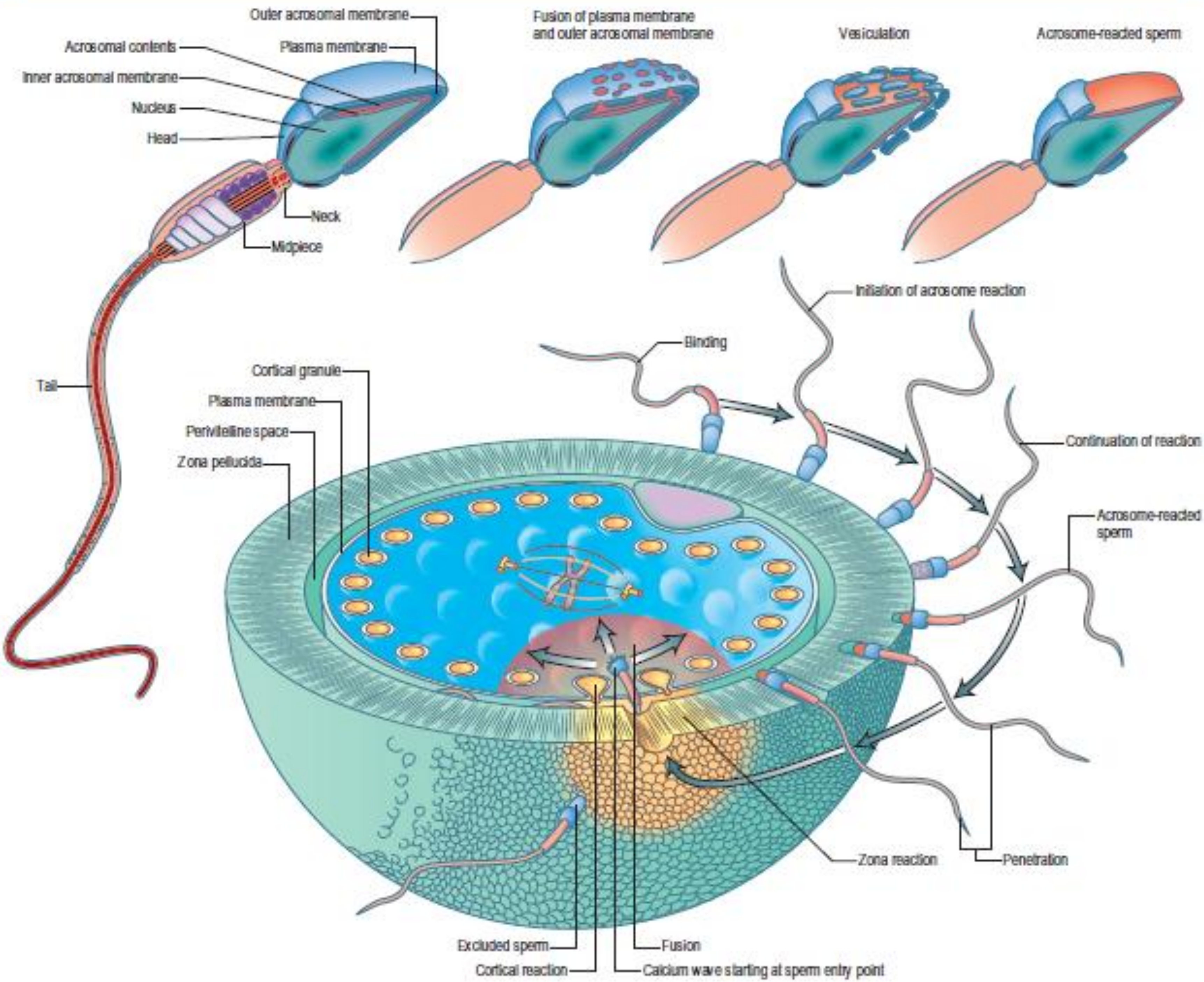


Outer acrosomal membrane
Acrosomal contents
Plasma membrane
Inner acrosomal membrane
Nucleus
Head
Neck
Midpiece
Tail
Fusion of plasma membrane
and outer acrosomal membrane
Vesiculation
Acrosome-reacted sperm
Initiation of acrosome reaction
Binding
Cortical granule
Plasma membrane
Perivitelline space
Zona pellucida
Continuation of reaction
Acrosome-reacted
sperm
Zona reaction
Penetration
Excluded sperm
Fusion
Cortical reaction
Calcium wave starting at sperm entry point

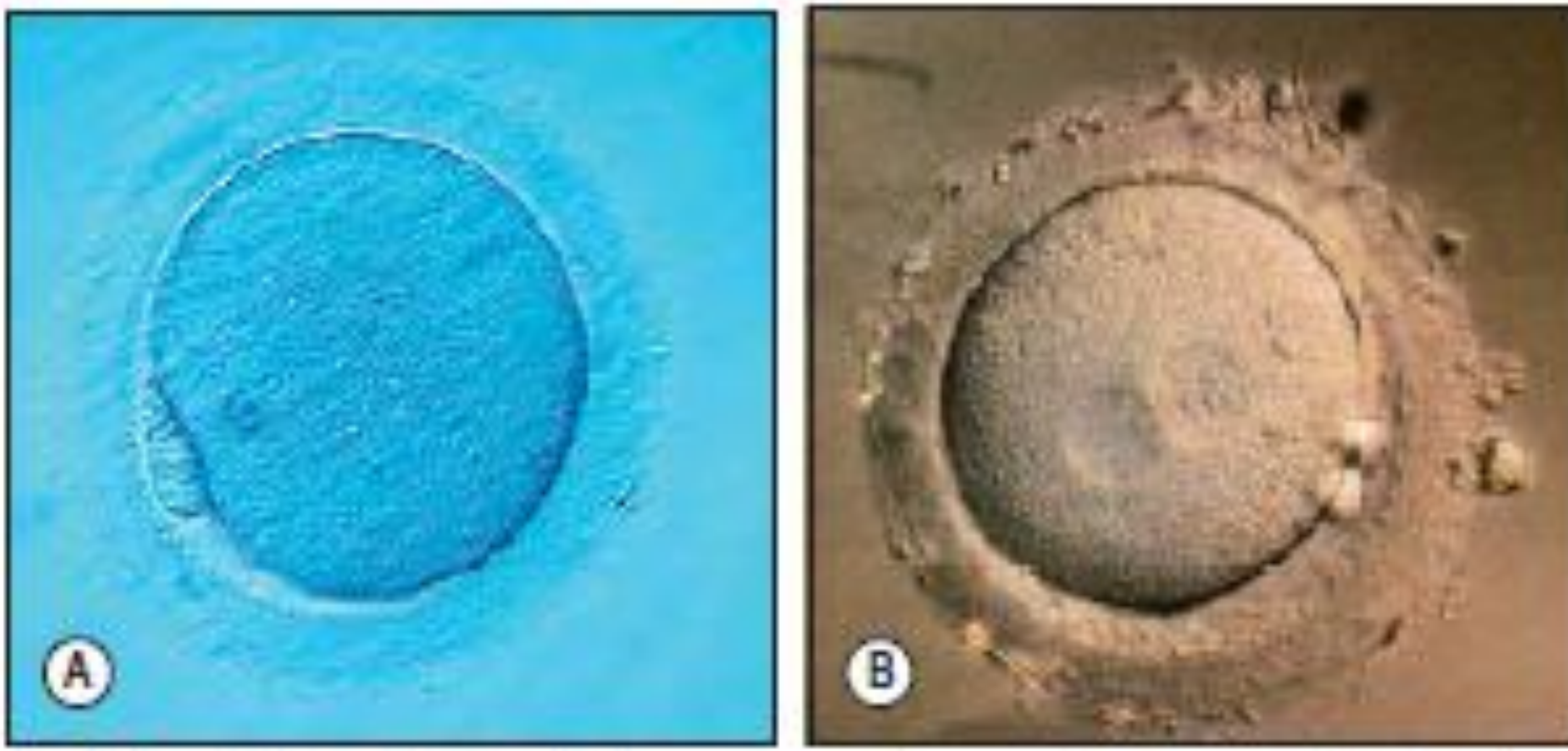


Fig. 8.5 **A**, An unfertilized human secondary oocyte surrounded by the zona pellucida; the first polar body can be seen. Spermatozoa can be seen outside the zona pellucida. **B**, Fertilized human ootid before fusion of the pronuclei. Two polar bodies can be seen beneath the zona pellucida.

MITTELSCHMERZ AND OVULATION

A variable amount of abdominal pain—*mittelschmerz*—accompanies ovulation in some women. Mittelschmerz may be used as a secondary **sign of ovulation**; however, there are better primary indicators, including slight elevation of basal body temperature, fertile cervical mucus, and change in the cervical position.

ANOVULATORY MENSTRUAL CYCLES

In anovulatory cycles, the endometrial changes are minimal; the proliferative endometrium develops as usual, but ovulation does not occur and no **corpus luteum** forms (see Fig. 2-8). Consequently, the endometrium does not progress to the **luteal phase**; it remains in the proliferative phase until menstruation begins. The estrogen in **oral contraceptives**, with or without **progesterone** (pregnancy hormone), suppresses ovulation by acting on the hypothalamus and pituitary gland; this inhibits secretion of gonadotropin-releasing hormone, follicle-stimulating hormone, and luteinizing hormone.

Read only

SPERM COUNTS

Semen analysis is an important part of evaluating patients for infertility. Sperms account for less than 5% of the volume of semen. The remainder of the ejaculate consists of secretions of the seminal glands (60%), prostate (30%), and bulbourethral glands (5%). The ejaculate of normal males usually contains more than 100 million sperms per milliliter of semen. Although there is much variation in individual cases, men whose semen contains a minimum of 20 million sperms per milliliter, or 50 million in the total specimen, are probably fertile. A man with less than 10 million sperms per milliliter is likely to be sterile, especially when the specimen contains immotile and abnormal sperms. For potential fertility, at least 40% of the sperms should be motile after 2 hours, and some should be motile after 24 hours. Male infertility may result from endocrine disorders, abnormal spermatogenesis, reduced levels of seminal plasma proteins, or obstruction of a genital duct (e.g., the ductus deferens). Male infertility is found in 30% to 50% of involuntarily childless couples.

VASECTOMY

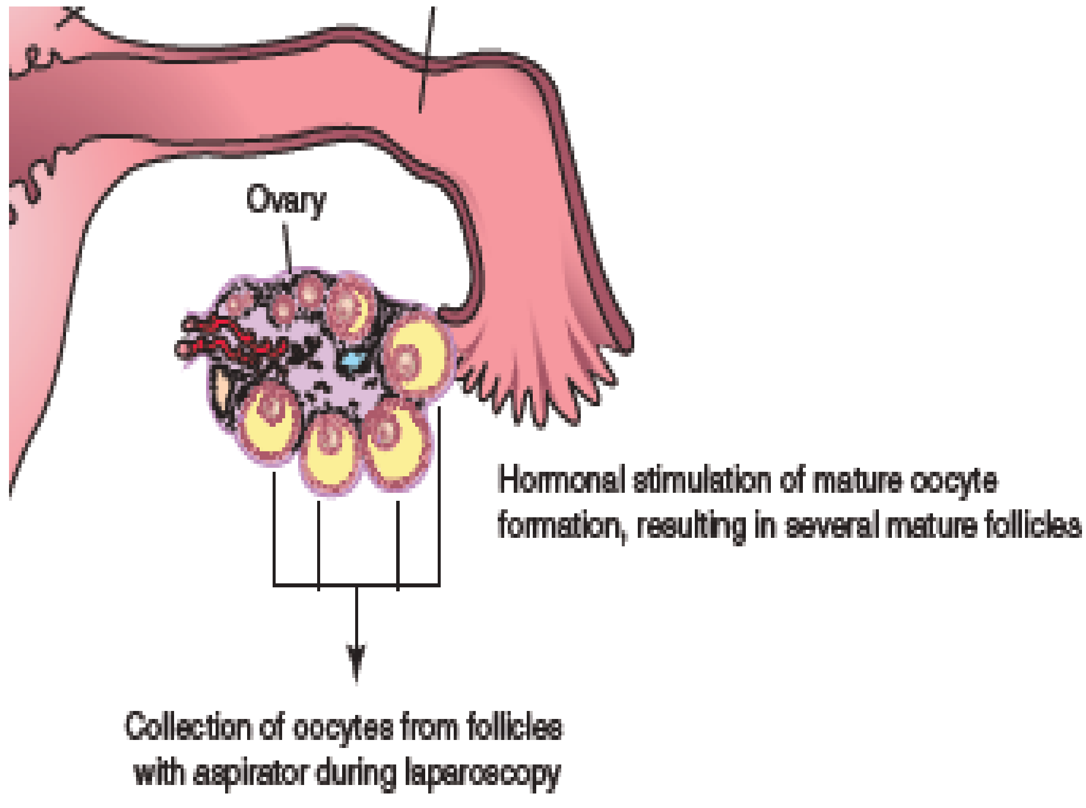
An effective method of contraception in males is **vasectomy**—excision of a segment of the ductus deferens (see Fig. 2-1*B*). Two to 3 weeks after vasectomy, there are no sperms in the ejaculate, but the amount of seminal fluid is the same as before the procedure.

<u>Fertilization of human gametes *in vitro*</u>

(IVF)

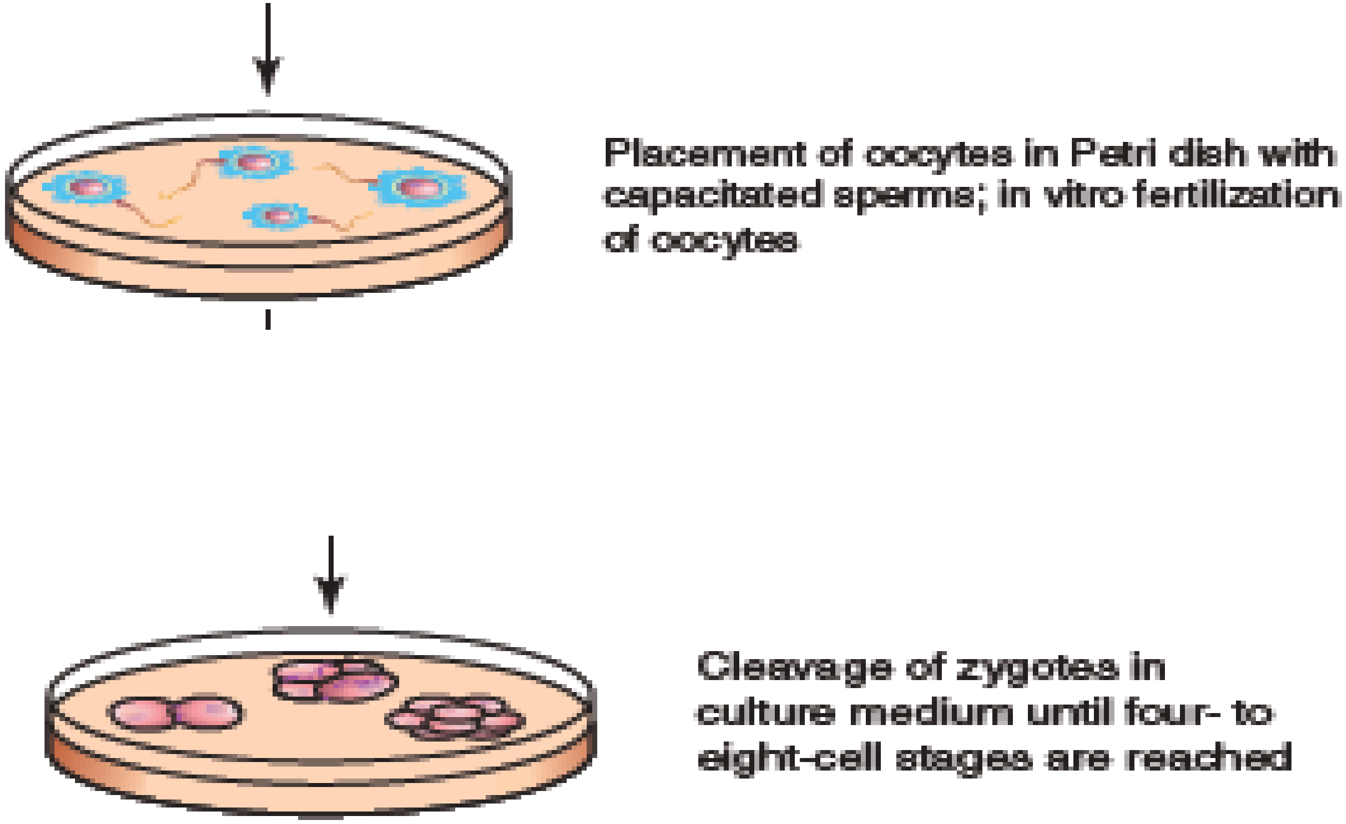
is a successful way of overcoming most forms of infertility

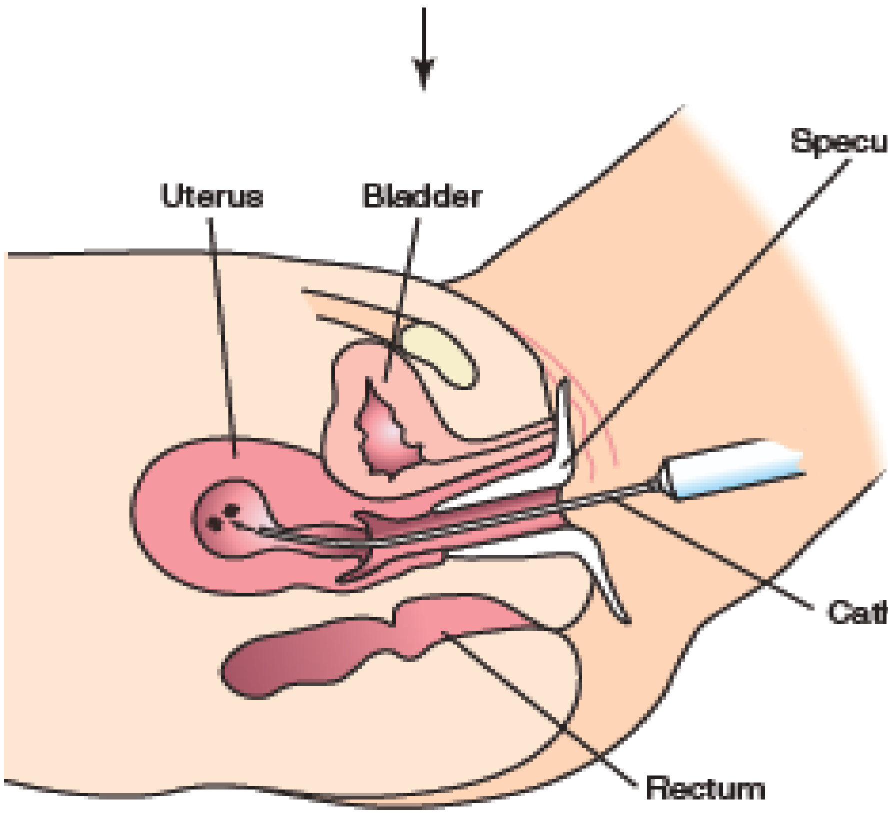
Controlled stimulation of the ovaries enables many preovulatory oocytes
(often 10 or more) to be recruited and matured, and **then aspirated either by laparoscopy or transvaginally using ultrasound guidance,**



https://www.youtube.com/watch?v=utkUkvYq-zM

These oocytes are then incubated overnight with motile spermatozoa
in a specially formulated culture medium, to achieve successful fertilization *in vitro.*





Transfer of one or two cleaving embryos into uterine cavity by way of a catheter inserted through the vagina and cervical canal

In cases of severe male-factor infertility, in which
there are insufficient normal spermatozoa to achieve fertilization *in vitro,*
Individual spermatozoa can be directly injected into the oocyte in
a process known as **intracytoplasmic injection of sperm**, which is as successful as routine *in vitro fertilization.*

In cases in which there are
no spermatozoa in the ejaculate, suitable material can sometimes be directly **aspirated from the epididymis or surgically retrieved from the testes**,
and the extracted sperm are then used for intracytoplasmic injection of sperm.

It is also now possible, in some cases, to test embryos
for the presence of a particular genetic or chromosomal abnormality in
a process known as preimplantation genetic diagnosis.

sexual cycles

At puberty the female begins to undergo **regular monthly cycles** called

sexual cycles

Sexual cycles are under the control of the

<u>Hypothalamus</u>

The hypothalamus acts as a pulse generator which generates the pulsatile release of

Gonadotropin releasing hormone (GnRH)

(GnRH)
Controls the release of the Gonadotropin

The follicle-stimulating hormone (FSH)

luteinizing hormone (LH)

from the anterior part of the pituitary gland

FSH and LH

Control

THE OVARIAN CYCLE

Controls

The endometrial cycle (menstrual cycle)

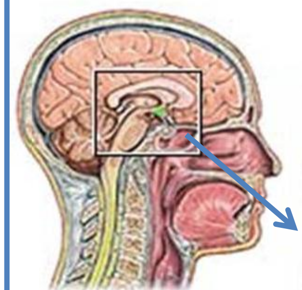
Emotional disturbances
Or
Nutrition problems

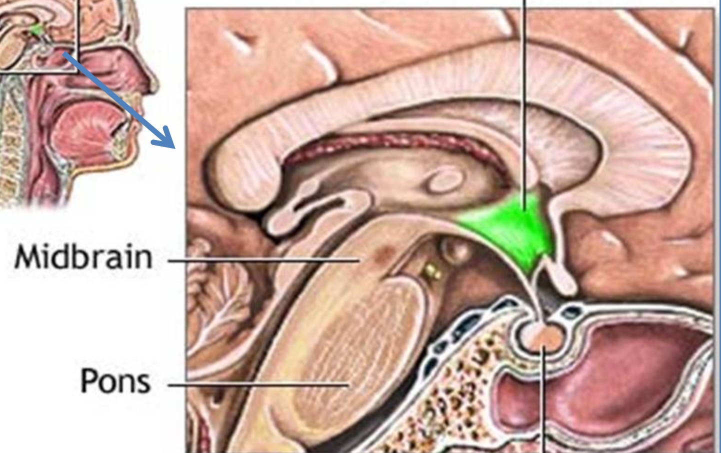
Affect
Higher centers
(The Brain)

Suppression of GnRH

Woman becomes **amenorhoeic**

1- Hypothalamus





Gonadotropin releasing hormone (GnRH)

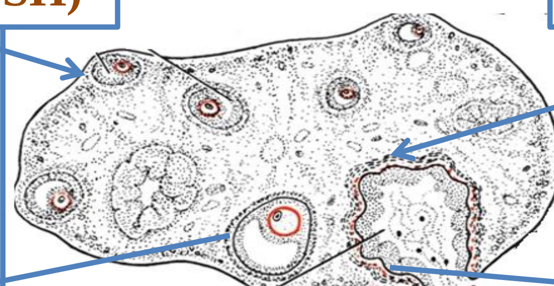
2- nterior lobe (adenohypophysis) of the pituitary gland

Gonadotropins

Follicle-stimulating hormone (FSH)

Luteinizing hormone (LH)

3- Ovary

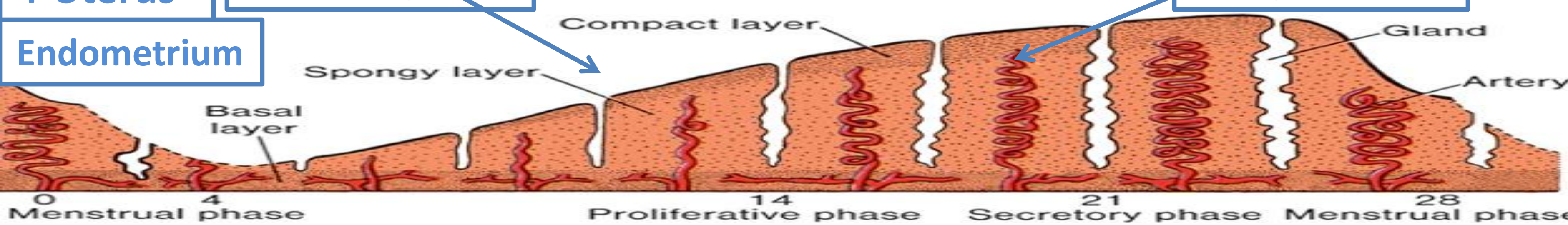


Estrogen

Progesterone

4-Uterus

Endometrium



Ovarian Cycle

FSH and LH produce cyclic changes in the ovaries

development

of ovarian follicles

ovulation

formation the corpus luteum

Follicular Development

Growth and differentiation of a primary oocyte
• Proliferation of follicular cells
• Formation of the zona pellucida
• Development of a connective tissue capsule surrounding the follicle—***theca folliculi. Thecal cells are believed*** to produce an *angiogenic factor that promotes growth* of blood vessels that provide nutritive support for follicular development.

only one of them usually develops into a mature follicle and ruptures, expelling its oocyte

The endometrial cycle (menstrual cycle)

Menstrual cycle is under the control of the ovaries

- **Remembe**r that the primary, secondary and graafian follicles all contain theca interna and granulosa cells which secret **estrogens**

Also remember that the ovulated egg leaves behind it;

1-The cells of theca interna
2- Granulosa cells
attached to the walls of the ruptured follicle.

These cells become **vascularized** and under **the influence of LH hormone** they develop ***a yellowish pigment and change into lutean cells***, which form
the corpus luteum

Corpus luteum starts to secrete **estrogens** and **progesterone**

Both **estrogen** and **progesterone** control and maintain the menstrual cycle

How?

Remember that:

The endometrium is mad of tow layers:

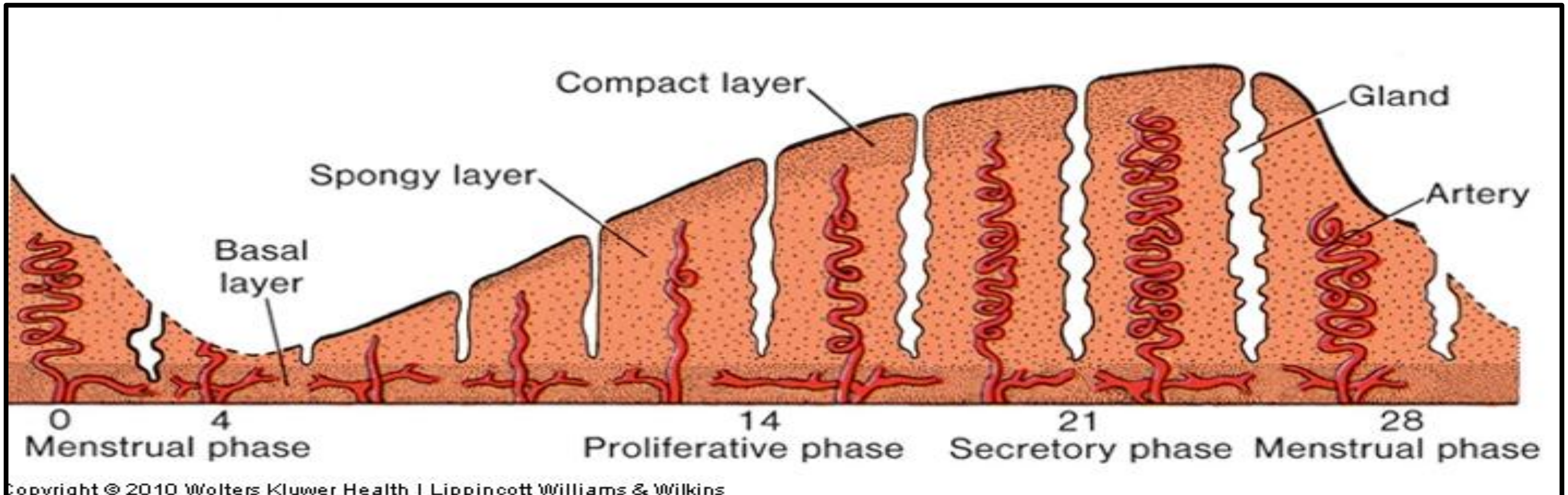
1- **Stratum basalis:** Adjacent to the mometrium

-Unresponsive to hormonal stimulation

-Remains intact throughout the menstrual cycle

2- **Functional layer made of** **A) STRATUM SPONGIOSUM**

B) STRATUM COMPACTUM



Menstrual cycle consists of three phases;

1- Follicular or proliferative phase

2- Secretory progestational phase

3- Menstrual phase

A) Begins at the end of the menstrual phase
B) Is under the influence of estrogen
C) Parallels growth of the ovarian follicles.

Begins approximately 2 to 3days after ovulation in response to progesterone produced by the corpus luteum.

1-Follicular /proliferative phase

Estrogen ⇨ mitotic activity in the glands & stroma ⇨

↑ enometrial thickness from 2 to 8 mm

(from basalis to opposed basalis layer)

2-Luteal /secretory phase

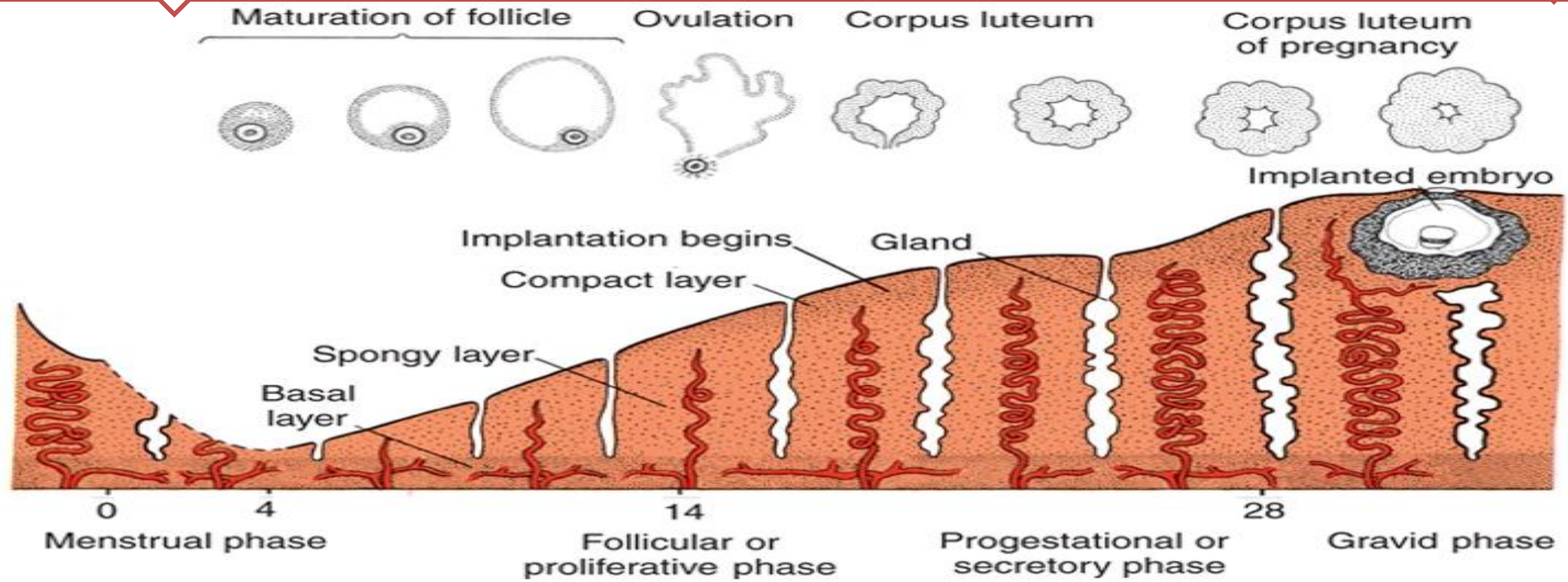
Progestrone ⇨- Mitotic activity is severely restricted

-Endometrial glands produce then secretes glycogen rich vacules

-Stromal edema

-Stromal cells enlargement

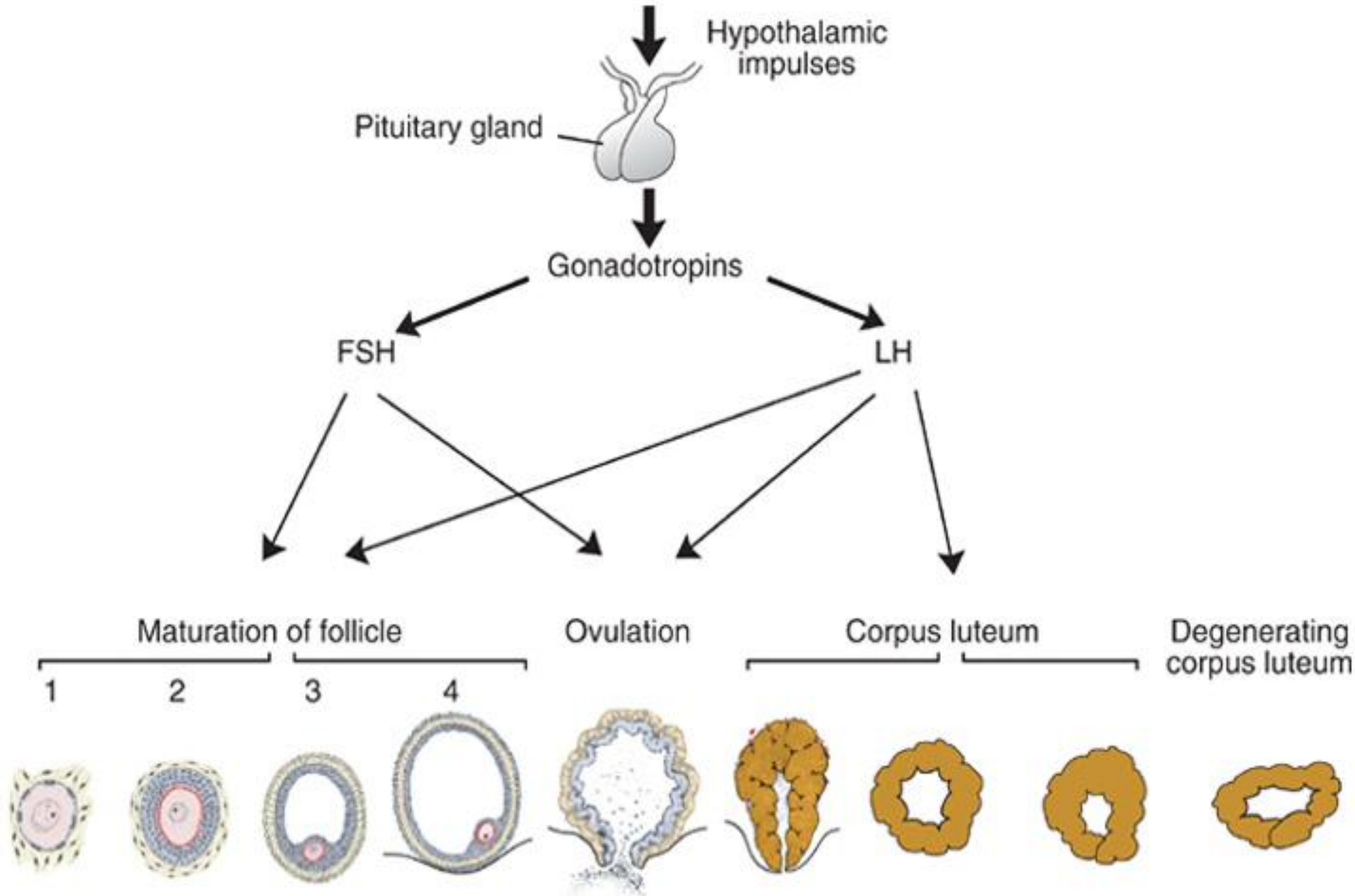
-Spiral arterioles develop, lengthen & coil



3-MENSTRUATION

- Periodic desquamation of the endometrium
- The external hallmark of the menstrual cycle
- Just before menses the endometrium is infiltrated with leucocytes
- Prostaglandins are maximal in the endometrium just before menses
- Prostaglandins ⇨ constriction of the spiral arterioles ⇨ischemia & desquamation

Followed by arteriolar relaxation, bleeding & tissue breakdown


Hypothalamic impulses
Pituitary gland
Gonadotropins
FSH
LH
Maturation of follicle
1
2
3
4
Ovulation
Corpus luteum
Degenerating corpus luteum

Menstrual cycle

DEFINITION

Rhythmical series of physiological changes that occur in fertile women

- The menstrual cycle averages **28 days**

- **Variations** between **21 and 35** days are **normal**

- **Irregular** and **infrequent** cycles may occur for a few months after puberty and in the few years proceeding **the menopause**

Menarche: a woman's first menstruation

typically occurs around age 12

occurrence depends on overall health and diet

Menopause: end of a woman's reproductive phase, commonly occurs between 45-55 years. Less than 2% occur before age 40.

age of menopause is largely the result of genetics

Factors associated with early menopause

Cigarette smoking

Family history

Chemo / Radiation / Genetic factors

Peri-menopause

- Transitional period
- Hallmark is menstrual irregularities
- Shortened cycle length
- Skipped cycles
- 10% of women will have abrupt cessation of menses

Menstrual irregularities is the primary reason women seek medical attention

Symptoms

Hot Flushes

Subjective feeling of intense heat followed by skin flushing and diaphoresis

Atrophic vaginitis, urethritis, recurrent UTIs,

Sexual Disturbances

Decreased interest in sexual activity

Sleep Disturbances

Estrogen appears related to producing restful, deep-stage sleep

Mood Swings / Irritability / Depression

Osteoporosis

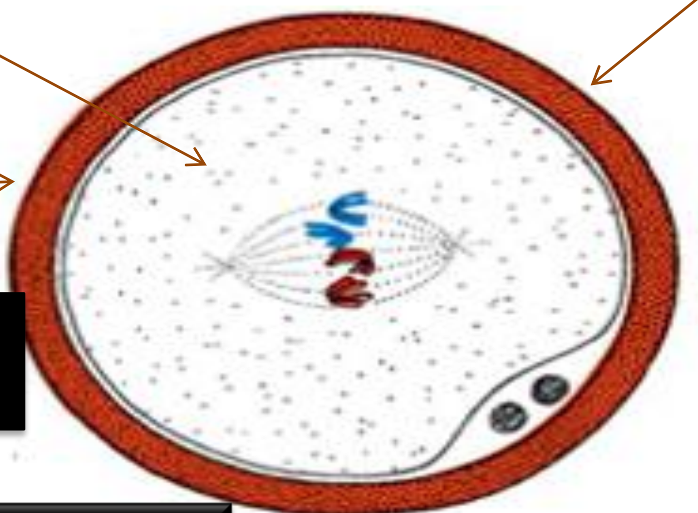
IMPLANTATION AND FIRST WEEK OF DEVELOPMENT

So …

What we HAVE at the end of fertilization ?!

Fertilized Oocyte covered by Zona pellucida

THE ZYGOTE



Why does the zygote need zona pellucida?

To prevent early implantation. And …….

The Zygote's Journey to the Uterus

➢Takes approximately **3 to 4 day**

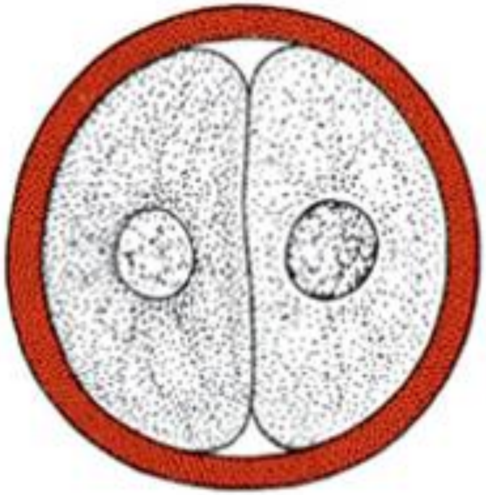
➢**In this journey the zygote undergoes** a series of mitotic divisions called **Cleavage**, that results in an increase in cells number.

The two cellular stage. (two cells)

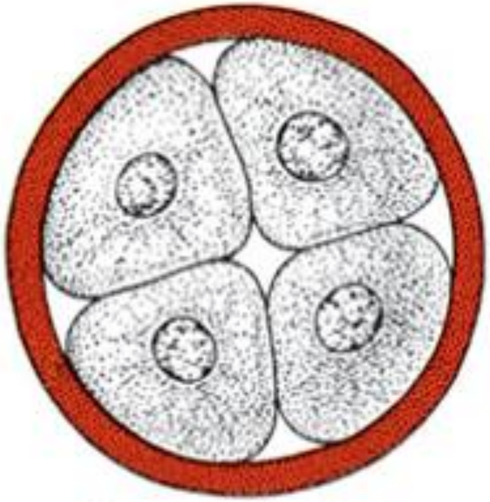
Four-cell stage

Eight-cell stage

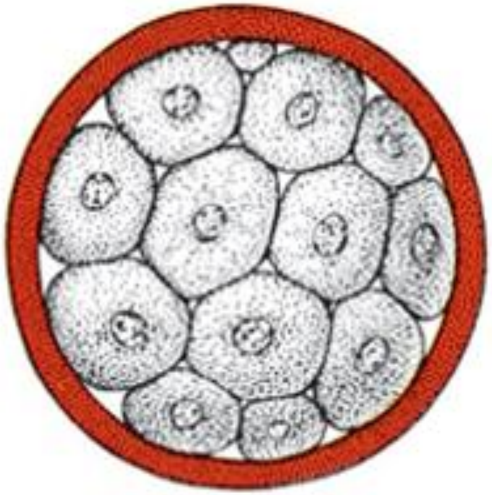
These cells are called <u>Blastomeres</u>



Two-cell stage



Four-cell stage



Morula

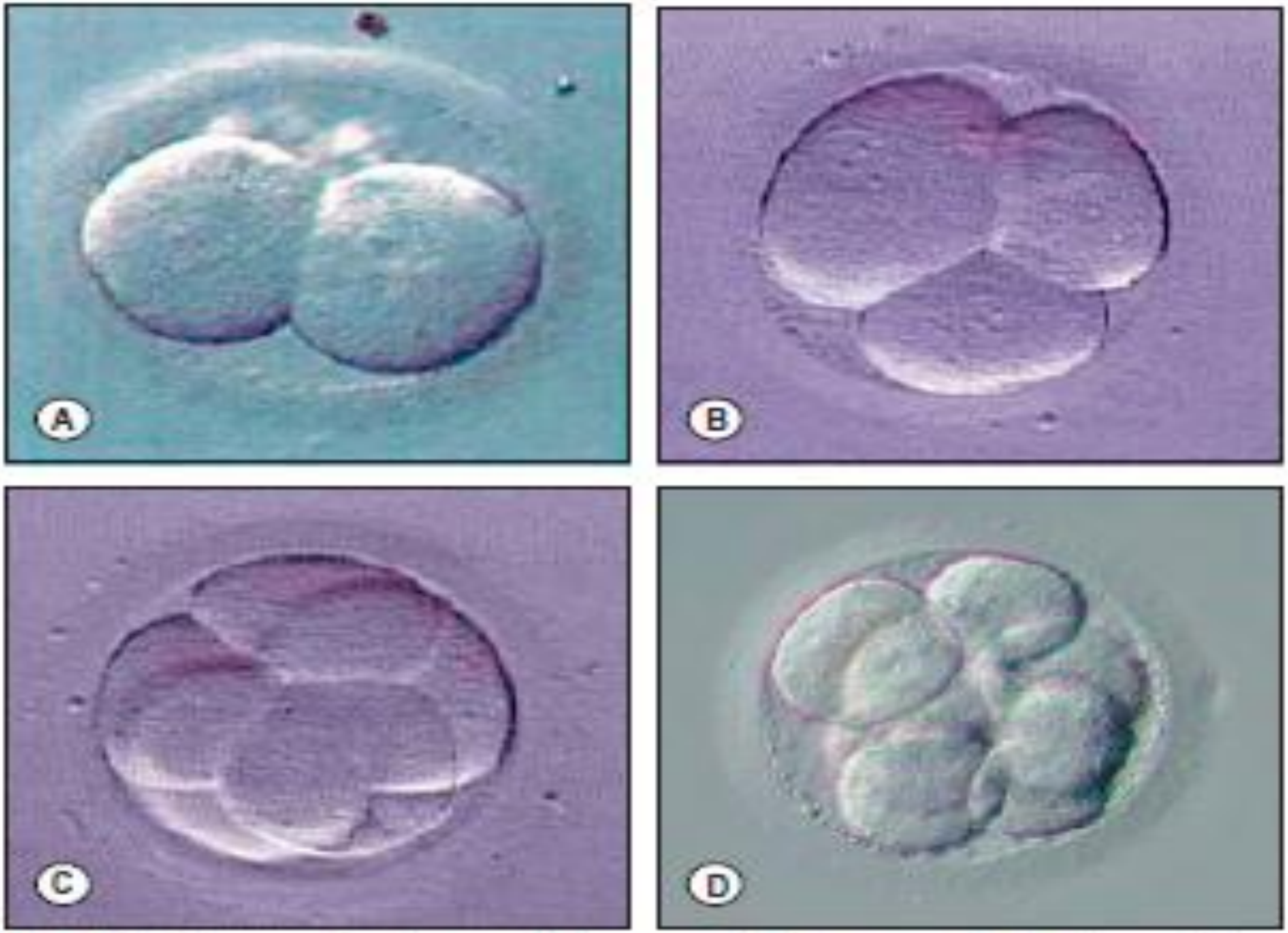


Fig. 8.6 Successive stages of cleavage of a human ootid. **A**, Two-cell stage; **B**, three-cell stage; **C**, five-cell stage; **D**, eight-cell stage.

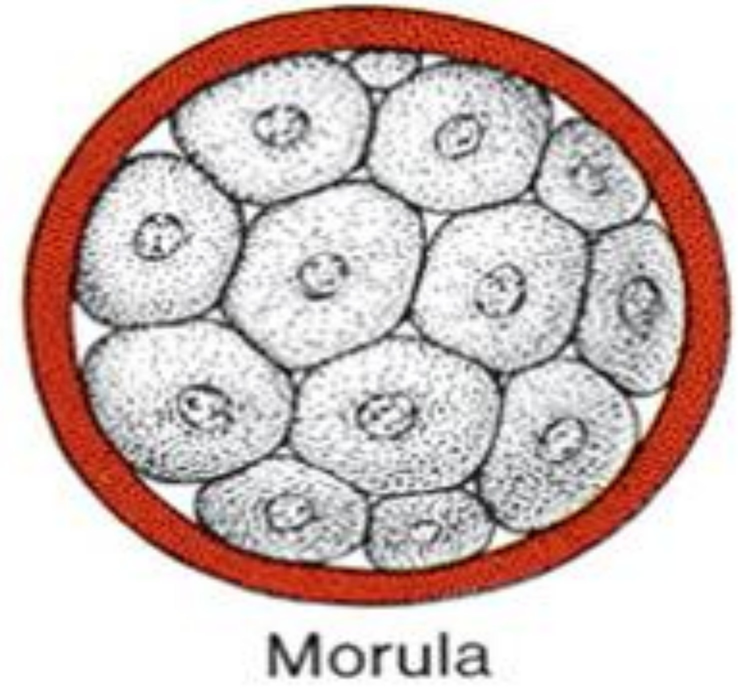
➢Approximately **3 days after fertilization, the** **B l a s t o m e r e s** divide again to **form a 16-cell morula (mulberry). !** (too many cells they push out the zona pellucida, zona pellucida bulges here and there and it becomes full of bulgings which look like **mulberry**, but we will call it **morula** from Latin.

➢Inner cells of the morula constitute

the inner cell mass

➢The surrounding cells compose

the outer cell mass



➢The inner cell mass gives rise to tissues of

the embryo proper

➢ The outer cell mass forms the

trophoblast, which later contributes to the

placenta.

Fig. 8.7 Human embryos. Formation of a morula and blastocyst within the zona pellucida and blastocyst hatching from the zona pellucida. **A**, A ball of cells, the morula, with the cells undergoing compaction; **B**, the blastocyst cavity is developing and the inner cell mass can be seen on one side of the cavity; **C**, the blastocyst is beginning to hatch from the zona pellucida.

The morula is heading to the uterus!

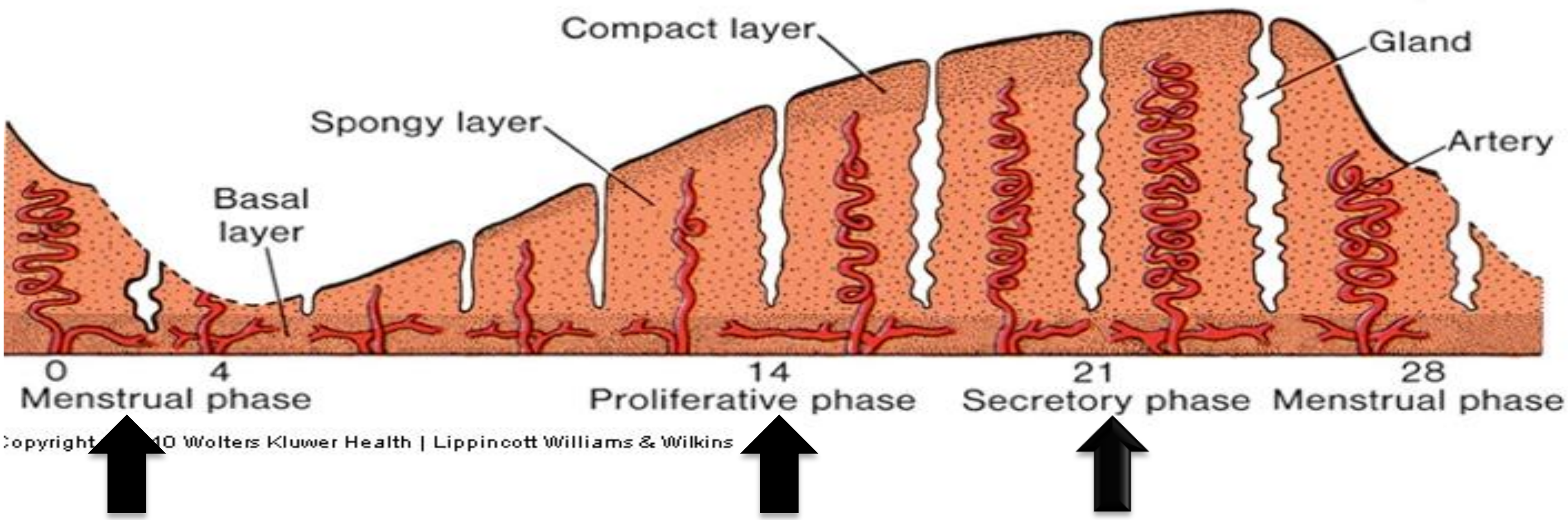
In which stage is the mucosa of the uterus?

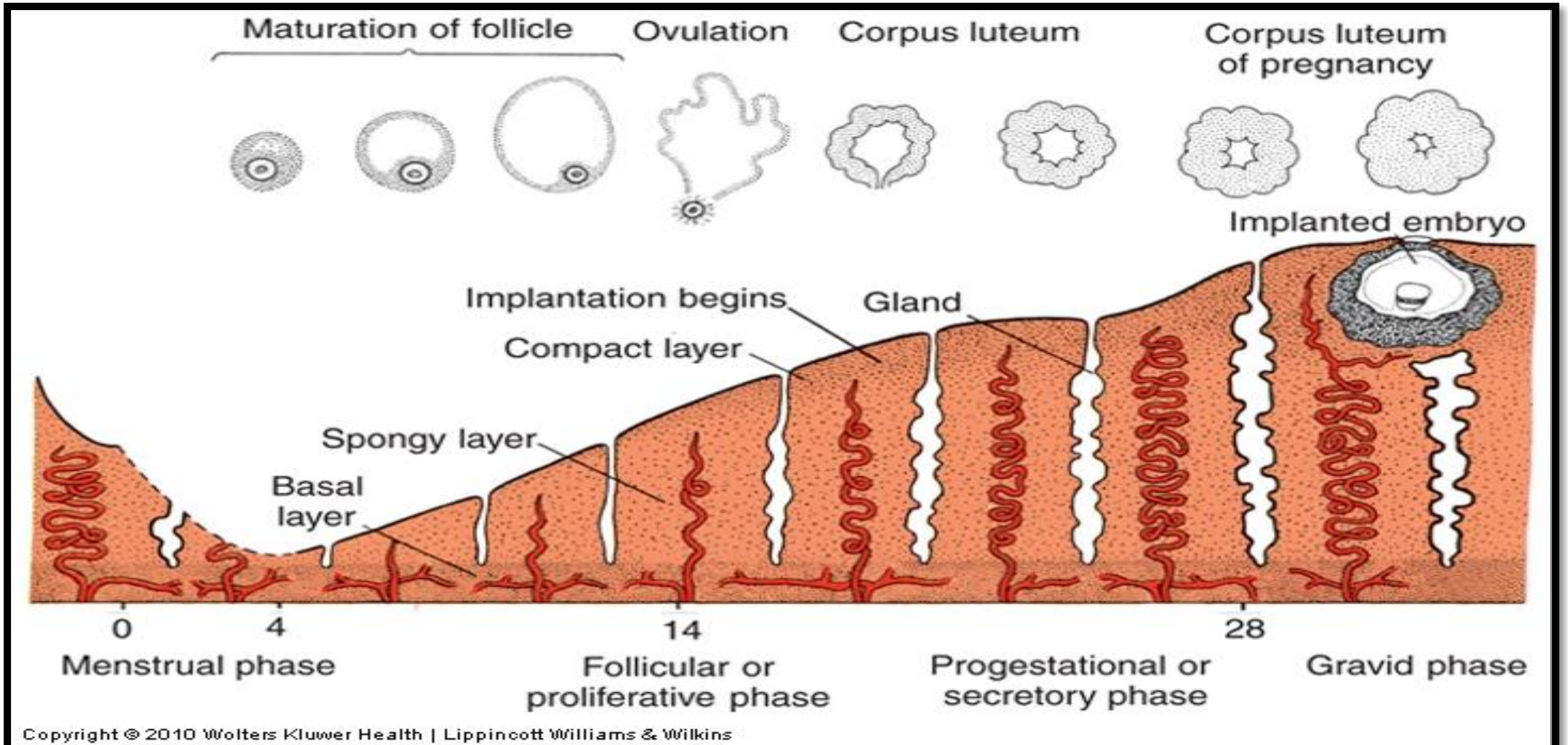
The endometrium is mad of tow layers

1- **Stratum basalis**

2- **Functional layer made of** **A) STRATUM SPONGIOSUM**

B) STRATUM COMPACTUM





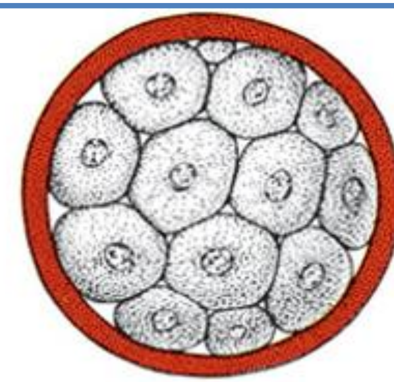
At the time that the morula reaches the uterus, the mucosa of the uterus is in the secretory phase during which:

Uterine glands and Arteries become coiled and the tissue become succulent.

The morula enters the uterine cavity

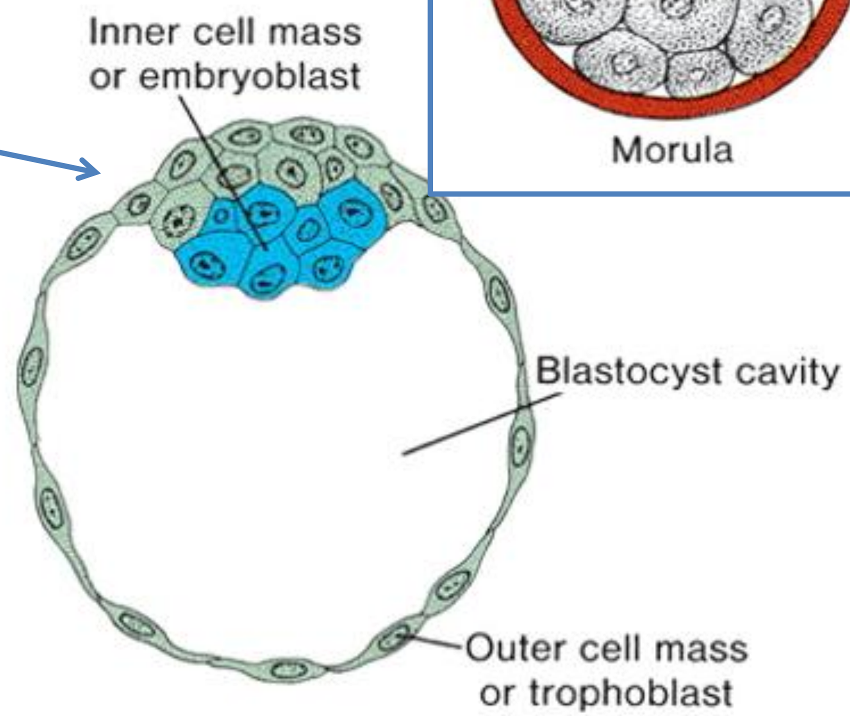
Day 4 after fertilization

- Uterine fluid begins to penetrate through **the zona pellucida** into the intercellular spaces of **the inner cell mass**.
- Gradually, the intercellular spaces become **confluent, and a single cavity, the blastocele, forms.**



Morula

- At this time, the embryo is a blastocyst.
- Cells of the inner **cell mass**, now called the **embryoblast**, are at one pole, and those of the outer cell mass, or trophoblast flatten and form the **epithelial wall of the blastocyst**

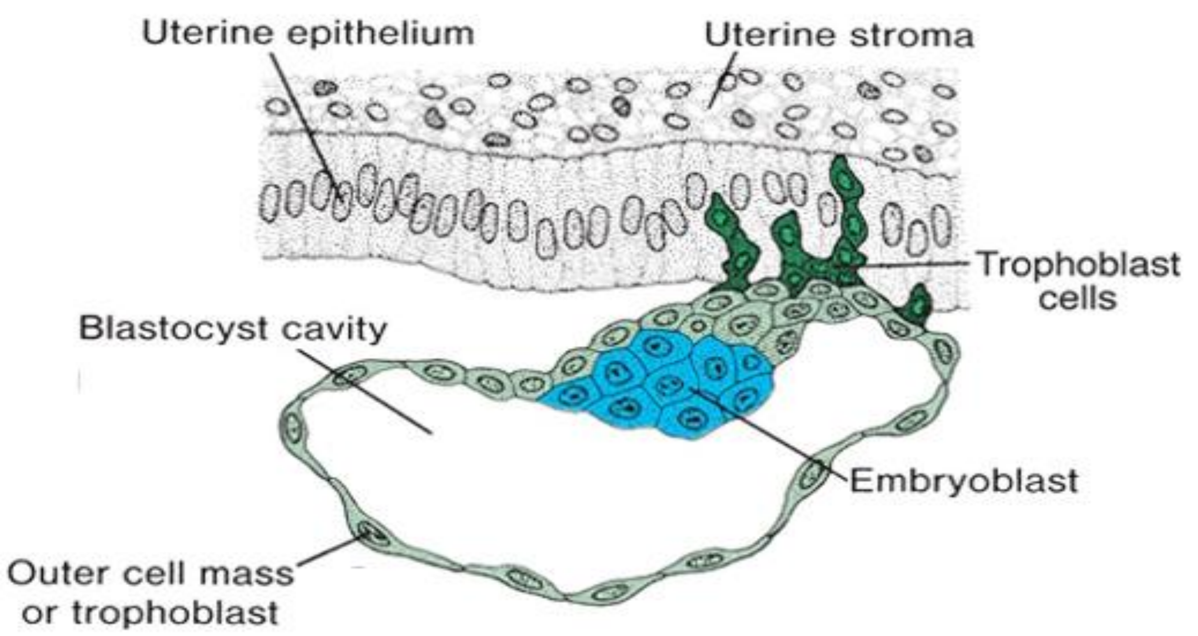


- ***The zona pellucida disappears to allow implantation***

Fig. 8.8 Human blastocyst nearly completely hatched from the zona pellucida. The blastocyst can now expand to its full size.

Day 6 after fertilization

Trophoblastic cells over the embryoblast pole begin to *penetrate* between the epithelial cells of the *uterine mucosa* on about *the sixth day*
(Early implantation)



Pregnancy starts at *Day 6* when Blastocyst loosely attached to endometrium.

Read only

Preimplantation and postimplantation reproductive failure occurs often.
Even in some fertile women under optimal conditions for pregnancy, 15% of oocytes are not fertilized, and 10%to 15% start cleavage but fail to implant.Of the 70% to 75% that implant, only 58% survive until the second week, and 16% of those are abnormal. Hence, when the first expected menstruation is missed, only 42% of the eggs exposed to sperm are surviving.
Of this percentage, a number will be aborted during subsequent weeks and a number will be abnormal at the time of birth.

An immunosuppressant protein

the **early pregnancy factor—is secreted by the trophoblastic** cells and appears in the maternal **<u>serum within 24 to 48 hours</u>** after implantation.

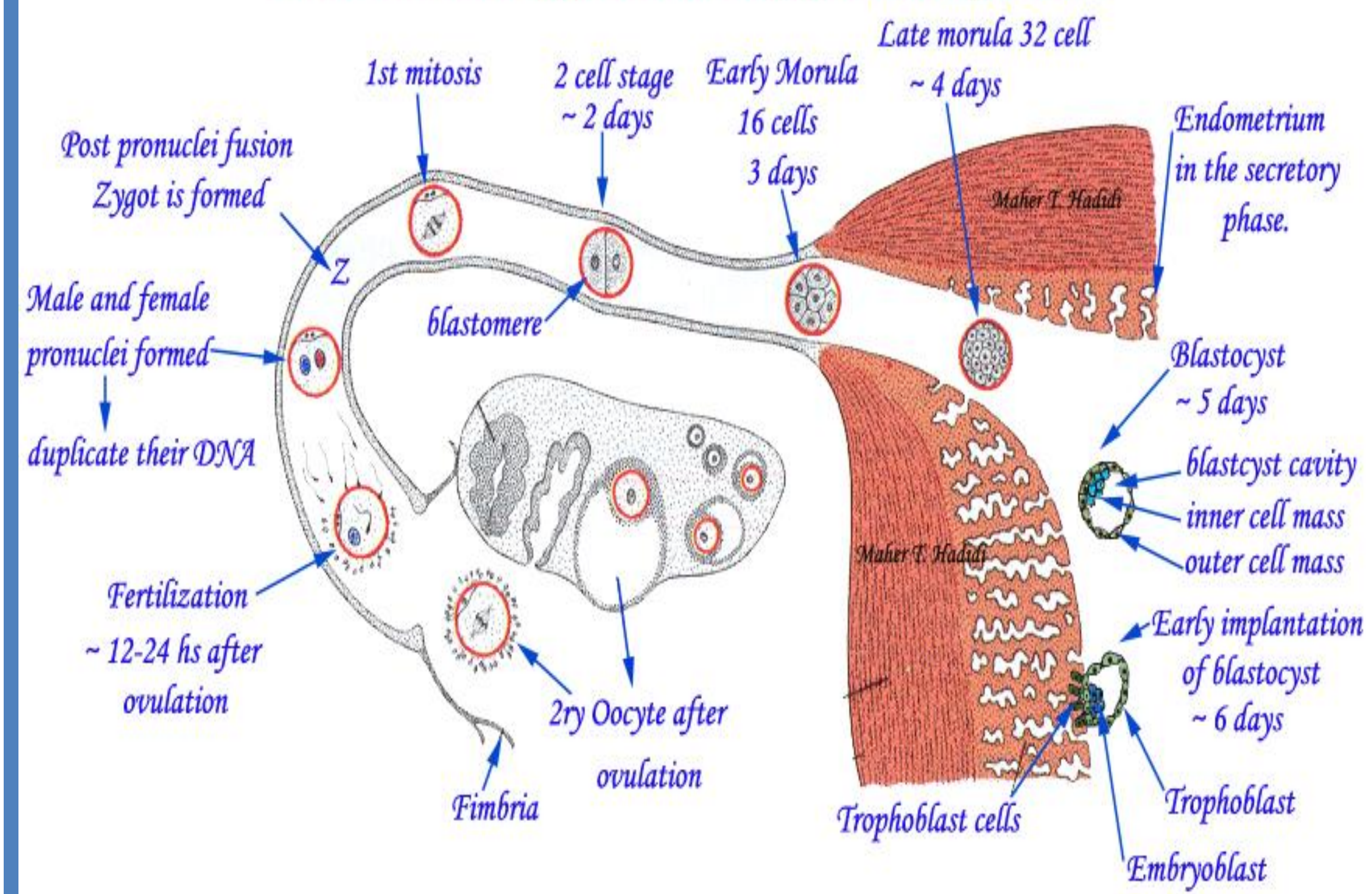
The early pregnancy factor forms the basis for a pregnancy test applicable during the **first 10 days of development.**

If fertilization does not occur, the **corpus luteum** reaches maximum development approximately 9 days after ovulation. Subsequently, the corpus luteum shrinks because of degeneration of lutean cells and forms a mass of fibrotic scar tissue, the **corpus albicans**.

If the oocyte is fertilized, degeneration of the corpus luteum is prevented by **human chorionic gonadotropin (hCG),** a hormone secreted by the **syncytiotrophoblast of the developing embryo**. The corpus luteum continues to grow and forms the **corpus luteum of pregnancy (corpus luteum graviditatis).**

By the end of the third month, this structure **(corpus luteum graviditatis)** may be one third to one half of the total size of the ovary. Yellowish luteal cells continue to secrete progesterone until **the end of the fourth month**; thereafter, they regress slowly as secretion of progesterone **by the trophoblastic component of the placenta becomes adequate** for maintenance of pregnancy.

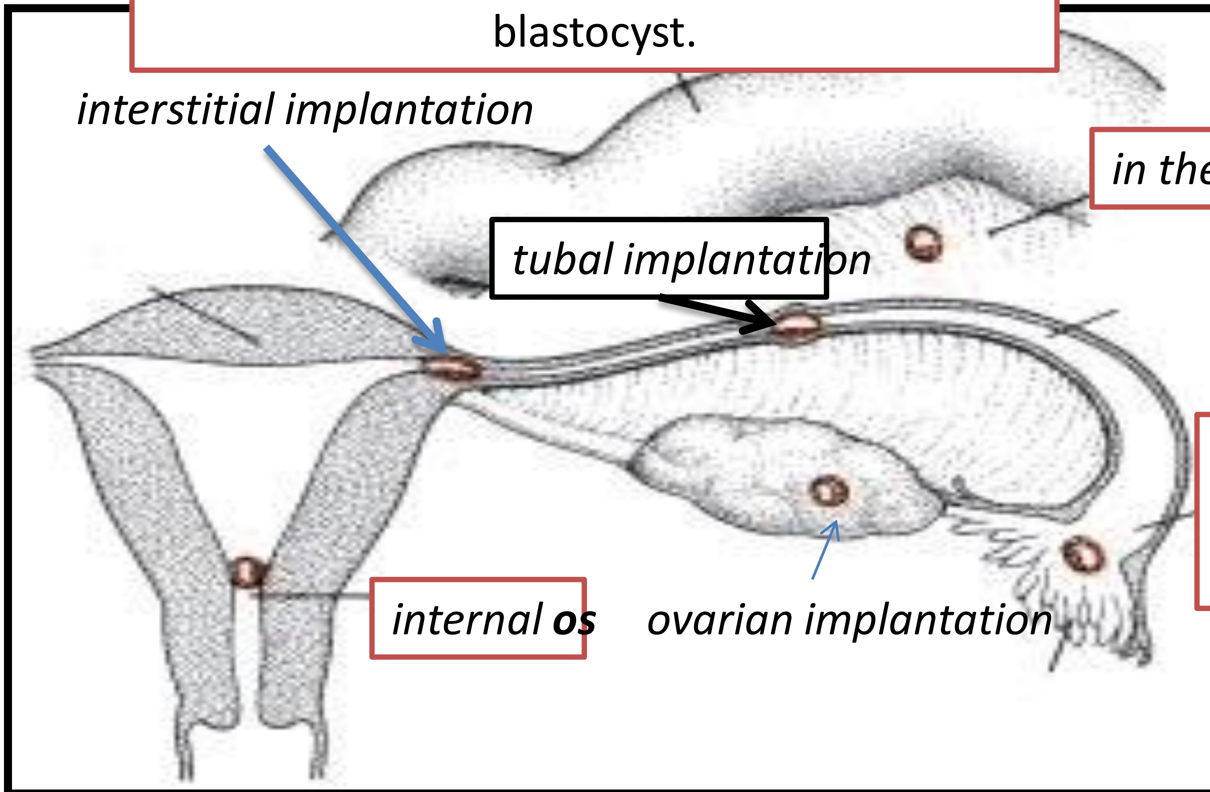
Events during first week of development



ABNORMAL EMBRYOS AND SPONTANEOUS ABORTIONS

Many early embryos abort spontaneously. The early implantation stages of the blastocyst are critical periods of development that may fail to occur because of inadequate production of progesterone and estrogen by the corpus luteum (see Chapter 2, Fig. 2-8). Clinicians occasionally see a patient whose last menstrual period was delayed by several days and whose last menstrual flow was unusually profuse. Very likely, such patients have had an early spontaneous abortion. *The overall early spontaneous abortion rate is believed to be approximately 45%*. Early spontaneous abortions occur for a variety of reasons, an important one being the presence of chromosomal abnormalities.

Abnormal implantation sites of the blastocyst.



1- implantation in the abdominal cavity.
The ovum most frequently implants in **the rectouterine cavity (Douglas'pouch)**
2-implantation in the ampullary region of the tube.
3-tubal implantation.
4- interstitial implantation, that is, in the narrow portion of the uterine tube.
5- implantation in the region of the internal ***os,***
6- ovarian implantation.

the rectouterine cavity
(Douglas' pouch)