

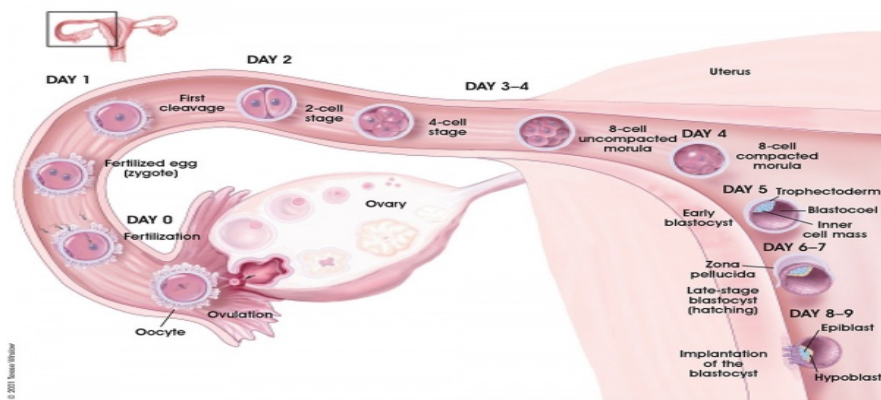
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Discuss the second week of development.

Week 1 and 2 development



Key events of human

development during the second week (week 2) following fertilization or clinical gestational age (GA) week 4, based on last menstrual period. Week 2 is about the implantation process and blastocyst differentiation. Note that all cells produced from the initial fertilization event are defined as the "conceptus" and will include cells with both embryonic and extraembryonic futures. In the conceptus, this is a period of blastocyst "hatching" rapid blastocyst differentiation into extraembryonic and embryonic tissues and proliferation. In placental animals, this is the first physical interaction between the conceptus and the maternal uterine wall with adplantation and the commencement of implantaion.

The implanting conceptus releases a hormone (human Chorionic Gonadotropin or hCG) that initiates maternal hormonal changes, stopping the menstrual cycle. Detection of hCG in maternal urine or blood is also the basis of many modern pregnancy tests.

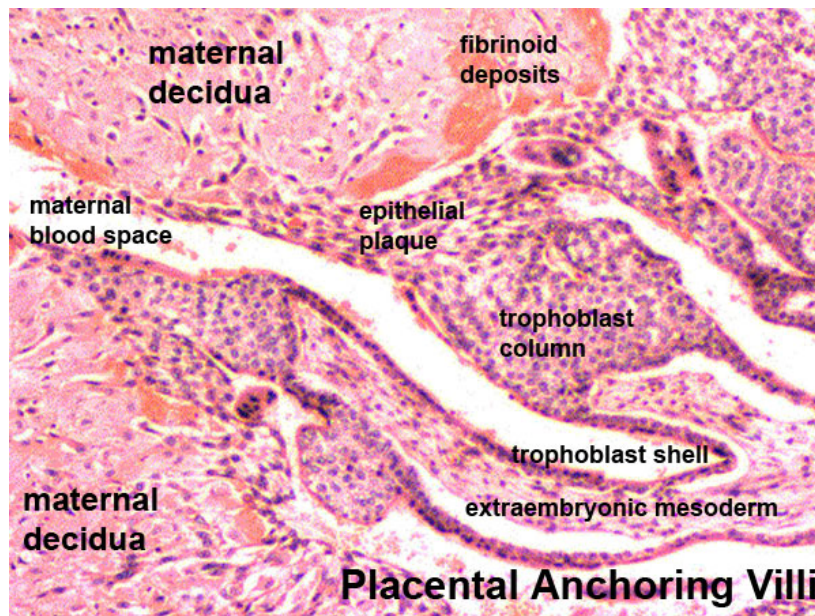
## Implantation

The second week of human development is concerned with the process of implantation and the differentiation of the blastocyst into early embryonic and placental forming structures.

- ★ implantation commences about day 6 to 7

- ★ Adplantation - begins with initial adhesion to the uterine epithelium
- ★ blastocyst then slows in motility, "rolls" on surface, aligns with the inner cell mass closest to the epithelium and stops
- ★ Implantation - migration of the blastocyst into the uterine epithelium, process complete by about day 9
- ★ coagulation plug - left where the blastocyst has entered the uterine wall day 12
- ★ Normal Implantation Sites - in uterine wall superior, posterior, lateral

## Decidual reaction



- ★ occurs initially at site of implantation and includes both cellular and matrix changes
- ★ reaction spreads throughout entire uterus, not at cervix
- ★ deposition of fibrinoid and glycogen and epithelial plaque formation (at anchoring villi)
- ★ presence of decidual cells are indicative of pregnancy

Cervix - at mouth of uterus, secretes mucus (CMP), forms a plug/barrier, mechanical and antibacterial  
 Vascular - increased number of blood vessels

## Decidua

The endometrium becomes the decidua and forms 3 distinct anatomical regions (at approx 3 weeks)

- ★ Decidua Basalis at implantation site
- ★ Decidua Capsularis enclosing the conceptus
- ★ Decidua Parietalis the remainder of uterus
- ★ Decidua Capsularis and Parietalis fuse eventually fuse and uterine cavity is lost by 12 weeks

## **Bilaminar Embryo**

Human development about day 8 to 9

The embryoblast (inner cell mass) forms the epiblast and hypoblast layers. This early stage of embryo development is referred to as the bilaminar embryo.

The inner cell mass forms an inner layer of larger cells is also called the "embryoblast" is a cluster of cells located and attached on one wall of the outer trophoblast layer. In week 2 this mass will differentiate into two distinct layers the epiblast and hypoblast, also called the bilaminar embryo.

## **Epiblast**

The epiblast layer will form the entire embryo and undergoes gastrulation in week three to form the 3 germ layers. It also forms an epithelial layer lining the amniotic cavity.

## **Hypoblast**

The hypoblast (or primitive endoderm) is a transient epithelial layer facing towards the blastocoel, it is replaced in week three by the gastrulation migrating endoderm cells.

## **Syncytiotrophoblasts**

secrete proteolytic enzymes, enzymes break down extracellular matrix around cells

Allow passage of blastocyst into endometrial wall, totally surround the blastocyst

generate spaces that fill with maternal blood- lacunae

secrete Human Chorionic Gonadotropin (hCG), hormone, maintains decidua and corpus luteum. This hormone is diagnostically the basis of pregnancy tests, and is present in maternal.

Later in development placenta will secrete hCG

## Human Chorionic Gonadotropin

(hCG) Placental hormone initially secreted by cells (syncytiotrophoblasts) from the implanting conceptus during week two, supporting the ovarian corpus luteum, which in turn supports the endometrial lining and therefore maintains pregnancy.[1] Hormone can be detected in maternal blood and urine and is the basis of many pregnancy tests. Hormone also stimulates the onset of fetal gonadal steroidogenesis, high levels are teratogenic to fetal gonadal tissues. Other potential cellular sources can include: hyperglycosylated hCG produced by cytotrophoblast cells, free beta-subunit made by multiple primary non-trophoblastic malignancies, and pituitary hCG made by the gonadotrope cells of the anterior pituitary.

The molecular weight of hCG is approximately 36,000 (36 KDa) for the  $\alpha$ -subunit and a  $\beta$ -subunit that are held together by both non-covalent hydrophobic and ionic interactions.

### Human Levels

levels peak at 8 to 10 weeks of pregnancy, then decline and are lower for rest of pregnancy

- 0-1 week: 0-50 mIU/ml
- 1-2 weeks: 40-300 mIU/ml
- 3-4 weeks: 500-6,000 mIU/ml
- 1-2 months: 5,000-200,000 mIU/ml
- 2-3 months: 10,000-100,000 mIU/ml
- 2nd trimester: 3,000-50,000 mIU/ml
- 3rd trimester: 1,000-50,000 mIU/ml
- Non-pregnant females: <5.0 mIU/ml Postmenopausal females: <9.5 mIU/ml

## Functions

1. Promotion of corpus luteal progesterone production

2. Angiogenesis of uterine vasculature
3. Cytotrophoblast differentiation
4. Immuno-suppression and blockage of phagocytosis of invading trophoblast cells
5. Growth of uterus in line with fetal growth
6. Quiescence of uterine muscle contraction
7. Promotion of growth and differentiation of fetal organs
8. Umbilical cord growth and development
9. Blastocysts signals endometrium prior to implantation
10. hCG in sperm and receptors found in fallopian tubes suggesting pre-pregnancy communication
11. hCG receptors in adult brain hippocampus, hypothalamus and brain stem, may cause pregnancy nausea and vomiting
12. hCG and implantation of pregnancy, hCG stimulates metalloproteinases of cytotrophoblast cell

Week 2 Abnormalities

## **Abnormal Implantation**

### **Ectopic tubal pregnancy**

Abnormal implantation sites or Ectopic Pregnancy occurs if implantation is in uterine tube or outside the uterus.

sites - external surface of uterus, ovary, bowel, gastrointestinal tract, mesentry, peritoneal wall

If not spontaneous then, embryo has to be removed surgically

Tubal pregnancy - 94% of ectopic pregnancies

if uterine epithelium is damaged (scarring, pelvic inflammatory disease)

if zona pellucida is lost too early, allows premature tubal implantation

embryo may develop through early stages, can erode through the uterine horn and reattach within the peritoneal cavity

**Hydatidiform Mole:** Another type of abnormality is when only the conceptus trophoblast layers proliferates and not the embryoblast, no embryo develops, this is called a "hydatidiform mole", which is due to the continuing presence of the trophoblastic layer, this abnormal conceptus can also implant in the uterus. The trophoblast cells will secrete human chorionic gonadotropin (hCG), as in a normal pregnancy, and may appear maternally and by pregnancy test to be "normal". Prenatal diagnosis by ultrasound analysis demonstrates the absence of a embryo.

There are several forms of hydatidiform mole: partial mole, complete mole and persistent gestational trophoblastic tumor. Many of these tumours arise from a haploid sperm fertilizing an egg without a female pronucleus (the alternative form, an embryo without sperm contribution, is called parthenogenesis). The tumour has a "grape-like" placental appearance without enclosed embryo formation. Following a first molar pregnancy, there is approximately a 1% risk of a second molar pregnancy

## **Mole Types**

Complete mole - chromosomal genetic material from the ovum (egg) is lost, by an unknown process. Fertilization then occurs with one or two sperm and an androgenic (from the male only) conceptus (fertilized egg) is formed. With this conceptus the embryo (fetus, baby) does not develop at all but the placenta does grow but it is abnormal and forms lots of cysts and has no blood vessels. These cysts look like a cluster of grapes and that is why it is called a hydatidiform mole (grape like). A hydatidiform mole miscarries by about 16 to 18 weeks gestational age. Since the diagnosis can be made by ultrasound before that time, it is better for you to have an evacuation of the uterus (D & C) so that there is no undue bleeding and no infection. Human chorionic gonadotropin (hCG) will assist in making the diagnosis.

Partial mole - three sets of chromosomes instead of the usual two and this is called triploidy. With such a pregnancy the chromosomal (genetic) material from the ovum (egg) is retained and the egg is fertilized by one or two sperm. Since with partial mole there are maternal chromosomes there is a fetus but because of the three sets of chromosomes this fetus is always grossly abnormal and will not survive. (Text modified from: International Society for the Study of Trophoblastic Diseases, see also JRM Gestational Trophoblastic Disease)

## **Tumour Growth**

Like any tumour, unless removed there is a risk of progression:

Stage I: Tumor confined to uterus (non-metastatic)

Stage II: Tumor involving pelvic organs and/or vagina

Stage III: Tumor involving lungs, with or without involving pelvic structures and/or vagina

Stage IV: Tumor involving distant organs

#### Placental Mesenchymal Dysplasia

Due to a similar "grape-like" placental appearance, this rare disorder has been mistaken both clinically and macroscopically for a partial hydatidiform molar pregnancy. This disorder also has a high incidence of intrauterine growth restriction (IUGR) and fetal death.

### **Twin Pregnancy Mole**

Hydatidiform mole and co-existent healthy fetus is a very rare condition with only 30 cases documented in detail in the literature.

### **Uterus Abnormalities**

Endometriosis endometrial tissue located in other regions of the uterus or other tissues. This misplaced tissue develops into growths or lesions which respond to the menstrual cycle hormonal changes in the same way that the tissue of the uterine lining does; each month the tissue builds up, breaks down, and sheds.

### **Monoygotic Twinning**

Monozygotic twins (identical) produced from a single fertilization event (one fertilised egg and a single spermatozoa, form a single zygote), these twins therefore share the same genetic makeup. Occurs in approximately 3-5 per 1000 pregnancies, more commonly with aged mothers. The later the twinning event, the less common are initially separate placental membranes and finally resulting in conjoined twins.