Second Week of Development: Bilaminar Germ Disc

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Although the rate of development usually variable, the following major events could be approximately described:
1. The second week of development is known as the week of twos.

Formation of what structures supports this statement?
2. During implantation, the trophoblast is invading maternal tissues, and because it contains approximately 50% paternal genes, it is a foreign body. Why is the conceptus not rejected by an immunologic response from the mother's system?
Question 3

3. A woman who believes she is pregnant complains of edema and vaginal bleeding.

Examination reveals high plasma human chorionic gonadotropin concentrations and placental tissue, but no evidence of an embryo.

How would you explain this condition?
4. A young woman who has missed two menstrual periods complains of intense abdominal pain.

What might an initial diagnosis be, and how would you confirm it?
The blastocyste is partially embedded in the uterine mucosa. In the area over the embryoblast.
**DAY 8**

The *trophoblast* at the embryoblast form two layers:

a. Inner mononucleated cytotrophoblastic cells that divide by mitosis forming layer b.

b. Outer multinucleated syncytiotrophoblastic zone of fused cell losing their membrane, also called the syncytium.
The inner cell mass cells (the *embryoblast*) forms the two layers of the bilaminar germ disc;

a. small cubiodal *hypoblastic* cells near the blastocele.

b. high columnar *epiblastic* cells. The amniotic cavity develops between these cells.
Amniotic cavity is lined by the epiblast proper cells,

The endometrial mucosa is edematous, highly vascular, and secrete glycogen and mucus from its large glands. Epiblast cells adjacent to the cytotrophoblast are called amnioblasts; together with the rest of the epiblast, they line the amniotic cavity.
The endometrial stroma adjacent to the implantation site is edematous and highly vascular. The large, tortuous glands secrete abundant glycogen and mucus.
Summary

- human blastocyst, partially embedded in the endometrial stroma.
- The trophoblast consists of an inner layer with mononuclear cells, the cytotrophoblast, and an outer layer without distinct cell boundaries, the syncytiotrophoblast.
- The embryoblast is formed by the epiblast and hypoblast layers.
- The amniotic cavity appears as a small cleft.
The *blastocyst* embedded more, the small defect closed by fibrin coagulum.
Summary
A 9-day human blastocyst.

- The syncytiotrophoblast shows a large number of lacunae.
- Flat cells form the exocoelomic membrane.
- The bilaminar disc consists of a layer of columnar epiblast cells and a layer of cuboidal hypoblast cells.
- The original surface defect is closed by a fibrin coagulum.
Vacules in syncytiun, fusion form lacunae thus (lacunar stage) of development.
Flat cells originate from the hypoblast forming the exocoelomic Heuser's membrane forming the exocoelomic cavity or called the primitive yolk sac.
DAY 11 & 12

1. The blastocyst is completely embedded.
2. Defect is almost covered by the mucosal cells.
2-The blastocyst now produces a slight protrusion into the lumen of the uterus
The trophoblast is characterized by lacunar spaces in the syncytium that form an intercommunicating network.

This network is particularly evident at the embryonic pole; at the abembryonic pole, the trophoblast still consists mainly of cytотrophoblastic cells.
Human blastocyst of approximately 12 days.

The trophoblastic lacunae at the embryonic pole are in open connection with maternal sinusoids in the endometrial stroma.

Extraembryonic mesoderm proliferates and fills the space between the exocoelomic membrane and the inner aspect of the trophoblast.
3-The intercommunicating network of lacunae at the embryonic pole penetrate the maternal sinusoidal capillaries and the maternal blood begin to flow in the trophoblast lacunae establishing the uteroplacental circulation.
In the meantime, a new population of cells appears between the inner surface of the cytотrophoblast and the outer surface of the exocoelomic.
4-New cells originate from the yolk sac cells forming the extraembryonic mesodermal connective
DAY 11 & 12

- Except connecting stalk region, cavitations of this mesoderm will form the chorionic cavity or called the extraembryonic coelom.
The chorionic cavity divides the extraembryonic mesoderm into two parts;
DAY 11 & 12

a. Somatopleuric mesoderm (or called the chorionic plate) lining the cytotrophoblast and the amnion.

b. Splanchnopleuric mesoderm covering the primitive yolk sac.
**DAY 11 & 12**

Decidual reaction occur in the endometrial cells of the uterine mucosa, the mucosal cells become polyhedral, loaded with glycogen and lipid.
The mucosal defect heals.

Sometimes bleeding occurs from the increased lacunar blood flow, this bleeding may be confused with the normal menstrual bleeding as it occurs near the 28th day of the cycle. This bleeding called false menstruation.
DAY 13

1-Primary villi formation
The hypoblast will form a new cellular layer lining the inside of the exocoelomic membrane. The new cavity formed by these new cells called the secondary or definitive yolk sac.
The exocoelomic membrane lining the exocoelomic cavity is largely pinched off forming the exocoelomic cysts that are often seen floating in the chorionic cavity.
DAY 14

- The epiblast forms the floor of the amniotic cavity, and the hypoblast forms the roof of the definitive yolk sac.

- The buccopharyngeal membrane appears as a thickening in the cephalic region of the hypoblast that is firmly attached to the epiblast.
15 Days

- Trophoblast: Cytotrophoblast & Syncytiotrophoblast
- Extraembryonic Mesoderm: Visceral (splanchnic) & Parietal (somatic) Layers
- Embryonic Disc: Epiblast & Hypoblast
- Cavities: Amniotic cavity & Yolk sac

2nd Week = Week of Two’s
CLINICAL CORRELATES

Syncytium...... hCG ....the end of 2\textsuperscript{nd} week......
detected by RIA (basis for PT)

(The syncytiotrophoblast is responsible for
to hormone production (see Chapter6), including
human chorionic gonadotropin (hCG). By
the end of the second week, quantities of this
hormone are sufficient to be detected by
radioimmunoassays,(RIA) which serve as the
basis for pregnancy testing.
CLINICAL CORRELATES

- in blood: 6-12 days after ovulation.
- Urine PT done 1 week after missed period.
Because 50% of the implanting embryo’s genome is derived from the father, it is a foreign body that potentially should be rejected by the maternal system.

Recent evidence suggests that a combination of factors protects the conceptus, including production of immunosuppressive cytokines and proteins and the expression of an unusual major histocompatibility complex class IB molecule (HLA-G) that blocks recognition of the conceptus as foreign tissue.

If the mother has autoimmune disease, for example systemic lupus erythematosus, antibodies generated by the disease may attack the conceptus and reject it.
What makes the conceptus not to be rejected by the mother immune system?

- Placental trophoblast does not express the polymorphic class I and class II MHC genes and instead expresses HLA-G, a non-polymorphic gene. Therefore, antibodies against the fetal proteins are not developed.

- The production of immunosuppressive cytokines and proteins.

- There is a Fas ligand on the surface of the placenta, and this bonds to T cells, causing them to undergo Apoptosis.
ABNORMAL IMPLANTATION

Primary ov preg
mostly
Placenta previa

Modified from: Before we are born, Moore and Persaud, 1998
ABNORMAL IMPLANTATION

Normally …. Ant. Or post. Wall of the uterus

Implants close to the int os …. Placenta previa (antepartum hemorrhage in form of painless vaginal bleeding in the third trimester, 10% diagnosed incidentally by ultrasonography or at term.)

ABRUPTIO PLACENTAE, (premature separation of the normally implanted placenta, may result in fetal death) Clinically: painful vaginal bleeding in association with uterine tenderness, hyperactivity, and increased tone

ECTOPIC PREG (EXTRAUTERINE PREG):
- 95% …. Uterine tube… and mostly in the ampula
Abnormal implantation sites of the blastocyst.

1. implantation in the abdominal cavity. The ovum most frequently implants in the rectouterine cavity (Douglas’ pouch) but may implant at any place covered by peritoneum.

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, frequently resulting in placenta previa.

6. ovarian implantation.
Placenta previa
ABNORMAL IMPLANTATION

Tubal Pregnancy
ABNORMAL IMPLANTATION

Ectopic Pregnancy

UNSW Embryology
ABNORMAL IMPLANTATION

Ectopic Pregnancy

Heart
ABNORMAL IMPLANTATION

Ectopic Pregnancy

Limb Buds
ABNORMAL IMPLANTATION

Ectopic Pregnancy
ABNORMAL IMPLANTATION

In the abd cavity the blastocyst most frequently attach to the peritoneal lining of douglas pouch. And st to the peritoneum covering the intestine or to the omentum.
ABNORMAL IMPLANTATION

- In most ectopic preg the embryo dies in the second month of gestation... causing sever hrg and abd pain
- Most abnormal blastocyst would not have any signs of preg bec of inferior trophoblast... no hCG ... corp luteum not persist
- In some cases the trophoblast developed and form placental memb with little or no embryonic tissues ... haydatidiform mole
High hCG...invasive mole or choriocarcinoma
ABNORMAL IMPLANTATION

- Uterine cavity
- Uterine wall
- Hydatidiform mole
- Uterine wall
Genetic analysis of hydatidiform moles indicates ...male and female pronuclei may be genetically equivalent, they differ functionally.

cells of moles are diploid, their entire genome is paternal.

These suggest that paternal genes regulate most of the development of the trophoblast,

This tissue differentiates even in the absence of a female pronucleus.
ABNORMAL IMPLANTATION

Other examples of functional differences ….. certain genetic diseases depend on whether the defective or missing gene is inherited from the father or the mother.

Example, inheritance of a deletion on chromosome 15 from a father produces Prader-Willi syndrome, If from the mother results in Angelman syndrome.
ABNORMAL IMPLANTATION

pws
Angelman Syndrome is a rare neurological disorder characterized by severe congenital mental retardation, unusual facial appearance, and muscular abnormalities.
Ovulated oocyte

- 85% fertilized
- 15% Not fertilized

  - 70-75% Implanted
  - 10-15% Not implanted

    - 58% Survive to 2\textsuperscript{nd} week
      - 42% Survive & normal
      - 16% abnormal

    - 12% not reach 2\textsuperscript{nd} week (die)
    - 42% Survive & normal

Normal
Abnormal at birth
Aborted
A 23-year-old woman consulted her physician about severe right lower abdominal pain. She said that she had missed two menstrual periods. A diagnosis of ectopic pregnancy was made.

A. What techniques might be used to enable this diagnosis?

B. What is the most likely site of the extrauterine gestation (pregnancy)?

C. How do you think the physician would likely treat the condition?
THE END

THANK YOU