DISCUSS THE 2ND WEEK OF EMBRYONIC DEVELOPMENT.

The following events take place during the second week of embryonic development;

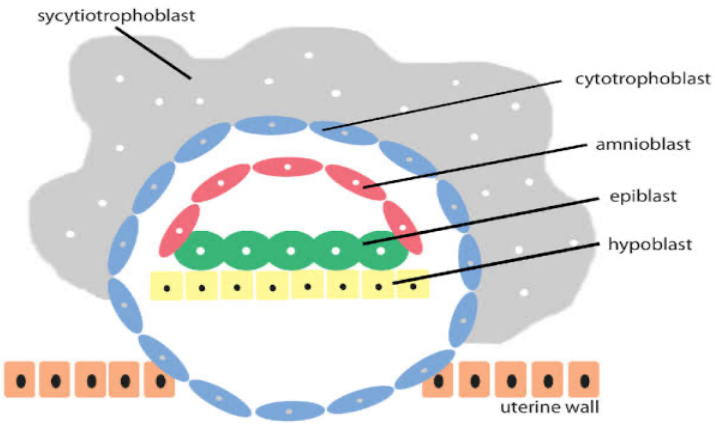
- Completion of implantation of the blastocyst.
- Formation of the bilaminar embryonic disc (epiblast and hypoblast).
- Formation of extra embryonic structures (amniotic cavity, amnion, umbilical vesicle/yolk sac, connective stalk and chorionic sac).

DAY8.

The blastocyst is partially embedded in the endometrium. The syncytiotrophoblast will continue to erode the endometrium thereby eroding endometrial blood vessels and glands. More cells in the cytotrophoblast divide and migrate into the region of the syncytiotrophoblast where they fuse and lose their individual cell membranes. Cells of the embryoblast (inner cell mass) also differentiate into 2 layers:

1. Hypoblast layer; which is made up of small cuboidal cells and it is adjacent to the blastocytic cavity.
2. Epiblast layer; made up of high columnar cells and it is adjacent to the amniotic cavity.

The hypoblast and epiblast layers together form a flat ovoid shaped disc called the bilaminar embryonic disc. At the same time, a small cavity appears within the epiblast which enlarges to form the amniotic cavity. Epiblast cells adjacent to the cytotrophoblast are called amnioblasts. Amnioblasts together with the rest of the epiblast, line the amniotic cavity. The endometrium adjacent to the implantation site is swollen with an excessive accumulation of fluid and highly vascular.



DAY 9.

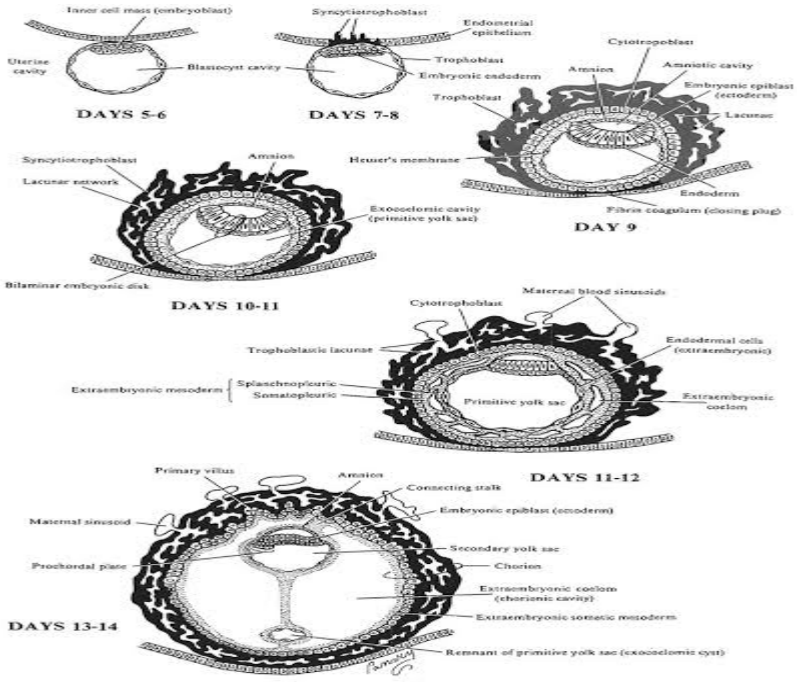
The blastocyst is more deeply embedded in the endometrium. The syncytiotrophoblast continues to erode the endometrium. The cells of the cytotrophoblast will continue to divide and migrate into the region of the syncytiotrophoblast. The penetration defect in the surface epithelium is closed by a coagulum called fibrin. Vacuoles appear at the region of the trophoblast and they fuse to form larger lacunae. This phase of trophoblast development is known as the lacunar stage. The cells of the hypoblast adjacent to the cytotrophoblast form a thin membrane called the exocoelomic (Heuser's) membrane. This membrane lines the inner surface of the cytotrophoblast. The exocoelomic membrane together with the hypoblast forms the lining of the exocoelomic cavity/primitive yolk sac/primary umbilical vesicle.

DAY 11-12.

The blastocyst is completely embedded in the endometrium and the surface epithelium almost entirely covers the original defect in the uterine wall. The syncytiotrophoblast continues to erode the endometrium. The cells of the cytotrophoblast will continue to divide and migrate into the region of the syncytiotrophoblast. The blastocyst now produces a slight protrusion into the lumen of the uterus. Cells of syncytiotrophoblast penetrate deeper into the stroma and endothelial lining of the endometrial capillaries. These ruptured endometrial capillaries are called sinusoids. The lacunae then begin to communicate with sinusoids and maternal blood enters the lacunar system. The communication of the eroded endometrial capillaries with the lacunae establishes the primordial uteroplacental circulation. When maternal blood flows into the lacunae, oxygen and nutritive substances are available to the embryo. A new population of cells appears between the inner surface of cytotrophoblast and the outer surface of the exocoelomic cavity. These cells which are derived from the yolk sac cells form a fine, loose connective tissue called the extraembryonic mesoderm. Soon large cavities develop in the extra embryonic mesoderm and when those become confluent they form a space know as the extra embryonic cavity or extra embryonic mesoderm. This space surrounds the primitive yolk sack and amniotic cavity, except where the germ disc is connecting stalk (which develops into the umbilical cord). The extraembryonic mesoderm lining the cytotrophoblast and amnioblast and amnioblast called the extra embryonic somatic mesoderm extra embryonic somatic mesoderm also forms the connecting stalk. The lining covering the yolk sack (amnioblast and exocoelomic cavity) is called the extra embryonic splanchnic mesoderm. As the conceptus implants, the endometrial connective tissues cells undergo a transformation, the cells of the endometrium swell because of the accumulation of glycogen and lipid in the cytoplasm, and they are known as decidual residual cells. The main function of the decidual reaction is to provide nutrition for the early embryo and an immunologically privileged site for the conceptions.

DAY 13.

The surface defect in the endometrium has been completely covered by the surface epithelium. Occasionally bleeding occurs at the implantation site as a result of increased blood flow into the lacunar spaces. Cells of the cytotrophoblast proliferate locally and penetrate into the syncytiotrophoblast; forming cellular columns with the syncytial covering are known as primary villi. The primary yolk sac becomes reduced in size and is known as secondary yolk sac/definitive yolk sac/secondary umbilical cord. In humans the yolk sac contains no yolk but is important for transfer of nutrients between the fetus and mother. The yolk sac is much smaller than the original exocoelomic cavity/primitive yolk sac. During its formation, large portions of the exocoelomic cavity are pinched off to form exocoelomic cyst. Exocoelomic cysts are often found in the extraembryonic cavity or chorionic cavity or extra embryonic coelom. The extraembryonic coeolom expands and forms a large cavity called chorionic cavity. The extra embryonic mesoderm lining the outside of the cytotrophoblast is then known as chorion plate. The only place where extra embryonic mesoderm traverses the chorionic cavity is the connecting stalk. With development of blood vessels, the connecting stalk becomes the umbilical cord.



CLINICAL COORELATES.

Human chorionic gonadotropin: Pregnancy test

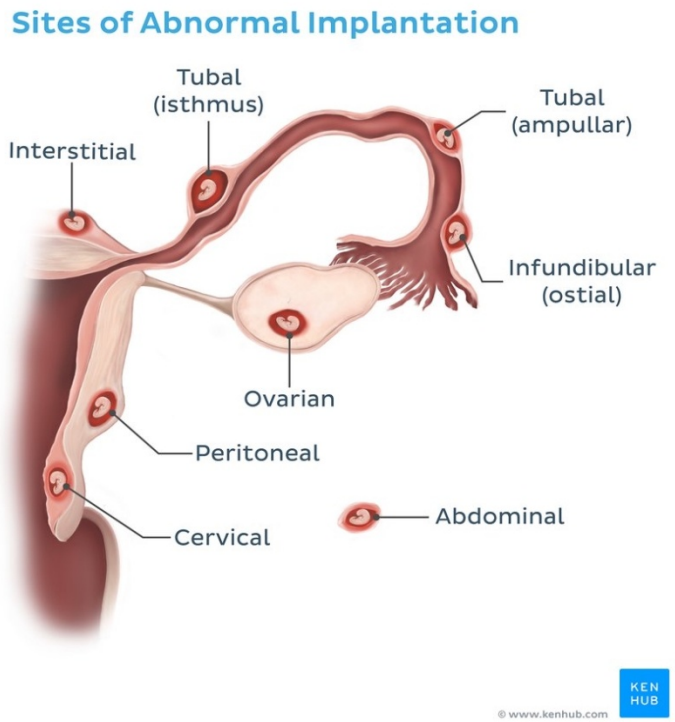
Implantation spotting can be misinterpreted as the beginning of the menstrual period. Consequently, most pregnant females may not realize that they are pregnant. However, home pregnancy kits rely on the presence of β-hCG to determine whether or not the individual is pregnant.

hCG (human chorionic gonadotropin) is a glycoprotein that is made up of alpha and beta subunits. As hCG accumulates in the **maternal serum**, it is **metabolized** into the constituent alpha and beta subunits, filtered by the kidneys and excreted in urine. Unlike the alpha subunit, which is homologous to the alpha units in other reproductive hormones (FSH, LH, etc), the **beta (β) moiety** is unique to hCG and therefore can be used as the basis of the **pregnancy test**. Throughout the pregnancy, the β-hCG levels will continue to increase and then decrease as the pregnancy comes closer to term. This can be used to monitor the viability of the conceptus throughout the gestational period.

ECTOPIC PREGNANCY.

Implantation ideally occurs within the **body of the uterus**; usually either on the anterior or posterior wall. However, there are instances when the blastocyst may implant in an area other than the corpus uteri. This process is referred to as an **ectopic pregnancy**. These are obstetric emergencies that regrettably require termination of the pregnancy as they threaten the life of the mother and the implantation site cannot facilitate the projected fetal growth.

Of the numerous inappropriate sites that implantation can occur, **tubal ectopic pregnancies** are the most common. Within the fallopian tubes, an ectopic pregnancy is most likely to happen in the ampulla, then at the isthmus, followed by the infundibulum. Implantation in the **ovary** and abdominopelvic regions has also been reported. **Uterine scarring** (as a result of pelvic inflammatory disease, aggressive dilation and curettage, etc.), early **loss of the zona pellucida**, reduced motility of the cilia (caused for example, by smoking) can result in abnormal implantation.



Placenta previa

There are other cases where the blastocyst implants within the uterine cavity, but the placenta may cover the internal cervical os. Unlike ectopic pregnancies, these pregnancies may actually progress to term. But they are considered **high risk** pregnancies as they are likely to progress to preterm labor. This process is referred to as placenta previa.

Placenta previa can be subdivided into marginal and complete types. In **marginal placenta previa**, the leading edge of the placenta is within 2 cm of the internal vaginal os; while in **complete placenta**, the entire internal os is covered by the placenta. The leading theory behind the onset of placenta previa is that the cranial part of the corpus uteri is unfavorable for implantation. As a result, the blastocyst implants in the caudal part of the uterus, and the placenta develops near or over the internal os. As the **cervix** undergoes changes to facilitate delivery during the third trimester, the placenta loses its attachment to the endometrium.

Digital vaginal examination or coitus can result in painless bleeding from the vagina. This inevitably has unfavorable effects on both the mother and fetus. These patients should be admitted for maternal and fetal monitoring. The goal is to keep the mother hemodynamically stable and ascertain if an emergency cesarean delivery is indicated.

Uterine fibroids

Leiomyomata uteri or uterine fibroids are benign stromal tumors of the uterus. They are quite common among women of **reproductive age**. Clinical manifestation spans a spectrum of **asymptomatic** existence to **dysmenorrhea** and **infertility**. The impact of the leiomyoma is

dependent on its location and size. Essentially, large leiomyomas can distort the uterus, making implantation more challenging. Furthermore, they can obstruct the proximal fallopian ostium, preventing the zygote from entering the uterus.

Endometriosis

Endometriosis is another relatively common gynecological disorder that has been demonstrated to negatively affect **fertility**. Numerous mechanisms have been proposed in the effect of endometriosis on fertility. These include problems with follicular maturation, defective fertilization, and issues with implantation. Patients with endometriosis have demonstrated resistance to **progesterone** as well as decreased levels of **LIF** and **integrins**. These entities are known to positively influence implantation and as such, their absence would be detrimental to the process.

Hydrosalpinx

A hydrosalpinx is a mechanical obstruction of the **distal fallopian tube** associated with **fluid accumulation** in the tubular lumen. It is also relatively common among women with tubal disease and fertility issues. One of the proposed mechanisms by which hydrosalpinx interferes with implantation is **integrin** and **LIF deficiency**. Another is based on the fact that there is intermittent release of hydrosalpinx fluid into the uterine cavity. This coats the blastocyst and results in impaired attachment.