Implantation

The very early stage of pregnancy at which the embryo adheres to the wall of the uterus.

About Implantation

In humans implantation is the very early stage of pregnancy at which the conceptus adheres to the wall of the uterus (Pic.1). At this stage of prenatal development, the conceptus is called blastocyst. It is by this adhesion that the foetus receives oxygen and nutrients from the mother to be able to grow. Implantation of a fertilized ovum is most likely to occur about 9 days after ovulation, ranging between 6 and 12 days.

Implantation window

The reception-ready phase of the endometrium of the uterus is usually termed the "implantation window" and lasts about 4 days. The implantation window follows around 6 days after the peak in luteinizing hormone levels. With some disparity between sources, it has been stated to occur from 7 days after ovulation until 9 days after ovulation, or days 6-10 postovulation. On average, it occurs during the 20th to the 23rd day after the last menstrual period. The implantation window is characterized by changes to the endometrium cells, which aid in the absorption of the uterine fluid. These changes are collectively known as the plasma membrane transformation and bring the blastocyst nearer to the endometrium and immobilize it. During this stage the blastocyst can still be eliminated by being flushed out of the uterus. Scientists have hypothesized that the hormones cause a swelling that fills the flattened out uterine cavity just prior to this stage, which may also help press the blastocyst against the endometrium. The implantation window may also be initiated by other preparations in the endometrium of the uterus, both
structurally and in the composition of its secretions.

**Predecidualization**

The endometrium increases thickness, becomes vascularized and its glands grow to be tortuous and boosted in their secretions. These changes reach their maximum about 7 days after ovulation. Furthermore, the surface of the endometrium produces a kind of rounded cells, which cover the whole area toward the uterine cavity. This happens about 9 to 10 days after ovulation. These cells are called decidual cells, which emphasizes that the whole layer of them is shed off in every menstruation if no pregnancy occurs, just as leaves of deciduous trees. The uterine glands, on the other hand, decrease in activity and degenerate already 8 to 9 days after ovulation in absence of pregnancy. The decidual cells originate from the stromal cells that are always present in the endometrium. However, the decidual cells make up a new layer, the decidua. The rest of the endometrium, in addition, expresses differences between the luminal and the basal sides. The luminal cells form the zona compacta of the endometrium, in contrast to the basalolateral zona spongiosa, which consists of the rather spongy stromal cells.

**Decidualization**

Decidualization succeeds predecidualization if pregnancy occurs. This is an expansion of it, further developing the uterine glands, the zona compacta and the epithelium of decidual cells lining it. The decidual cells become filled with lipids and glycogen and take the polyhedral shape characteristic for decidual cells. It is likely that the blastocyst itself makes the main contribution to this additional growing and sustaining of the decidua. An indication of this is that decidualization occurs at a higher degree in conception cycles than in non-conception cycles. Furthermore, similar changes are observed when giving stimuli mimicking the natural invasion of the embryo.

**Parts of decidua**

The decidua can be organized into separate sections, although they have the same composition:

- Decidua basalis - this is the part of the decidua which is located basalolateral to the embryo after implantation.
- Decidua capsularis - decidua capsularis grows over the embryo on the luminal side, enclosing it into the endometrium. It surrounds the embryo together with decidua basalis.
- Decidua parietalis - all other decidua on the uterine surface belongs to decidua parietalis.

**Pinopodes**
Pinopodes are small, finger-like protrusions from the endometrium. They appear between day 19 and day 21 of gestational age. This corresponds to a fertilization age of approximately 5 to 7 days, which corresponds well with the time of implantation. They only persist for 2 to 3 days. The development of them is enhanced by progesterone but inhibited by estrogens. Pinopodes endocytose uterine fluid and macromolecules in it. By doing so, the volume of the uterus decreases, taking the walls closer to the embryoblast floating in it. Thus, the period of active pinocytes might also limit the implantation window.

**Nutrition**

The embryoblast spends approximately 72 hours in the uterine cavity before implanting. In that time, it cannot receive nourishment directly from the blood of the mother, and must rely on secreted nutrients into the uterine cavity, e.g. iron and fat-soluble vitamins. In addition to nourishment, the endometrium secretes several steroid-dependent proteins, important for growth and implantation. Cholesterol and steroids are also secreted. Implantation is further facilitated by synthesis of matrix substances, adhesion molecules and surface receptors for the matrix substances.

**Zona hatching**

Zona hatching is a phenomenon occurring during prenatal development. Prior to this event, the predecessor of the embryo, in the form of a blastocyst, is surrounded by a glycoprotein sphere called the zona pellucida. To be able to perform implantation on the uterine wall, the blastocyst first needs to get rid of the zona pellucida. This lysis of the zona pellucida is called the zona hatching.

**Adhesion and communication**

Adhesion is a much stronger attachment to the endometrium than the loose apposition. The trophoblasts adhere by penetrating the endometrium, with protrusions of trophoblast cells. There is massive communication between the blastocyst and the endometrium at this stage. The blastocyst signals to the endometrium to adapt further to its presence, e.g. by changes in the cytoskeleton of decidual cells. This, in turn, dislodges the decidual cells from their connection to the underlying basal lamina, which enables the blastocyst to perform the succeeding invasion. This communication is conveyed by:

- receptor-ligand-interactions
- both integrin-matrix
- proteoglycan ones
Another ligand-receptor system involved in adhesion is proteoglycan receptors, found on the surface of the decidua of the uterus. Their counterparts, the proteoglycans, are found around the trophoblast cells of the blastocyst. This ligand-receptor system also is present just at the implantation window.

**Invasion**

At the end of the first week, the blastocyst (Pic.2) comes in contact with the uterine wall and adheres to it, embedding itself in the uterine lining via the trophoblast cells. Thus begins the process of implantation, which signals the end of the pre-embryonic stage of development. Implantation can be accompanied by minor bleeding. The blastocyst typically implants in the fundus of the uterus or on the posterior wall. However, if the endometrium is not fully developed and ready to receive the blastocyst, the blastocyst will detach and find a better spot. A significant percentage (50–75 percent) of blastocysts fail to implant; when this occurs, the blastocyst is shed with the endometrium during menses. The high rate of implantation failure is one reason why pregnancy typically requires several ovulation cycles to achieve. When implantation succeeds and the blastocyst adheres to the endometrium, the superficial cells of the trophoblast fuse with each other, forming the syncytiotrophoblast (Pic.3), a multinucleated body that digests endometrial cells to firmly secure the blastocyst to the uterine wall. In response, the uterine mucosa rebuilds itself and envelops the blastocyst. The trophoblast secretes human chorionic gonadotropin (hCG), a hormone that directs the corpus luteum to survive, enlarge, and continue producing progesterone and estrogen to suppress menses. These functions of hCG are necessary for creating an environment suitable for the developing embryo. As a result of this increased production, hCG accumulates in the maternal bloodstream and is excreted in the urine. Implantation is complete by the middle of the second week. Just a few days after implantation, the trophoblast has secreted enough hCG for an at-home urine pregnancy test to give a positive result.

Most of the time an embryo implants within the body of the uterus in a location that can support growth and development.

**Failure**

Implantation failure is considered to be caused by inadequate uterine receptivity in two-thirds of cases, and by problems with the embryo itself in the other third. Inadequate uterine receptivity may be caused by abnormal cytokine and hormonal signaling as well as epigenetic alterations. Recurrent implantation failure is a cause of female infertility. Therefore, pregnancy rates can be improved by optimizing endometrial receptivity for implantation. Evaluation of implantation markers may help to predict pregnancy outcome and detect
occult implantation deficiency. Luteal support is the administration of medication, generally progestins, for the purpose of increasing the success rate of implantation and early embryogenesis, thereby complementing the function of the corpus luteum.

In women with more than 3 implantation failures in assisted reproduction, a review of several small randomized controlled studies estimated that the use of adjunct low molecular weight heparin (LMWH) improves live birth rate by approximately 80%.

Find more about related issues

**Diagnoses**

**Adenomyosis**
Medical condition characterized by the presence of ectopic endometrial tissue within the myometrium.
Learn more at: [www.fertilitypedia.org/therapy/diag/adenomyosis](http://www.fertilitypedia.org/therapy/diag/adenomyosis)

**Amenorrhoea**
The absence of a menstrual period in women of reproductive age.
Learn more at: [www.fertilitypedia.org/therapy/diag/amenorrhoea](http://www.fertilitypedia.org/therapy/diag/amenorrhoea)

**Anorexia Nervosa**
An eating disorder characterized by the maintenance of a body weight below average, fear of gaining weight, and a distorted body image.
Learn more at: [www.fertilitypedia.org/therapy/diag/anorexia-nervosa](http://www.fertilitypedia.org/therapy/diag/anorexia-nervosa)

**Anovulation**
Failure of the ovaries to release an oocyte over a period of time generally exceeding 3 months.
Learn more at: [www.fertilitypedia.org/therapy/diag/anovulation](http://www.fertilitypedia.org/therapy/diag/anovulation)

**Antiphospholipid syndrome**
A condition when immune system mistakenly attacks some of the standard proteins in blood.
Learn more at: [www.fertilitypedia.org/therapy/diag/antiphospholipid-syndrome-do-rf](http://www.fertilitypedia.org/therapy/diag/antiphospholipid-syndrome-do-rf)
Asherman’s syndrome
A medical condition, where the walls of the uterus stick to one another due to bands of scar tissue.
Learn more at: www.fertilitypedia.org/therapy/diag/asherman-s-syndrome

Autoimmune disorders
A condition arising from an abnormal immune response to a normal body part.
Learn more at: www.fertilitypedia.org/therapy/diag/autoimmune-disorders-1

Bicornuate uterus
Inborn morphological deviation of the uterus - one of the Müllerian duct anomalies where the uterine cavity is divided in the upper part.
Learn more at: www.fertilitypedia.org/therapy/diag/bicornuate-uterus

Endometrial hyperplasia
Thickening of the lining of the uterus.
Learn more at: www.fertilitypedia.org/therapy/diag/endometrial-hyperplasia

Endometrial polyp
The finger like overgrowths attached to the inner wall of the uterus that extend into the uterine cavity which are made of endometrial tissue
Learn more at: www.fertilitypedia.org/therapy/diag/endometrial-polyp

Endometriosis
A state in which pieces of the tissue alike to the lining of the uterus (endometrium) grow in other parts of the body.
Learn more at: www.fertilitypedia.org/therapy/diag/endometriosis

Hysterectomy
A surgery performed to remove a woman's uterus.
Learn more at: www.fertilitypedia.org/therapy/diag/hysterectomy

Lupus erythematosus
Collection of autoimmune diseases in which the human immune system becomes hyperactive and attacks normal, healthy tissues.
Learn more at: www.fertilitypedia.org/therapy/diag/lupus-erythematosus
Menopause
The time in most women's lives when menstrual periods stop permanently, and the woman is no longer able to have children.
Learn more at: www.fertilitypedia.org/therapy/diag/menopause

Menstrual cycle disorders
An abnormal condition in a woman's menstrual cycle.
Learn more at: www.fertilitypedia.org/therapy/diag/menstrual-cycle-disorders

Obesity
A disease of excess body fat that can have a negative effect on health, leading to reduced life expectancy and other health problems.
Learn more at: www.fertilitypedia.org/therapy/diag/obesity

Oligomenorrhea
Light or infrequent menstrual flow at intervals of 39 days to 6 months or 5–7 cycles in a year.
Learn more at: www.fertilitypedia.org/therapy/diag/oligomenorrhea

Pelvic Inflammatory Disease
Infection of the upper part of the female reproductive system and a common complication of some sexually transmitted diseases.
Learn more at: www.fertilitypedia.org/therapy/diag/pelvic-inflammatory-disease-do-rf

Pyosalpinx
A distally blocked Fallopian tube filled with pus.
Learn more at: www.fertilitypedia.org/therapy/diag/pyosalpinx-do-rf

Repeated implantation failure
The absence of implantation after three or more transfers of high quality embryos or after placement of 10 or more embryos in multiple transfers.
Learn more at: www.fertilitypedia.org/therapy/diag/repeated-implantation-failure

Thyroid disorders
A medical condition impairing the function of the thyroid.
Learn more at: www.fertilitypedia.org/therapy/diag/thyroid-disorders

Tubal phimosis
The type of blockage that affects the part of the fallopian tube end towards the ovary.
Learn more at: www.fertilitypedia.org/therapy/diag/tubal-phimosis
**Uterine fibroids**
The most common benign smooth muscle tumors of the uterus encountered in women of reproductive age.
Learn more at: [www.fertilitypedia.org/therapy/diag/uterine-fibroids](http://www.fertilitypedia.org/therapy/diag/uterine-fibroids)

**Uterine malformations**
A type of female genital malformation resulting from an abnormal development of the Müllerian duct(s) during embryogenesis.
Learn more at: [www.fertilitypedia.org/therapy/diag/uterine-malformations](http://www.fertilitypedia.org/therapy/diag/uterine-malformations)

**Uterus duplex**
Congenital uterine malformation where both Müllerian ducts develop but fail to fuse, thus the woman has a "double uterus".
Learn more at: [www.fertilitypedia.org/therapy/diag/uterus-duplex](http://www.fertilitypedia.org/therapy/diag/uterus-duplex)

**Uterus septus**
A form of a congenital malformation where the uterine cavity is partitioned by a longitudinal septum. It is one of Müllerian duct anomalies.
Learn more at: [www.fertilitypedia.org/therapy/diag/uterus-septus](http://www.fertilitypedia.org/therapy/diag/uterus-septus)

**Uterus subseptus**
A form of a congenital malformation where the uterus is partially divided by a longitudinal septum. It is one of Müllerian duct anomalies.
Learn more at: [www.fertilitypedia.org/therapy/diag/uterus-subseptus](http://www.fertilitypedia.org/therapy/diag/uterus-subseptus)

**Vaginismus**
A physical or psychological condition in which woman cannot engage in any form of vaginal penetration.
Learn more at: [www.fertilitypedia.org/therapy/diag/vaginismus](http://www.fertilitypedia.org/therapy/diag/vaginismus)

**Reproductive cells**

**Embryo**
A multicellular diploid eukaryote in an early stage of embryogenesis, or development.
Learn more at: [www.fertilitypedia.org/edu/reproductive-cells/embryo](http://www.fertilitypedia.org/edu/reproductive-cells/embryo)

**Endometrial cell**
Cells composing an inner layer of the uterine lining.
Learn more at: [www.fertilitypedia.org/edu/reproductive-cells/endometrial-cell](http://www.fertilitypedia.org/edu/reproductive-cells/endometrial-cell)
Fertilization in humans. The sperm and ovum unite through fertilization, creating a conceptus that (over the course of 8-9 days) will implant in the uterine wall, where it will reside over the course of 9 months.

Sources

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