THE SECOND WEEK OF HUMAN DEVELOPMENT

Formation of the Amniotic Cavity and Embryonic Disc 31
Development of the Chorionic Sac 33
Implantation Sites of the Blastocyst 33
Clinically Oriented Questions 35
Implantation of the blastocyst is completed during the second week of embryonic development. As this crucial process occurs, changes occur in the embryoblast, producing a bilaminar embryonic disc composed of two layers, the epiblast and the hypoblast (Fig. 4-1). The embryonic disc gives rise to the germ layers that form all the tissues and organs of the embryo. Extraembryonic structures forming during the second week include the amniotic cavity, amnion, umbilical vesicle (yolk sac), connecting stalk, and chorionic sac.

Implantation of the blastocyst begins at the end of the first week. The actively erosive syncytiotrophoblast invades the endometrial connective tissue that supports the uterine capillaries and glands. As this occurs, the blastocyst slowly embeds itself in the endometrium. Syncytiotrophoblastic cells from this region displace endometrial cells in the central part of the implantation site. The endometrial cells undergo apoptosis (programmed cell death), which facilitates implantation. Proteolytic enzymes produced by the syncytiotrophoblast are involved in this process. The uterine connective tissue cells around the implantation site become loaded with glycogen and lipids and assume a polyhedral appearance. Some of these cells—decidual cells—degenerate adjacent to the penetrating syncytiotrophoblast. The syncytiotrophoblast engulfs these degenerating cells, providing a rich source of embryonic nutrition. As the blastocyst implants, more trophoblast contacts the endometrium and continues to differentiate into two layers (see Fig. 4-1A and B):

- The cytotrophoblast, a layer of mononucleated cells that is mitotically active and forms new trophoblastic cells that migrate into the increasing mass of syncytiotrophoblast, where they fuse and lose their cell membranes.
- The syncytiotrophoblast, a rapidly expanding, multinucleated mass in which no cell boundaries are discernible.

The syncytiotrophoblast produces a hormone, human chorionic gonadotropin (hCG), which enters the maternal blood in the lacunae in the syncytiotrophoblast (see Fig. 4-1C); hCG maintains the endocrine activity of the corpus luteum in the ovary during pregnancy and forms the basis for pregnancy tests. Highly sensitive radioimmunoassays are available for detecting hCG. Enough hCG is produced by the syncytiotrophoblast at the end of the second week to yield a positive pregnancy test, even though the woman is probably unaware that she is pregnant.

**FORMATION OF THE AMNIOTIC CAVITY AND EMBRYONIC DISC**

As implantation of the blastocyst progresses, changes occurring in the embryoblast result in the formation of a flattened, almost circular, bilaminar plate of cells—the embryonic disc—consisting of two layers (Figs. 4-1A and 4-2B):

- The epiblast, the thicker layer, consists of high, columnar cells related to the amniotic cavity.
- The hypoblast, the thinner layer, consists of small, cuboidal cells adjacent to the exocoelomic cavity.

Concurrently, a small cavity appears in the embryoblast, which is the primordium of the amniotic cavity (see Fig. 4-1A). Soon, amniogenic (amnion-forming) cells called amnioblasts separate from the epiblast and organize to form a thin membrane, the amnion, which encloses the amniotic cavity (see Fig. 4-1A).

The epiblast forms the floor of the amniotic cavity and is continuous peripherally with the amnion. The hypoblast...
forms the roof of the **exocoelomic cavity** and is continuous with the cells that migrated from the hypoblast to form the **exocoelomic membrane**. This membrane surrounds the blastocystic cavity and lines the internal surface of the cytotrophoblast. The exocoelomic membrane and cavity soon become modified to form the **primary umbilical vesicle**. The embryonic disc then lies between the amniotic cavity, the **primary umbilical vesicle** (yolk sac), and maternal blood flows into the lacunar networks. The degenerated endometrial stromal cells and glands, together with the maternal blood, provide a rich source of material for **embryonic nutrition**. Growth of the bilaminar embryonic disc is slow compared with the growth of the trophoblast.

As changes occur in the trophoblast and endometrium, the extraembryonic mesoderm increases and isolated extraembryonic coelomic spaces appear within it (see Fig. 4-2B). These spaces rapidly fuse to form a large, isolated cavity, the **extraembryonic coelom** (Fig. 4-3A). This fluid-filled cavity surrounds the amnion and the umbilical vesicle, except where they are attached to the chorion by the **connecting stalk**. As the extraembryonic coelom forms, the primary umbilical vesicle decreases in size and a smaller, **secondary umbilical vesicle** forms (see Fig. 4-3B). During formation of the secondary umbilical vesicle, a large part of the primary umbilical vesicle is pinched off. The human umbilical vesicle (yolk sac) contains no yolk. It may have a role in the selective transfer of nutritive materials to the embryonic disc. The trophoblast absorbs nutritive fluid from the lacunar networks in the syncytiotrophoblast; the fluid is then transferred to the embryo.
The end of the second week is characterized by the appearance of primary chorionic villi (Figs. 4-3A and 4-4A and C). Proliferation of the cytotrophoblastic cells produces cellular extensions that grow into the overlying syncytiotrophoblast. The growth of these cytotrophoblastic extensions is believed to be induced by the underlying extraembryonic somatic mesoderm. The cellular projections form primary chorionic villi, the first stage in the development of the chorionic villi of the placenta. The extraembryonic coelom splits the extraembryonic mesoderm into two layers (see Fig. 4-3A and B):

- The extraembryonic somatic mesoderm, which lines the trophoblast and covers the amnion
- The extraembryonic splanchnic mesoderm, which surrounds the umbilical vesicle

The extraembryonic somatic mesoderm and the two layers of trophoblast form the chorion. The chorion forms the wall of the chorionic sac (see Fig. 4-3A). The embryo and its amniotic sac and umbilical vesicle are suspended by the connecting stalk (see Figs. 4-3B and 4-4B). The amniotic sac and the umbilical vesicle are analogous to two balloons pressed together (at the site of the embryonic disc) and suspended by a cord (the connecting stalk) from the inside of a larger balloon (the chorionic sac). Transvaginal ultrasonography (endovaginal sonography) is used to measure the diameter of the chorionic (gestational) sac. This measurement is valuable for evaluating early embryonic development and pregnancy outcome.

The 14-day embryo still has the form of a flat, bilaminar, embryonic disc, but endodermal cells in a localized area are now columnar and form a thickened circular area called the prechordal plate (see Fig. 4-3B and C). This plate indicates the future site of the mouth and is an important organizer of the head region.

Implantation of a blastocyst begins at the end of the first embryonic week and normally occurs in the endometrium of the uterus, usually superiorly in the body of the uterus and slightly more often on the posterior than on the anterior wall.
Blastocysts may implant outside the uterus. Exauterine implantations result in **ectopic pregnancies**; most ectopic implantations occur in the uterine tube (Figs. 2-2B and 4-5A and B). Ectopic tubal pregnancy occurs in approximately 1 in 200 pregnancies in North America. A woman with a tubal pregnancy has the usual signs and symptoms of pregnancy, but she may also experience abdominal pain and tenderness because of distention of the uterine tube, abnormal bleeding, and irritation of the pelvic peritoneum. There are **several causes of tubal pregnancy**; however, they are often related to factors that delay or prevent transport of the cleaving zygote to the uterus (e.g., blockage of the uterine tube caused by scarring secondary to infection in the abdominopelvic cavity). Ectopic tubal pregnancies usually result in rupture of the uterine tube and hemorrhage into the peritoneal cavity during the first 8 weeks, followed by death of the embryo. Tubal rupture and hemorrhage constitute a threat to the mother’s life.

The administration of relatively large doses of estrogen ("morning-after pills") for several days, beginning shortly after unprotected sexual intercourse, usually does not prevent fertilization, but often prevents implantation. Normally, the endometrium progresses to the luteal (secretory) phase of the menstrual cycle as the zygote forms, undergoes cleavage, and enters the uterus. A large amount of estrogen, however, disturbs the normal balance between estrogen and progesterone that is necessary to prepare the endometrium for implantation. An **intrauterine device** inserted into the uterus through the vagina and cervix usually interferes with implantation by causing a local inflammatory reaction. Some intrauterine devices contain slow-release progesterone, which interferes with the development of the endometrium so that implantation does not usually occur.

**FIGURE 4-4.** A, Illustration of a section (outlined in B) of the wall of the chorionic sac. B, Illustration of a 14-day conceptus showing the chorionic sac and the chorionic cavity. C, Transverse section through a primary chorionic villus.
1. What is meant by the term *implantation bleeding*? Is this the same as *menses* (menstrual fluid)?
2. Can a drug taken during the first 2 weeks of pregnancy cause abortion of the embryo?
3. Can an ectopic pregnancy occur in a woman who has an intrauterine device?
4. Can a blastocyst that implants in the abdomen develop into a full-term fetus?
5. Can combined intrauterine and ectopic pregnancy occur?

The answers to these questions are at the back of the book.

**FIGURE 4-5.** A, Coronal section of the uterus and the uterine tube illustrating an ectopic pregnancy in the ampulla of the tube. B, Ectopic tubal pregnancy (6 weeks). The sonogram of the uterine tube (left) shows a small gestational sac (arrow). (B, Courtesy of E.A. Lyons, MD, Department of Radiology, Health Sciences Centre, University of Manitoba, Winnipeg, Manitoba, Canada.)