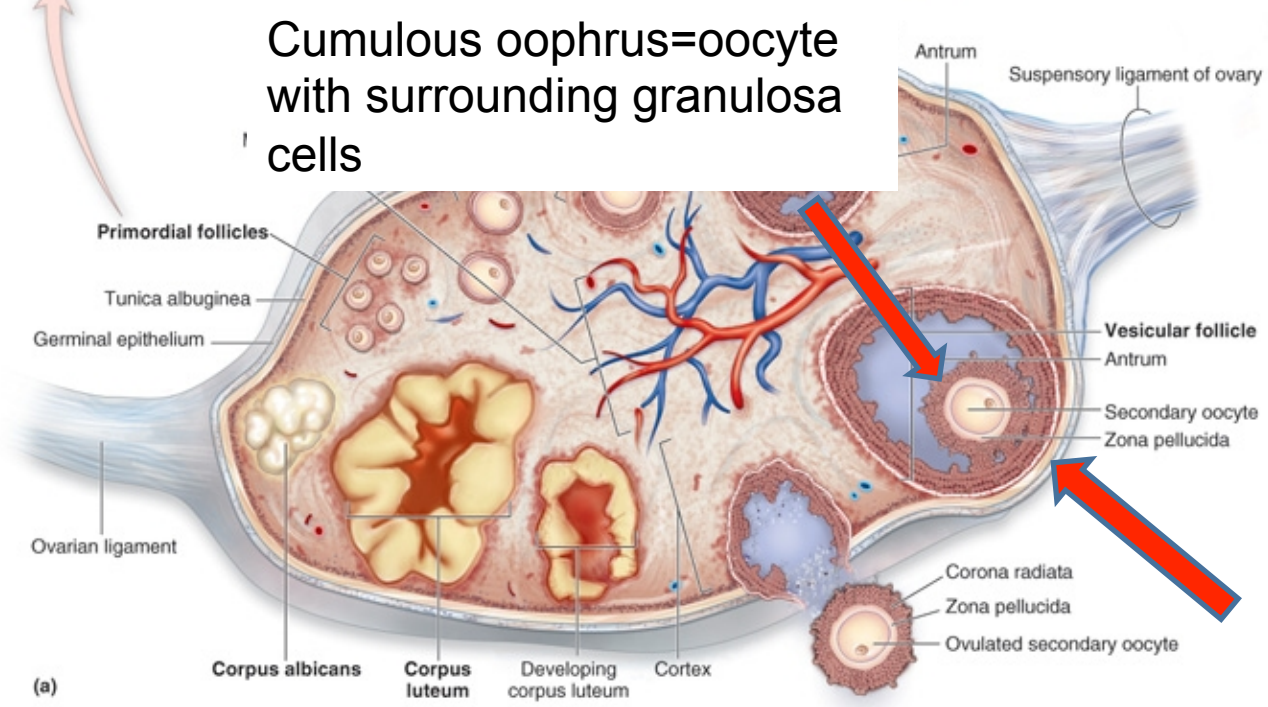
LH

•LH is responsible for ovulation („trigger”) and corpus luteum formation

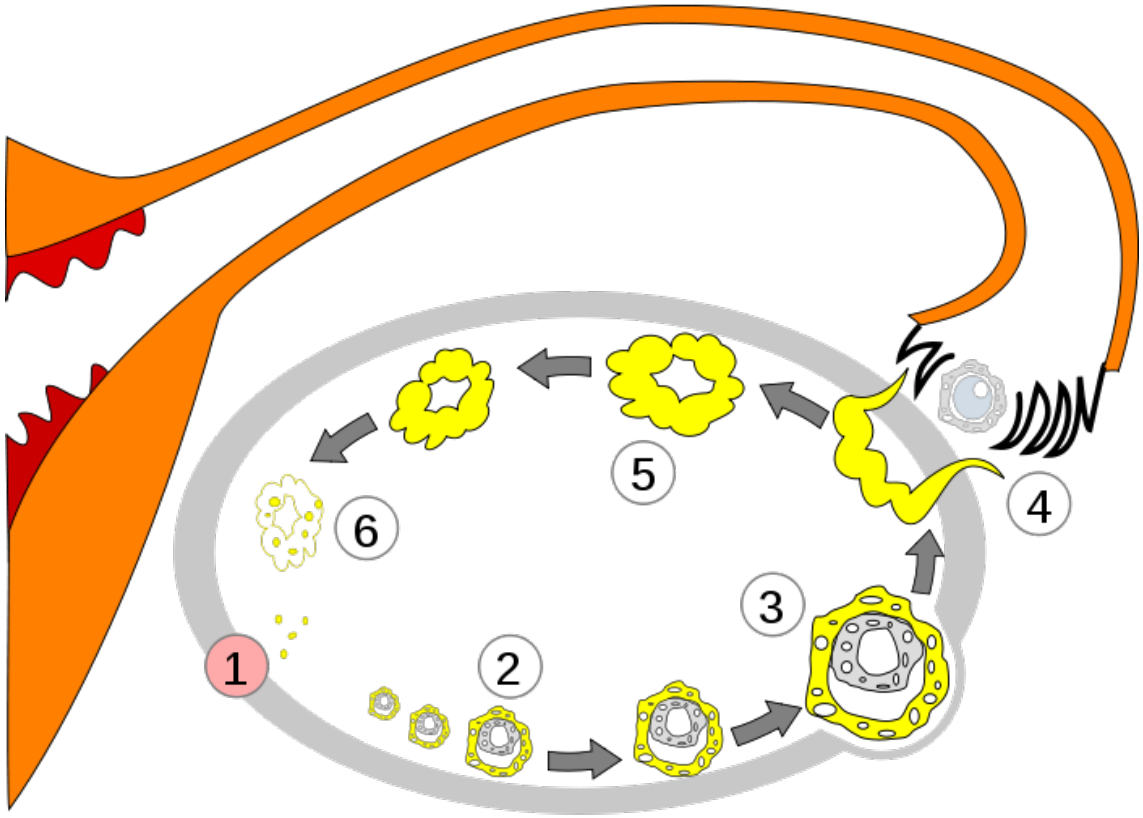
Preovulatory Follicle



Cumulous oophrus=oocyte with surrounding granulosa cells



STIGMA avascular spot buldging locally



!!!! LH surge

↓

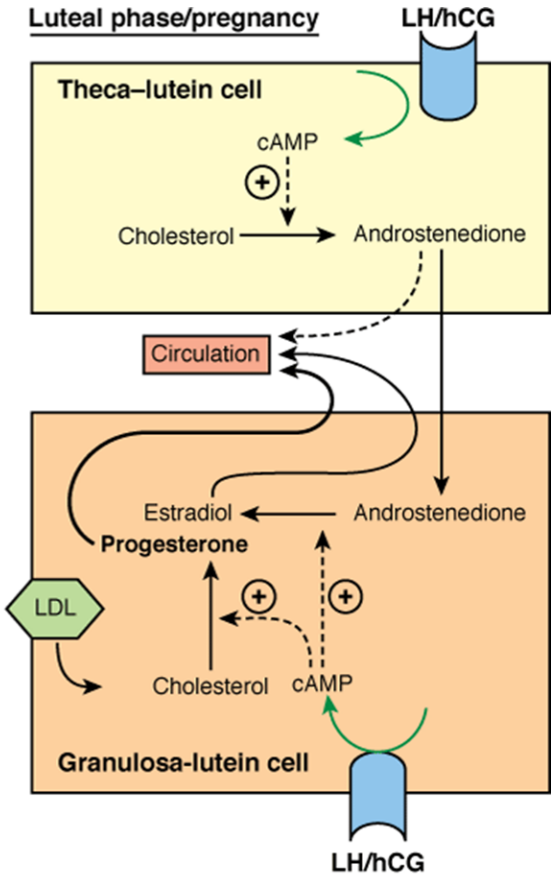
Preovulatory growth phase = Meiosis I is completed forming two daughter cells unequal sizes – 23 chromosomes each: SECONDARY OOCYTE FIRST POLAR BODY(with no cytoplasm) – lies between zona pellucida and cell membrane of oocyte in PERIVITELLINE SPACE.

↓

CELLS enters meiosis II and stops in METAPHASE approx. 3 h before ovulation until FERTILIZATION!

Luteal/Secretory Phase

The basement membrane separating the granulosa-lutein and theca-lutein cells break-down and by day 2 postovulation blood vessels and capillaries invade granulosa cell layer. These cells undergo hypertrophy and increase their capacity to synthetize hormones.



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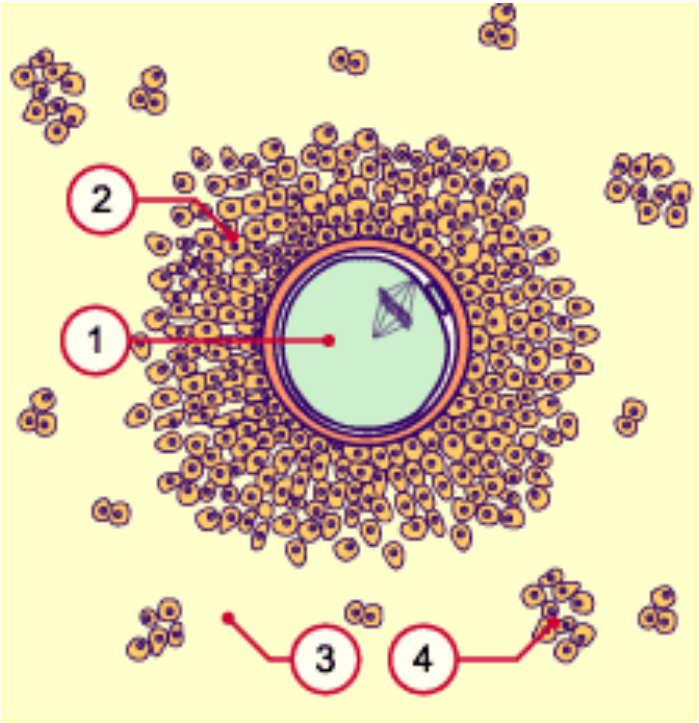
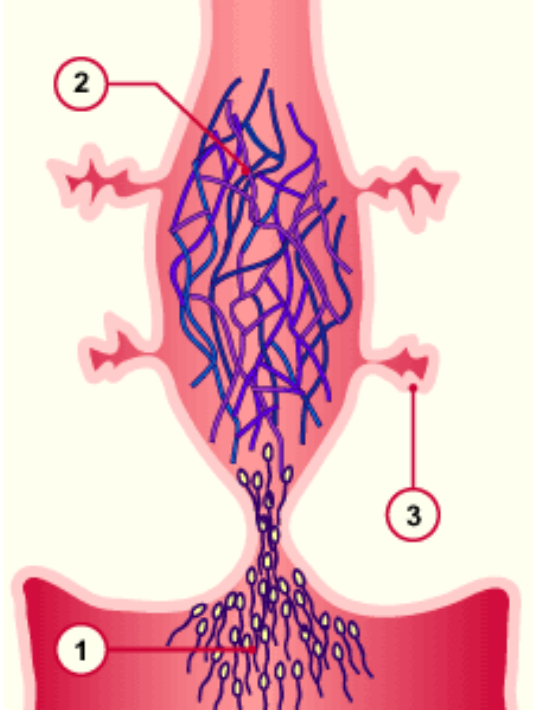
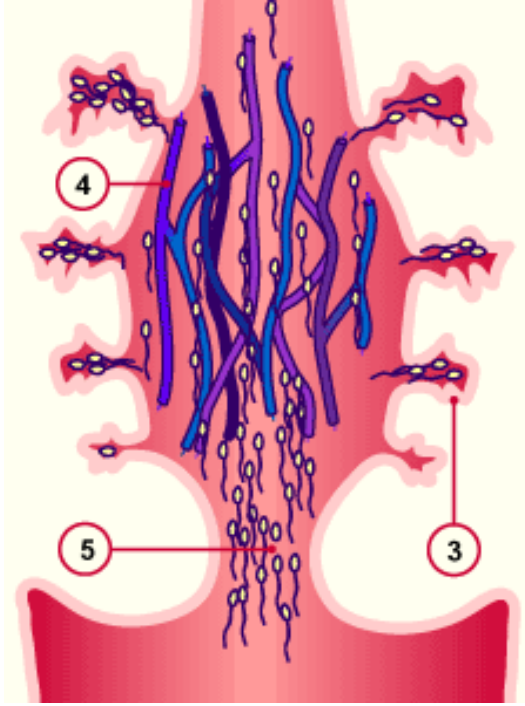


1 Secondary oocyte (in arrested metaphase of the 2nd meiosis)
2 Corona radiata
3 Follicle fluid
4 Scattered groups of cumulus cells



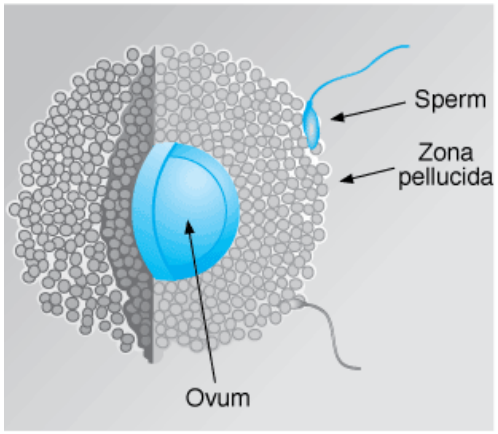


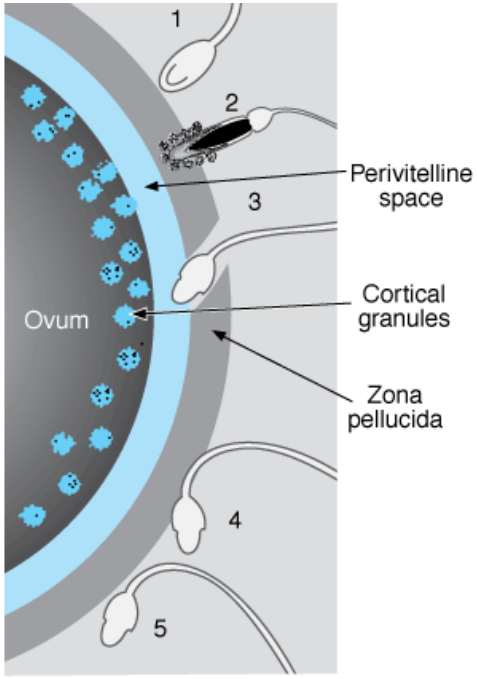
1 Sperm cells
2 Mucus fibers (strongly meshed)
3 Crypt of a cervix gland

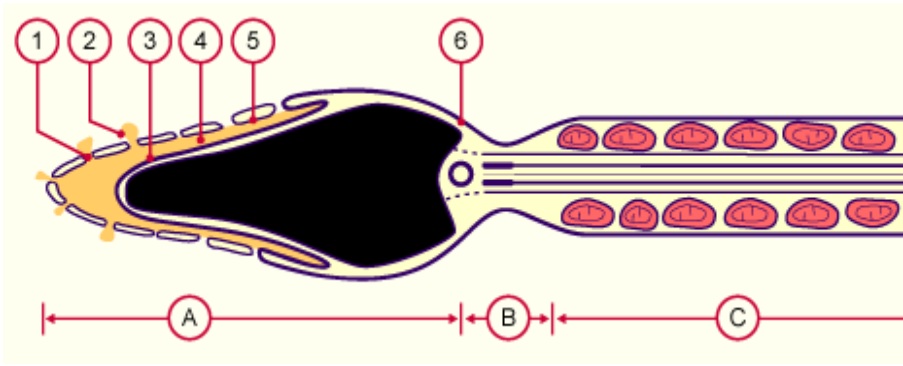
4 Mucus fibers (loosely meshed)
5 Portio entrance

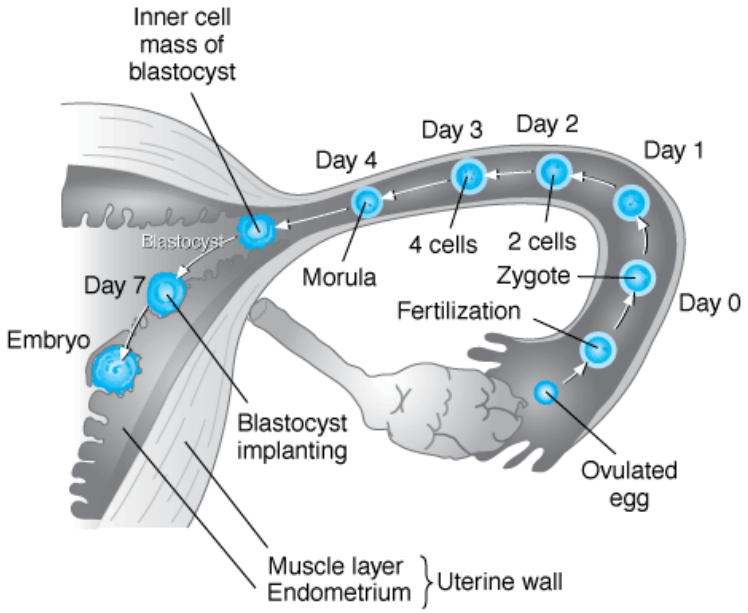
The trip from cervix to oviduct requires a minimum of 2 to 7 hours.

Capacitation is what one calls the changes that lead to hyperactivity of the spermatozoon and which later allow the spermatozoon to go through the acrosome reaction. **In the human it lasts approx. 7 hours.**



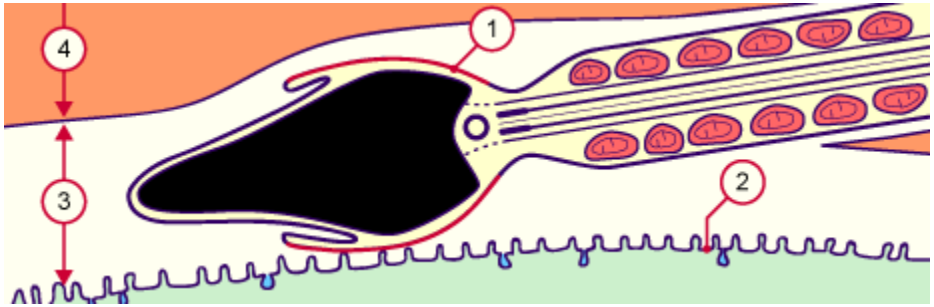






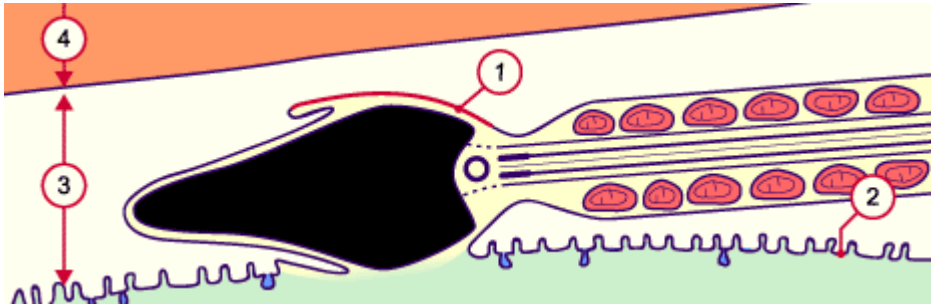
1 Pores
2 Emerging of the acrosomal contents
3 Inner acrosomal membrane
4 Acrosomal content (enzyme)
5 Outer acrosomal membrane
6 Cell membrane
A Head
B Neck
C Mid-piece

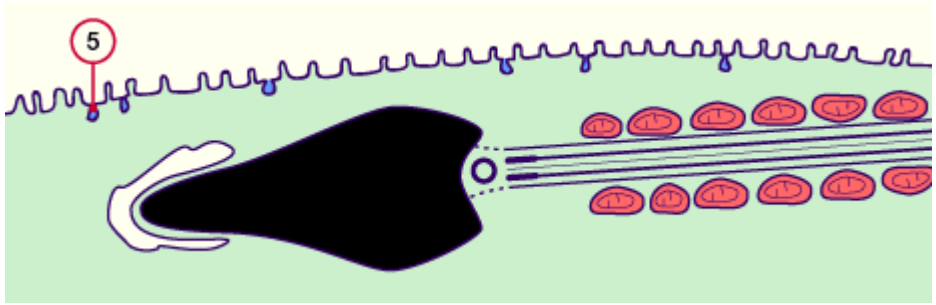
1. Passage through CORONA RADIATA
2. ACROSOME REACTION



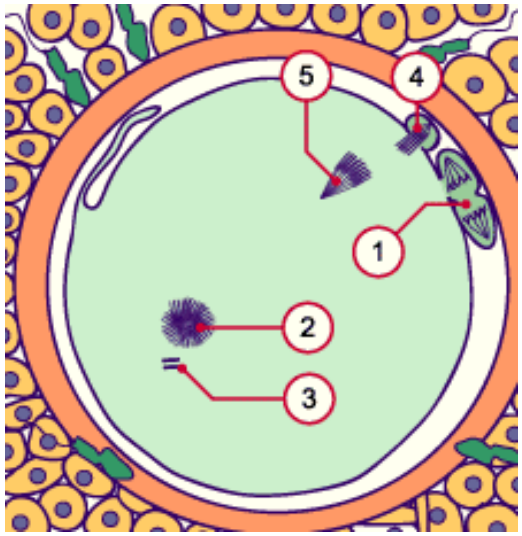
1 Post-acrosomal region
2 Oolemma with microvilli
3 Perivitelline space
4 Pellucid zone

FUSION





5 Cortical vesicle at the surface of the oocyte



1 1rst polar body

2 Nucleus (slightly unpacked) of the spermatozoon

3 Proximal centrosome of the spermatozoon

4 **2nd polar body** (being formed)

5 Remainder of the mitotic spindle with maternal chromosomes 1n,1C

The docking triggers a cascade of events with the following goals:

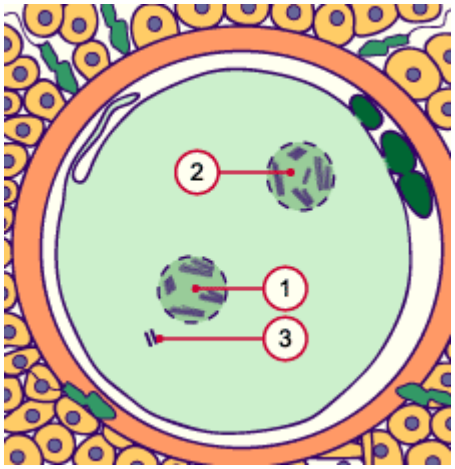
Polyspermy block: The penetration of further sperm cells should be hindered

Hardening of the pellucid zone as a mechanical protection of the embryo

Entry of the spermatozoon into the oocyte
Termination of the 2nd meiosis of the oocyte with expulsion of the 2nd polar body

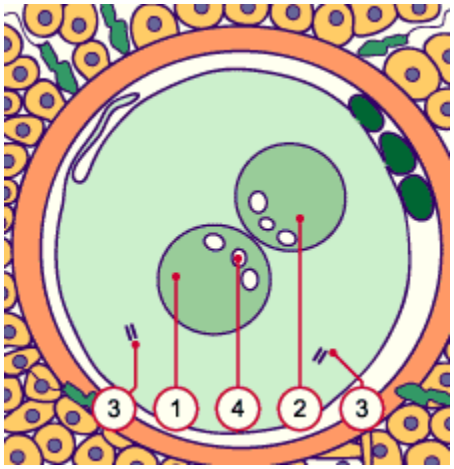
Preparation at the molecular level of the oocyte for unpacking the paternal DNA

4 hours after impregnation



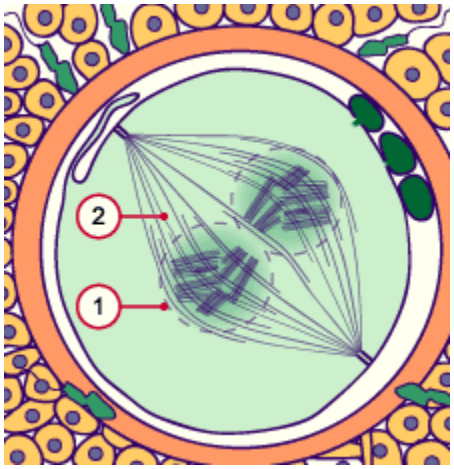
1 Paternal
2 pronucleus
3 Maternal pronucleus
Centrosome brought in by the spermatozoon

18 hours after impregnation

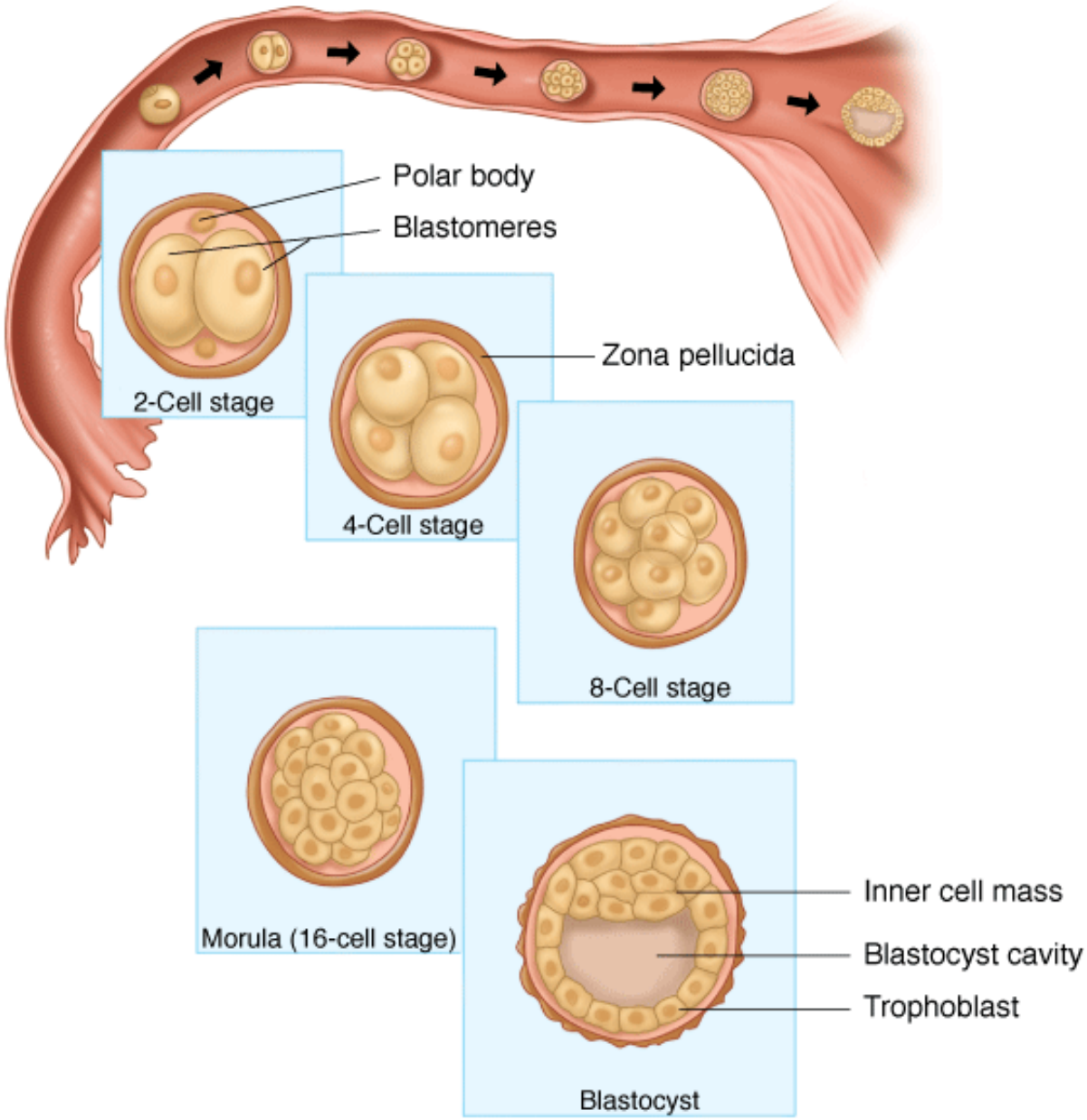


1 Paternal
2 pronucleus
3 Maternal
4 pronucleus
Duplicated paternal centrosome
"Inner bodies"

22hours after impregnations

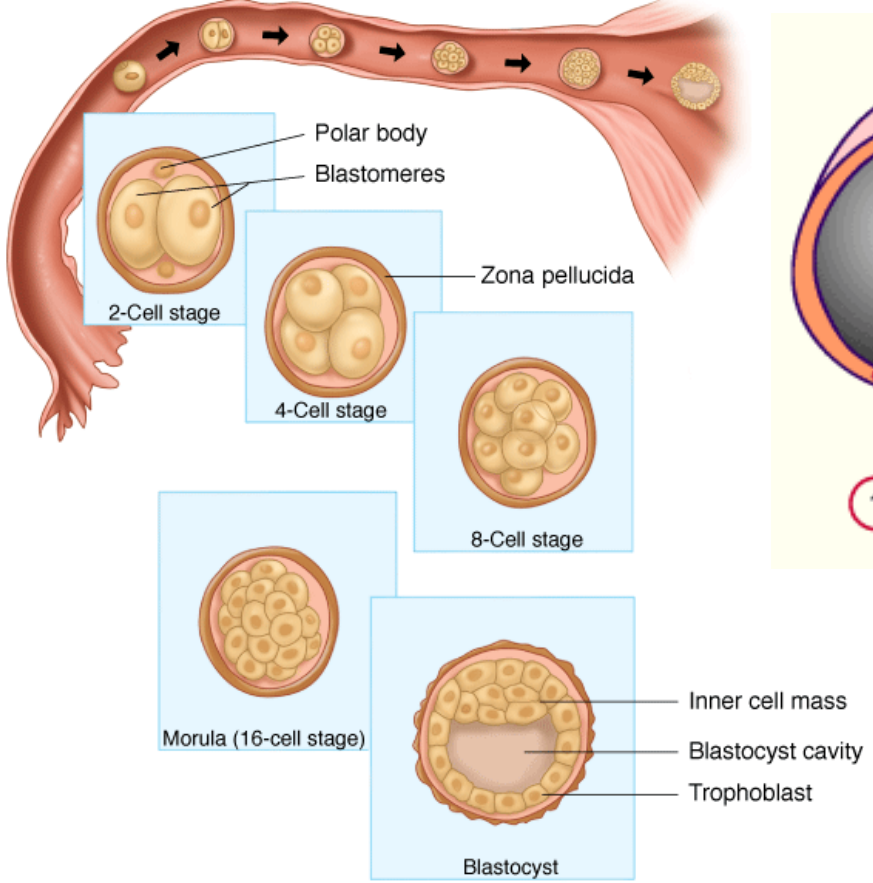


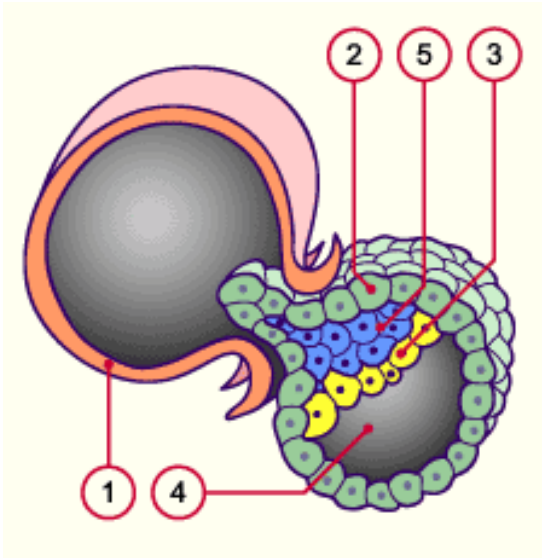
1 Nucleic membranes of the pronuclei, as they are dissolving
2 Microtubules of the mitotic spindle



- a **diploid** set of chromosomes
- The **zygote** - by definition the first cell of the embryo
- 12-32 cells - the **morula**
- The **blastocyst –** when blastocystic cavity appears.

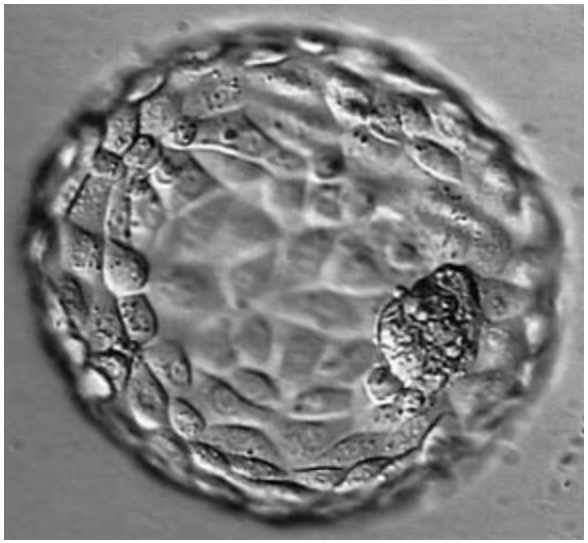
L. morus, mulberry





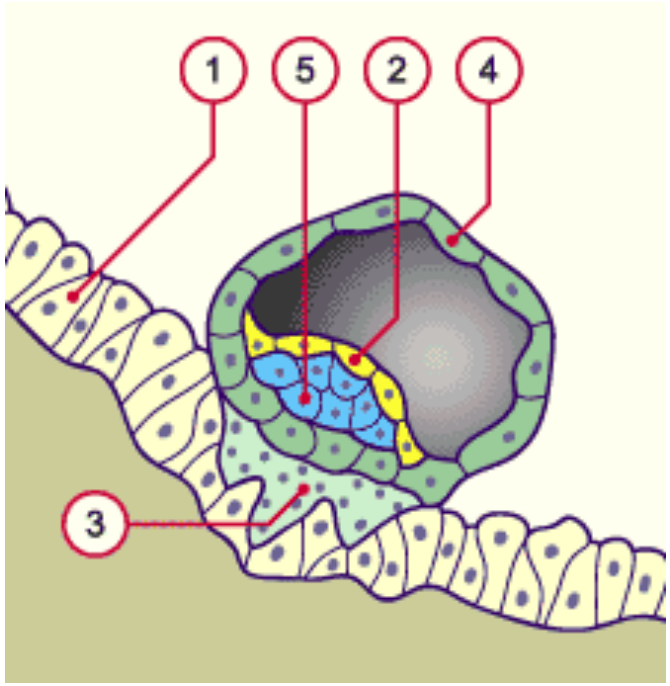
1. Pellucid zone
2. **Trophoblast** (outer cell mass)
3. **Hypoblast** (part of the inner cell mass)
4. Blastocyst cavity
5. **Epiblast** (part of the inner cell mass)

Blastocyst

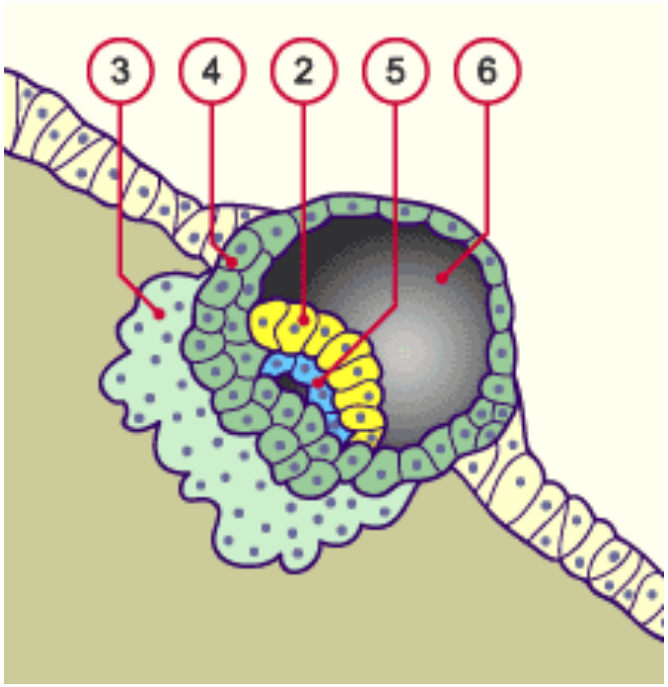


The two-cell stage is reached about 30 hours after fertilization.
The four-cell – 40 hours.
12-16 cell stage – 3 days.
Late morula stage – 4 days.
Zona Pellucida disappears at the end of 4th day.
Enters the cavity at the 4th day, when the morula become blastocyst.

Implantation: 6th –7th day

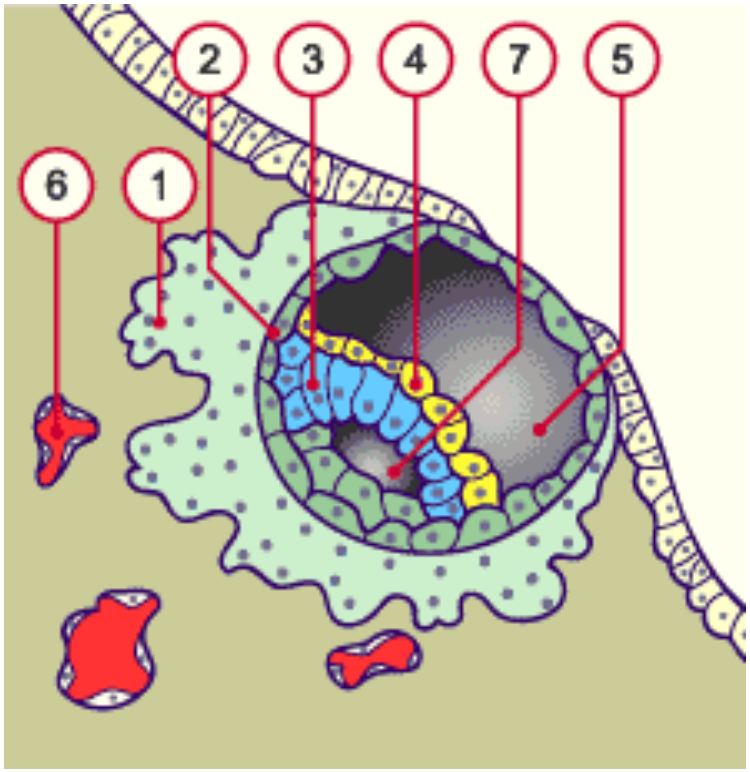


Implantation: 7th –8th day

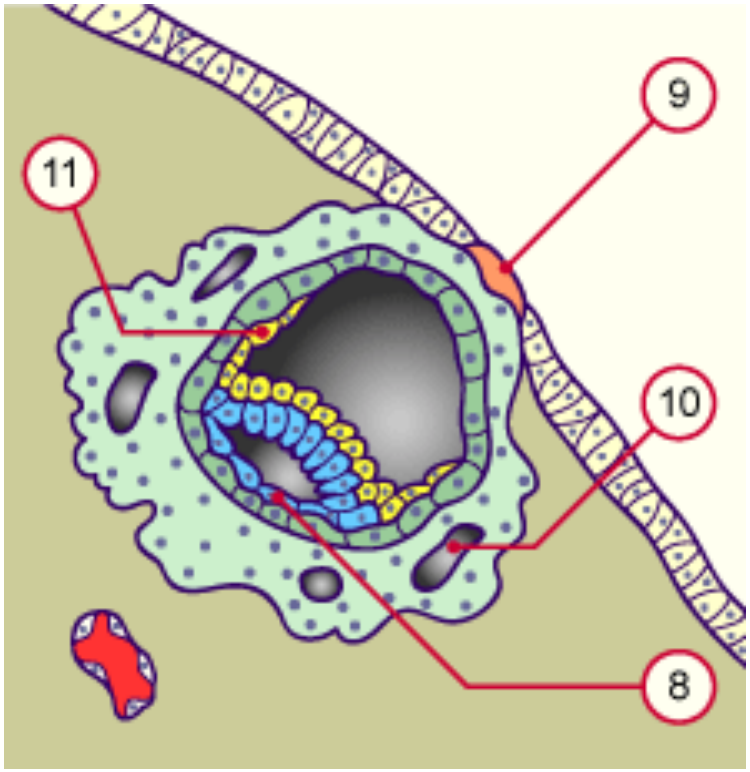


1 Epithelium of the uterine endometrium
2 **Hypoblast**
3 **Syncytiotrophoblast (ST)**
4 **Cytotrophoblast (CT)**
5 **Epiblast**
6 Blastocyst cavity

Implantation: 8th day



Implantation: 9th – 10th day

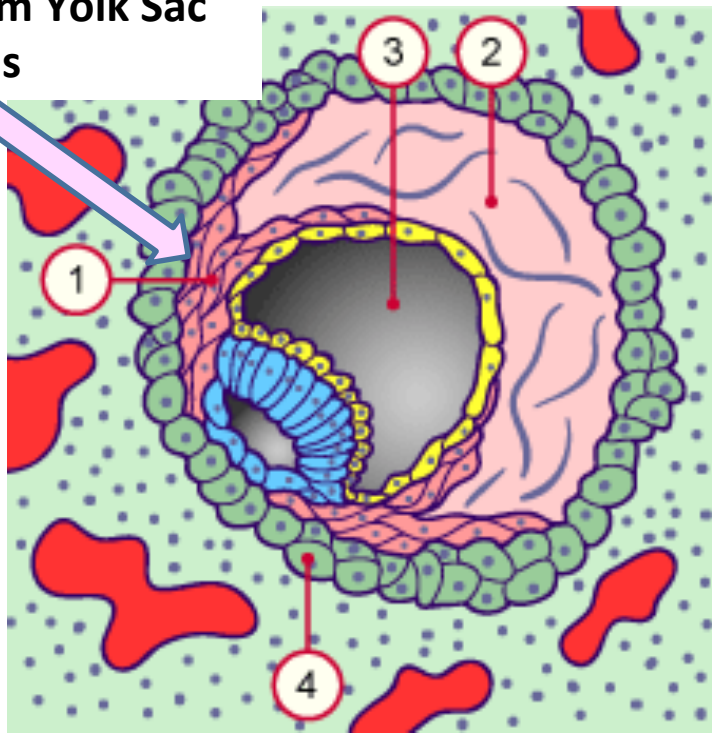


1 Syncytiotrophoblast (ST)
2 Cytotrophoblast (CT)
3 Epiblast
4 Hypoblast
5 Blastocyst cavity
6 Maternal blood capillary
7 **Amniotic cavity**

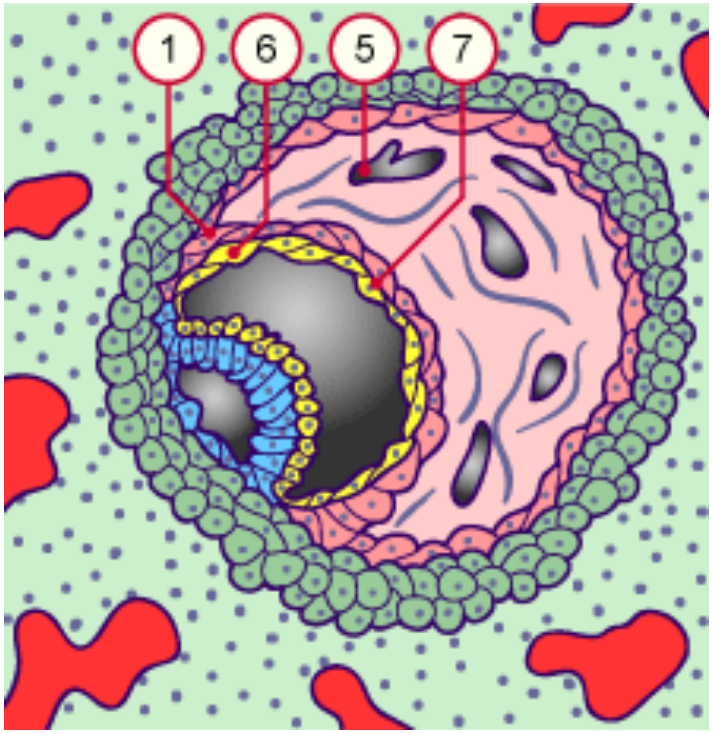
8 **Amnioblasts**
9 **Fibrin (closing) plug**
10 Syncytiothrophoblast lacuna
11 Multiplying hypoblast

Implantation: 11th day

From Yolk Sac Cells



Implantation: 12th day



1 Extra-embryonic mesoderm
2 Extra-embryonic reticulum
3 Primitive yolk sac (Exocoelomic cavity)
4 Cytotrophoblast

5 Lacunae in the reticulum
6 Hypoblast
7 **Heuser´s membrane** between hypoblast and mesoderm cells

MATERNAL BLOOD ENTERS THE LACUNES.