Implantation and Placenta

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During the ovary lecture, we left the oocyte right after ovulation and focused on the events that set up the uterine endometrium for implantation.

In the meantime, the oocyte + cumulus + corona radiata has been picked up by the fimbriated end of the oviduct.

It is transported to the ampulla where it will be fertilized.
Freshly Ovulated oocyte

This oocyte is seen in the center of a mass of cumulus cells.

Secondary oocyte is arrested in metaphase of meiosis II.
Fertilization and transport

- Fertilization occurs in ampulla of oviduct
- The oocyte completes meiosis and the pronucleus joins with the sperm pronucleus, restoring the diploid state.
- The zygote is then transported to the uterine lumen.
- The embryo develops to the morula and blastocyst stages and implants as a blastocyst.
Implantation

- Trophoblast cells begin to invade uterine endometrium. Digs deeper and eventually is enclosed in the endometrium.
- Uterine endometrium is in secretory stage, build up of glands and stroma that contain glycogen and other nutrients for embryo.
- Trophoblast over the inner cell mass differentiates into cytotrophoblast and syncytiotrophoblast.
  - Cytotrophoblast layer divides and adds cells to the syncytium in the syncytiotrophoblast layer
Lacunar spaces

- Syncytiotrophoblast by days 12-13 develop lacunae, spaces.
- As they invade, they break down maternal vessels (sinusoids) and the maternal blood spills in these spaces.
- Invasion continues and this becomes the initial route for the maternal blood support.
Primary villi
(end of second week)

- Projections of syncytiotrophoblast.
- Also include columns of cytotrophoblast.
- Don’t have any extraembryonic mesenchyme yet.
Third week

- Mesenchyme grows into primary villus and this forms a secondary villus.
- Mesenchyme will serve as a substrate and support for outgrowth of blood vessels.
- Once blood vessels have grown out, the villus is a tertiary villus.
Placental Blood supply

- Tertiary villi
- Anchoring villus
- Stem villus
- Free villus
Young placenta: Tertiary villus
Tertiary, free villi
Young placenta
Older placenta

- Cytotrophoblast is gone leaving only the syncytiotrophoblast
- Need for closer connection between vessels (maternal and fetal)
Older placenta
Anchoring villi
The placenta as an endocrine organ

- The syncytiotrophoblast produces human chorionic gonadotropin (identical to LH) which rescues and maintains the corpus luteum for about 60 days.
- As it develops, it also produces other types of hormones: thyrotropin, somatomammotropin, estrogens and progesterone.
- Eventually maintains uterine lining.
- Syncytiotrophoblast requires androgens to make estrogens: Gets them from fetal adrenal.
How does the uterus respond?

- As the blastocyst penetrates the endometrium, it repairs the penetration defect with a fibrin coagulum.
- Endometrial stroma become edematous and vascular.
- Glands secrete glycogen and mucus.
Response of Uterus

Stroma becomes a "decidua"; Cells enlarge and become foamy.
What stroma looked like before implantation

Secretory stage: Stromacells small; Spaces with edema
Response of uterus

Syncytiotrophoblast invading uterine endometrium.

Decidual cell
Regional specialization of uterus

Decidua basalis

Decidua capsularis

Decidua parietalis
Theory about what prevents an immune reaction against the placenta

- Father’s genes produce antigens, yet placenta is immunoprotected. The placenta does not express class II histocompatibility antigens.
- The class I histocompatibility antigens that it does express (HLA-E and HLA-G) are only weakly immunogenic.
- The cells of the placenta secrete progesterone, which is immunosuppressive.
More theories: Placenta foils the T cells

- In rats, the embryos (and the mother's endometrium) secrete corticotropin-releasing hormone (CRH).
  - Induces the expression of Fas ligand (FasL) on the cells of the placenta.
  - Activated T cells express Fas so any threatening T cells would commit suicide by apoptosis when they encounter FasL.

- In mice, the cells of the placenta degrade the amino acid tryptophan. Tryptophan is essential for T-cell function. (D. H. Munn, et. al., Science, 281: 1191, 21 Aug 1998.)
What about the placenta in twin pregnancies?

Example from dizygotic twins
Monozygotic twins
Blastomere Separation → Incomplete ICM Splitting → ICM Splits → Conjoined Twins

Modes of Monozygotic Twinning
IVF Retrieval

Graafian follicles after stimulation; retrieved about 12 eggs from both ovaries.

Oocyte retrieval (see needle)
Development after in vitro fertilization

Pronuclei of fertilized ovum

Polar body

Pronuclei of fertilized ovum
8 cell embryo and assisted hatching and co-culture
Human blastocysts
Embryo transfer: yellow dots indicate transfer Tube. Green=uterine lumen; blue=uterus

For women who are 35-39, they recommend transfer of 4-5 embryos (So, Couple can freeze the rest). With a 55% success rate, they are likely to have twins.
Cervix

- Connects uterus with vagina; projects into vagina
- Epithelium simple columnar + branched glands
- Epithelium becomes stratified squamous
- Produces serous and mucous secretions
  - Friendly to sperm at midcycle (watery, nutritive)
  - Unfriendly to sperm at other times in cycle (thick, viscous)
  - Thicker mucus protects against bacterial infections
  - Mucus plug formed during pregnancy
- Quality of mucus may be a factor in infertility
Cervix

Cervical epithelium

Cervical glands
Cervical Dysplasia
Cervical carcinoma: PAP smear
Vagina

- Wall: mucosa, muscularis, adventitia
- Muscular layer is smooth, except for sphincter at opening (skeletal)
- Mucosa: stratified squamous epithelium (non-keratinizing).
  - No muscularis mucosa
  - No glands in lamina propria; well vascularized
  - Numerous leukocytes
- Mucosa cells are light staining because of the presence of glycogen
  - converted to lactic acid
  - acidifies vagina to pH 3
  - protects against bacterial infections
- Lubrication: cervical glands; fluid exudate from lamina propria, glands in vestibule (external genitalia).
Vaginal epithelium: non-keratinizing; light staining
External genitalia

- **Labia majora and minora**: folds of skin with adipose tissue inside. Inside folds is the "vestibule"
- **Glands to lubricate area**
  - Bartholin
  - Vestibular glands
- **Clitoris**: between folds of the labia minora (anteriorly); projects just under pubic bone
  - Erectile tissue
  - Pacinian and Meissner’s corpuscles: Sensitive to touch, pressure during sexual arousal
  - Can be enlarged with abnormal androgen stimulation ("ambiguous genitalia"). Sex of baby may be difficult to determine