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QUESTION: Discuss the second week of development.

SECOND WEEK OF DEVELOPMENT

Week 2 is about the implantation process and blastocyst differentiation. 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 implantation. in the second week, 3 events take place; completion of implantation of the blastocyst, formation of bilaminar embryonic disc and formation of extraembryonic structures.

DAY 8

At the eighth day of development, the blastocyst is partially embedded in the endometrial stroma. In the area over the embryoblast, the trophoblast has differentiated into two layers:

(a) an inner layer of mononucleated cells, the cytotrophoblast

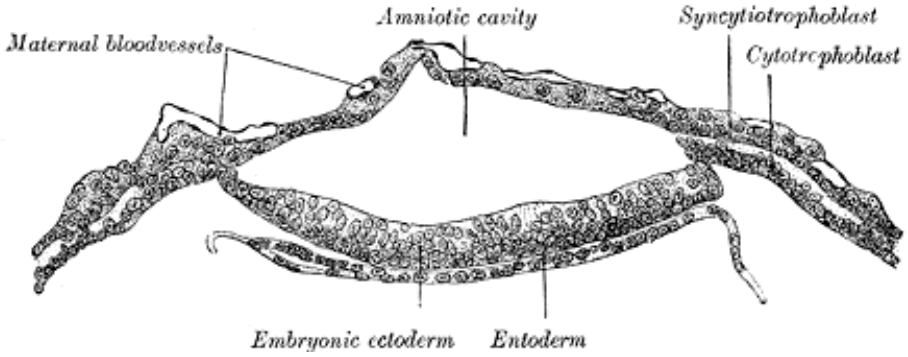
(b) an outer multinucleated zone without distinct cell boundaries, the syncytiotrophoblast.

Mitotic figures are found in the cytotrophoblast but not in the syncytiotrophoblast. Thus, cells in the cytotrophoblast divide and migrate into the syncytiotrophoblast, where they fuse and lose their individual cell membranes. Cells of the inner cell mass or embryoblast also differentiate into two layers:

(a) a layer of small cuboidal cells adjacent to the blastocyst cavity, known as the hypoblast layer.

(b) a layer of high columnar cells adjacent to the amniotic cavity, the epiblast layer .

Together, the layers form a flat disc. At the same time, a small cavity appears within the epiblast. This cavity enlarges to become the amniotic cavity. 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.



DAY 9

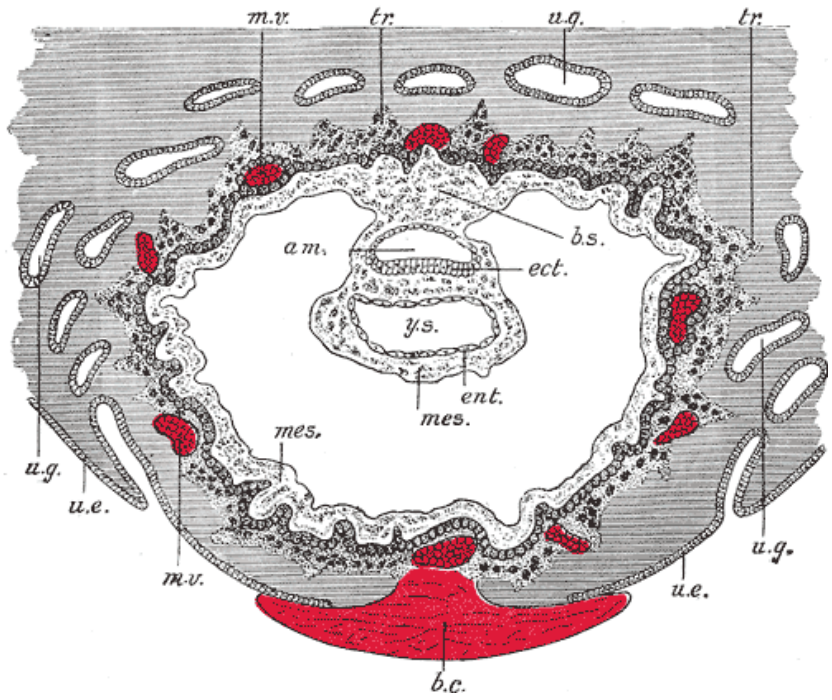
This process, called implantation, is completed by day 9 or 10. The wall of the blastocyst is one cell thick except in one area, where it is three to four cells thick. The inner cells in the thickened area develop into the embryo, and the outer cells burrow into the wall of the uterus and develop into the placenta.The blastocyst is more deeply embedded in the endometrium, and the penetration defect in the surface epithelium is closed by a fibrin coagulum. The trophoblast shows considerable progress in development, particularly at the embryonic pole, where vacuoles appear in the syncytium. When these vacuoles fuse, they form large lacunae, and this phase of trophoblast development is thus known as the lacunar stage. At the abembryonic pole, meanwhile, flattened cells probably originating from the hypoblast form a thin membrane, the exocoelomic (Heuser's) membrane, that lines the inner surface of the cytotrophoblast. This membrane, together with the hypoblast, forms the lining of the exocoelomic cavity, or primitive yolk sac.

Days 11 and 12

By the 11th to 12th day of development, the blastocyst is completely embedded in the endometrial stroma, and the surface epithelium almost entirely covers the original defect in the uterine wall . 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, cthe trophoblast still consists mainly of cytotrophoblastic cells. Concurrently, cells of the syncytiotrophoblast penetrate deeper into the stroma and erode the endothelial lining of the maternal capillaries.

These capillaries, which are congested and dilated, are known as sinusoids. The syncytial lacunae become continuous with the sinusoids and maternal blood enters the lacunar system. As the trophoblast continues to erode more and more sinusoids, maternal blood begins to flow through the trophoblastic system, establishing the uteroplacental circulation. In the meantime, a new population of cells appears between the inner surface of the cytotrophoblast and the outer surface of the exocoelomic 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. the original defect in the uterine wall. The blastocyst now produces a slight protrusion into the lumen of the uterus.

cavity. These cells, derived from yolk sac cells, form a fine, loose connective tissue, the extraembryonic mesoderm, which eventually fills all of the space between the trophoblast externally and the amnion and exocoelomic membrane internally. Soon, large cavities develop in the extraembryonic mesoderm, and when these become confluent, they form a new space known as the extraembryonic coelom, or chorionic cavity. This space surrounds the primitive yolk sac and amniotic cavity except where the germ disc is connected to the trophoblast by the connecting stalk. The extraembryonic mesoderm lining the cytotrophoblast and amnion is called the extraembryonic somatopleuric mesoderm; the lining covering the yolk sac is known as the extraembryonic splanchnopleuric mesoderm. Growth of the bilaminar disc is relatively slow compared with that of the trophoblast; consequently, the disc remains very small. Cells of the endometrium, meanwhile, become polyhedral and loaded with glycogen and lipids; intercellular spaces are filled with extravasate, and the tissue is edematous. These changes, known as the decidua reaction, at first are confined to the area immediately surrounding the implantation site but soon occur throughout the endometrium. Trophoblastic lacunae are present at the embryonic as well as the abembryonic pole, and the uteroplacental circulation has begun. Note the primary villi and the extraembryonic coelom or chorionic cavity. The secondary yolk sac is entirely lined with endoderm.



DAY 13

By the 13th day of development, the surface defect in the endometrium has usually healed. Occasionally, however, bleeding occurs at the implantation site as a result of increased blood flow into the lacunar spaces. Because this bleeding occurs near the 28th day of the menstrual cycle, it may be confused with normal menstrual bleeding and, therefore, cause inaccuracy in determining the expected delivery date. Note the amniotic cavity, yolk sac, and exocoelomic cyst in the chorionic cavity. Most of the lacunae are filled with blood.The trophoblast is characterized by villous structures. Cells of the cytotrophoblast proliferate locally and penetrate into the syncytiotrophoblast, forming cellular columns surrounded by syncytium. Cellular columns with the syncytial covering are known as primary villi. In the meantime, the hypoblast produces additional cells that migrate along the inside of the exocoelomic membrane. These cells proliferate and gradually form a new cavity within the exocoelomic cavity. This new cavity is known as the secondary yolk sac or definitive yolk sac. This yolk sac is much smaller than the original exocoelomic cavity, or primitive yolk sac. During its formation, large portions of the exocoelomic cavity are pinched off.

These portions are represented by exocoelomic cysts, which are often found in the extraembryonic coelom or chorionic cavity. Meanwhile, the extraembryonic coelom expands and forms a large cavity, the chorionic cavity. The extraembryonic mesoderm lining the inside of the cytotrophoblast is then known as the chorionic plate. The only place where extraembryonic mesoderm traverses the chorionic cavity is in the connecting stalk. With development of blood vessels, the stalk becomes the umbilical cord.

CLINICAL CORRELATES

Abnormal Implantation

The syncytiotrophoblast is responsible for hormone production (see Chapter 6), including human chorionic gonadotropin (hCG). By the end of the second week, quantities of this hormone are sufficient to be detected by radioimmunoassays, which serve as the basis for pregnancy testing. 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. Abnormal implantation sites sometimes occur even within the uterus.

EXTRAUTERINE IMPLANTATION

Ectopic pregnancies are caused by blastocysts implanting outside the uterus. **Ectopic pregnancy** is a complication of pregnancy in which the embryo attaches outside the uterus. Signs and symptoms classically include abdominal pain and vaginal bleeding. Fewer than 50 percent of affected women have both of these symptoms. The pain may be described as sharp, dull, or crampy. Pain may also spread to the shoulder if bleeding into the abdomen has occurred. Severe bleeding may result in a fast heart rate, fainting, or shock. With very rare exceptions the fetus is unable to survive.