Lecture - Week 1 and 2 Development

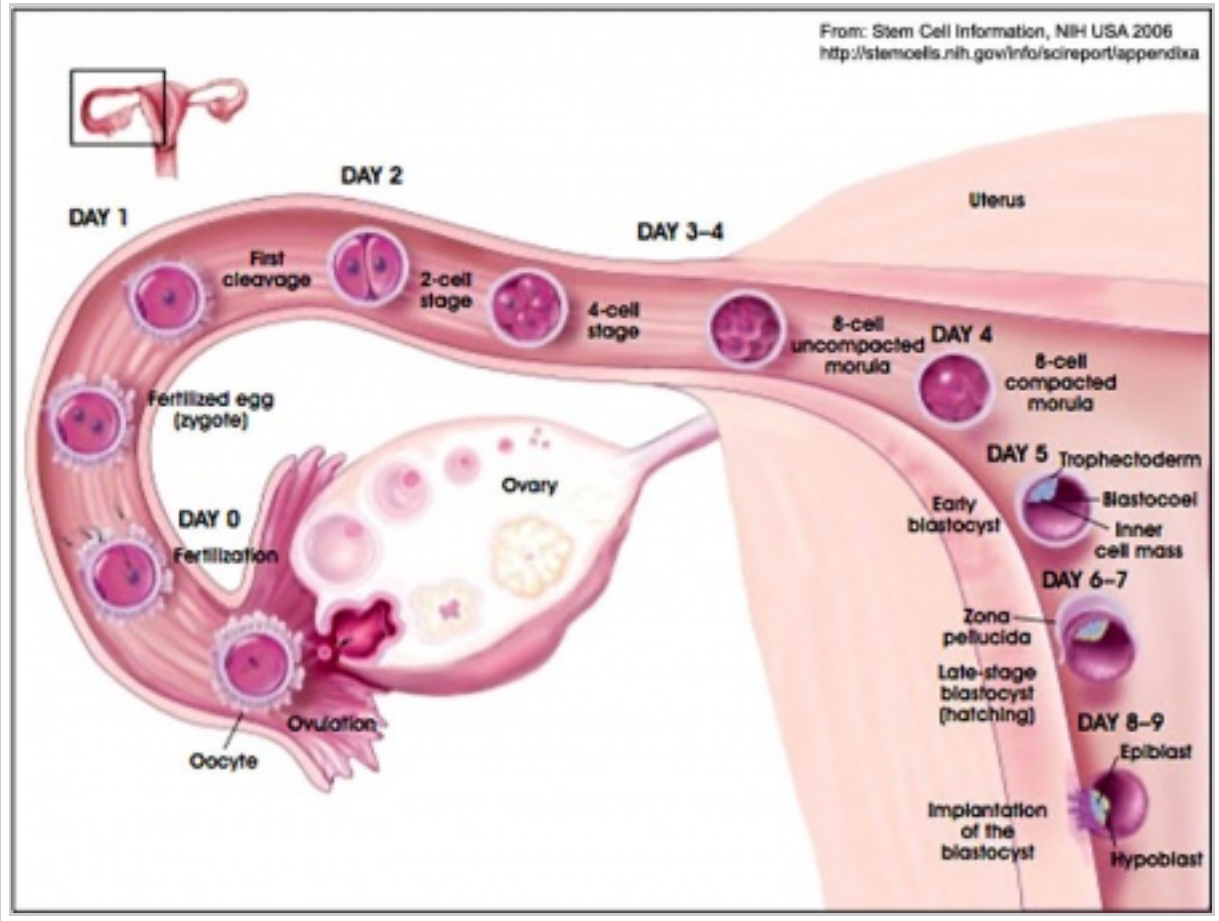
From Embryology

Zygote | Blastocyst | Implantation

Contents

Introduction

This lecture will discuss the first two weeks of human embryogenesis and describe the cleavage stages, blastocyst formation and hatching, and the generation of the bilaminar embryo. There will also be an introduction to the uterine changes at implantation, that will be covered in detail in the placentation lecture.



Week 1 and 2 Development (see Week 1 Movie)

Objectives

- Understand the events during week 1 of development (Zygote, Blastomeres, Morula, Blastocyst)
- Understand the events during week 2 of development (Trophoblast, Syncytiotrophoblast, Cytotrophoblast, Embryoblast, Implantation)
- Brief understanding of early placentation
- Brief understanding of maternal changes

Lecture Resources

Movies [Collapse]		
		
Day 3 to 6	**Contractions**	**Hatching**
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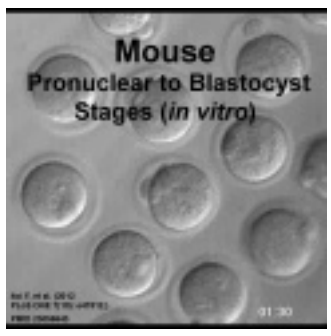	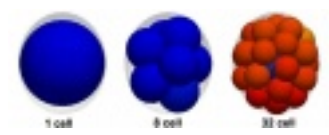	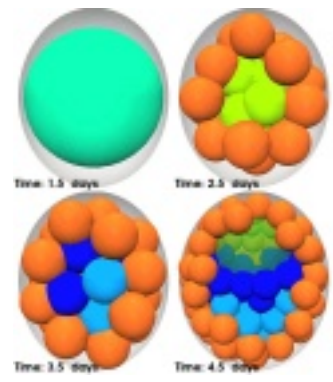
Mouse Blastocyst	**Morula Model**	**Blastocyst Model**
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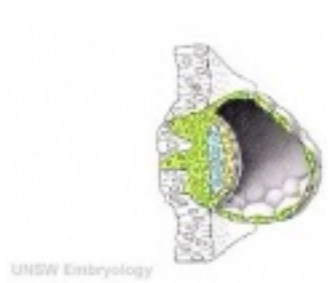
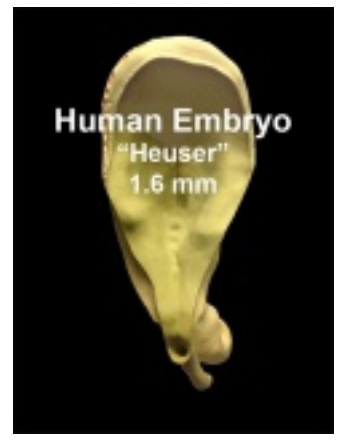
Week 2		
		
Week 2 - Implant	**Week 2 - Bilaminar**	**Embryo 1.6mm**
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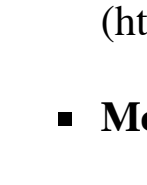
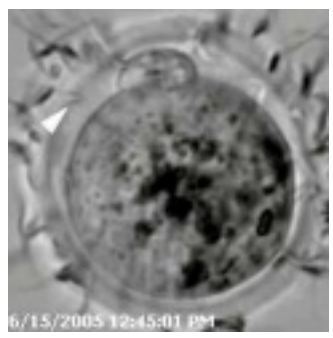
References [Collapse]	
Hill, M.A. (2014). *UNSW Embryology* (14th ed.) Retrieved August 11, 2014, from http://php.med.unsw.edu.au/embryology	▪ Menstrual Cycle | Week 1 | Week 2 | Implantation ▪ Lecture Archive: 2009 | 2010 | 2011 (http://embryology.med.unsw.edu.au/embryology/index.php?title=Lecture_-_Week_1_and_2_Development&oldid=61429) | 2012 (http://embryology.med.unsw.edu.au/embryology/index.php?title=Lecture_-_Week_1_and_2_Development&oldid=97577) | 2013
 Moore, K.L., Persaud, T.V.N. & Torchia, M.G. (2011). *The developing human: clinically oriented embryology* (9th ed.). Philadelphia: Saunders.	The following chapter links only work with a UNSW connection. ▪ Chapter 2 – First Week of Human Development (http://er.library.unsw.edu.au/er/cgi-bin/eraccess.cgi?url=http://www.mdconsult.com/books/page.do?eid=4-u1.0-B978-1-4377-2002-0..00002-3&isbn=978-1-4377-2002-0&uniqId=330028653-2#4-u1.0-B978-1-4377-2002-0..00002-3) ▪ Chapter 3 – Second Week of Human Development (http://er.library.unsw.edu.au/er/cgi-bin/eraccess.cgi?url=http://www.mdconsult.com/books/page.do?eid=4-u1.0-B978-1-4377-2002-0..00003-5&isbn=978-1-4377-2002-0&uniqId=330028653-2#4-u1.0-B978-1-4377-2002-0..00003-5)
 Schoenwolf, G.C., Bleyl, S.B., Brauer, P.R. & Francis-West, P.H. (2009). *Larsen's human embryology* (4th ed.). New York; Edinburgh: Churchill Livingstone.	The following chapter links only work with a UNSW connection. ▪ Chapter 1 - Gametogenesis, Fertilization, and First Week (http://www.mdconsult.com/books/linkTo?type=bookPage&isbn=978-0-443-06811-9&eid=4-u1.0-B978-0-443-06811-9..10001-6) ▪ Chapter 2 - Second Week: Becoming Bilaminar and Fully Implanting (http://www.mdconsult.com/books/linkTo?type=bookPage&isbn=978-0-443-06811-9&eid=4-u1.0-B978-0-443-06811-9..10002-8)

ECHO360 Recording [Expand]

Fertilization

- Fertilization usually occurs in first 1/3 of oviduct.
- Fertilization can also occur outside oviduct, associated with In Vitro Fertilization (IVF, GIFT, ZIFT...) and ectopic pregnancy.
- The majority of fertilized eggs do not go on to form an embryo.



Mouse Fertilisation

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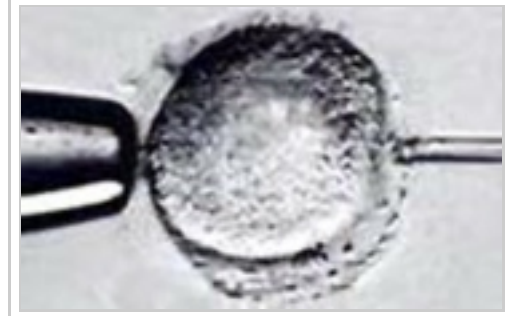
Antral Follicle and Oocyte

Fertilization - Spermatozoa

- **Sperm Binding** - zona pellucida protein ZP3 acts as receptor for sperm
- **Acrosome Reaction** - exyocytosis of acrosome contents (Calcium mediated) MBoC - Figure 20-31. The acrosome reaction that occurs when a mammalian sperm fertilizes an egg (http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.3741)
  - enzymes to digest the zona pellucida, exposes sperm surface proteins to bind ZP2
- **Membrane Fusion** - between spermatozoa and oocyte, allows spermatozoa nuclei passage into oocyte cytoplasm

Fertilization- Oocyte

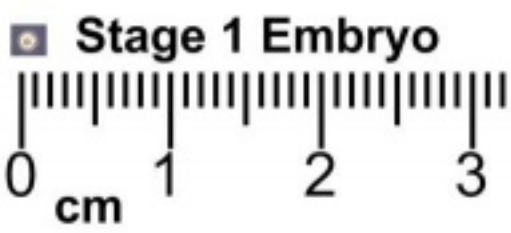
- **Membrane Depolarization** - caused by sperm membrane fusion, primary block to polyspermy
- **Cortical Reaction** - IP3 pathway elevates intracellular Calcium, exocytosis of cortical granules MBoC - Figure 20-32. How the cortical reaction in a mouse egg is thought to prevent additional sperm from entering the egg (http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.3743)
    - enzyme alters ZP3 so it will no longer bind sperm plasma membrane
- **Meiosis 2** - completion of 2nd meiotic division
    - forms second polar body (a third polar body may be formed by meiotic division of the first polar body)

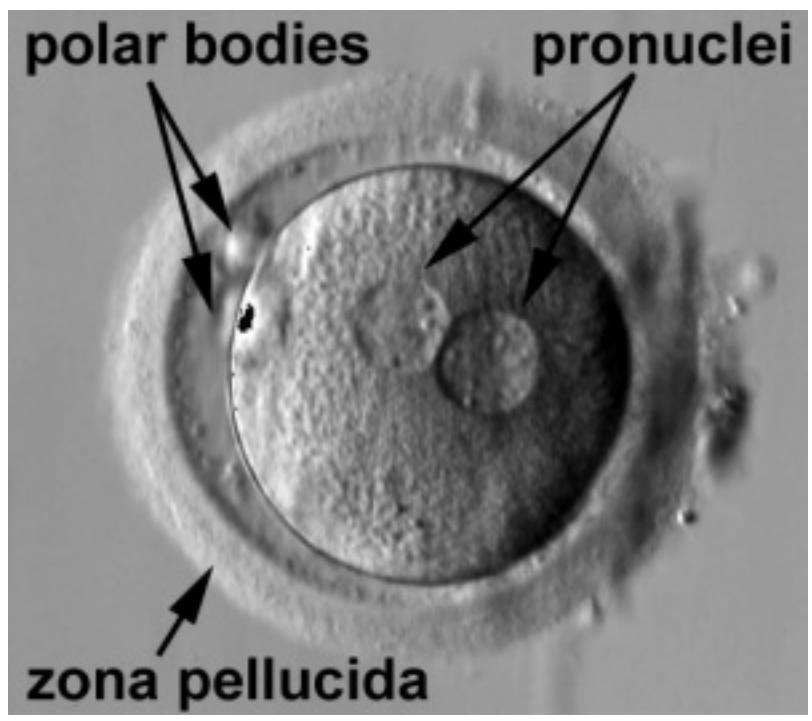


Intracytoplasmic sperm insemination (ART)

Zygote Formation

- zygote (Carnegie stage 1) is the first diploid cell formed following fertilisation.
- male and female pronuclei, 2 nuclei approach each other and nuclear membranes break down.
- DNA replicates, first mitotic division
- sperm contributes centriole which organizes mitotic spindle





Pronuclear Fusion and Parental Genomes Movies [Expand]

Conceptus *- the term refers to all material derived from this fertilised zygote, includes both the embryo and the non-embryonic tissues (placenta, fetal membranes).*

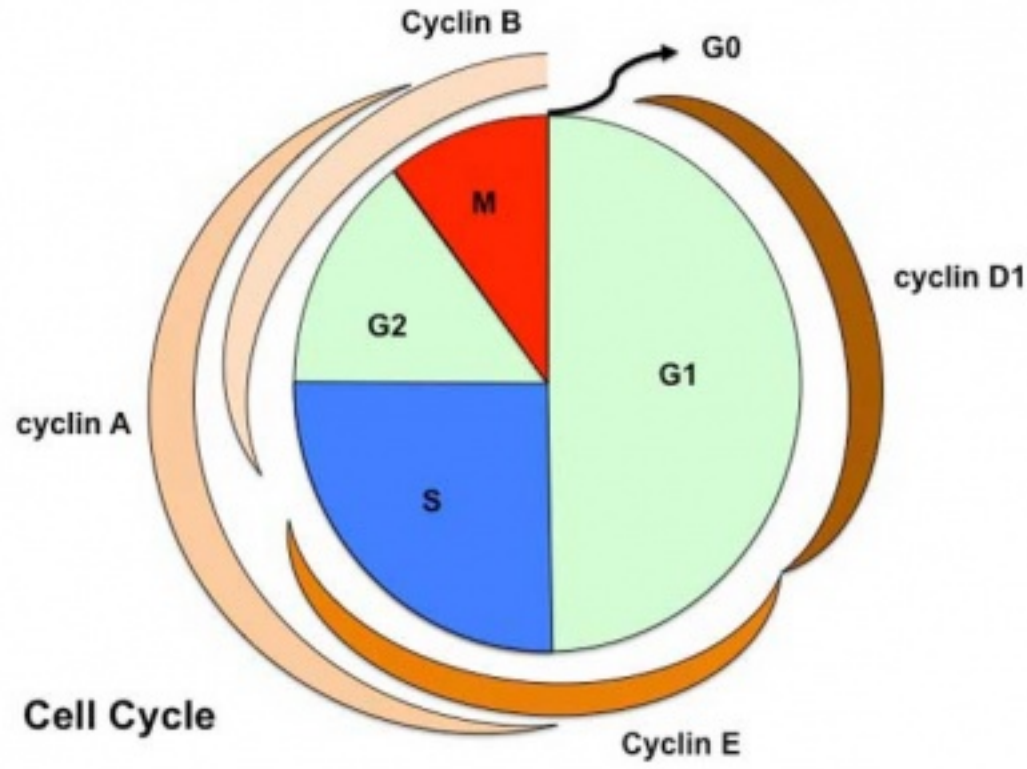
Links: Fertilization | Carnegie stage 1

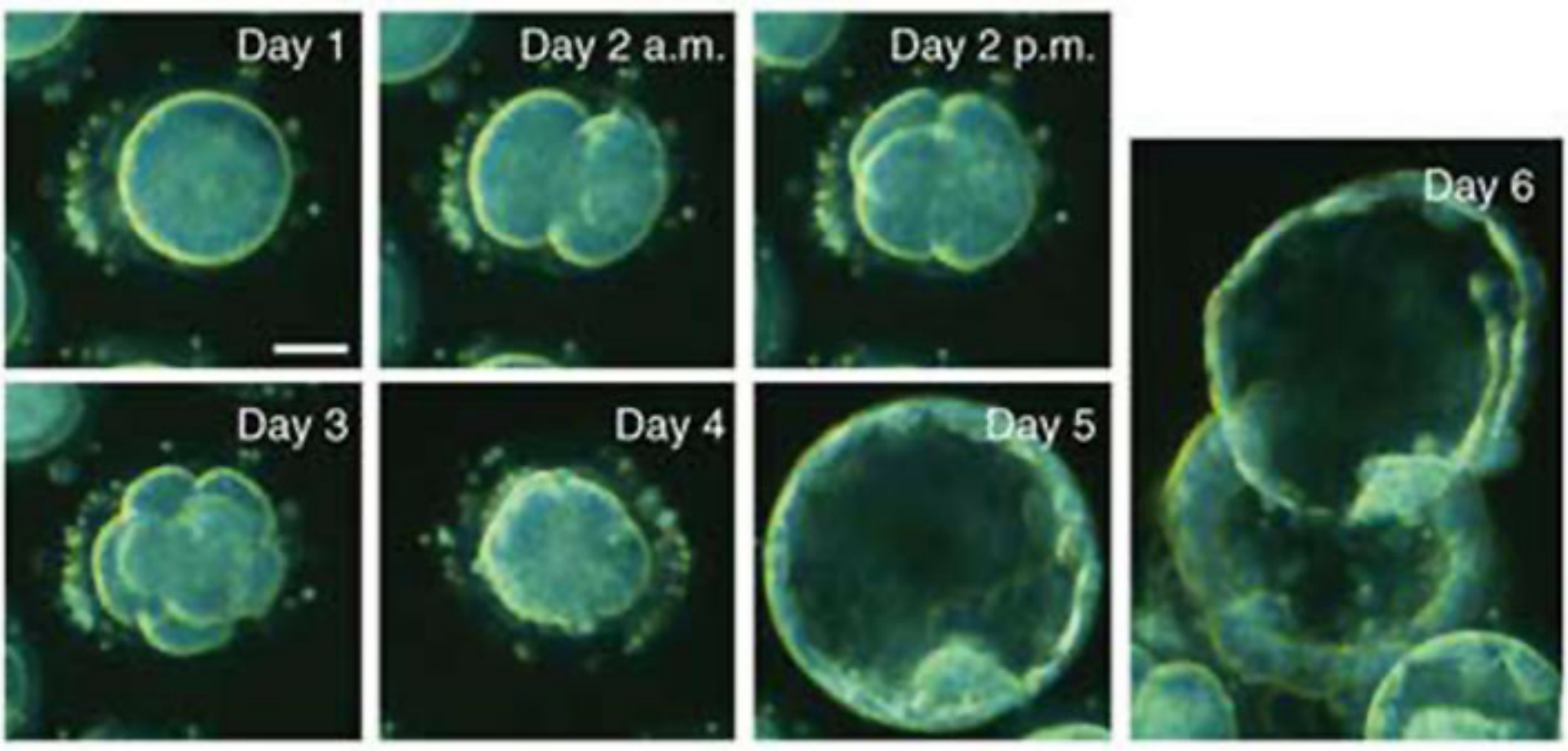
Cleavage of Zygote

- cleavage of zygote forms 2 blastomeres and is also cleavage with no cytoplasm synthesis.
    - special "embryonic" cell cycle **S** phases and **M** phases alternate without any intervening **G1** or **G2** phases (MSMSMSMS, adult MG1SG2)

therefore individual cell volume decreases.

- cell division is initially synchronous, then asynchronously
- cell division becomes slower (centre cells, larger) and faster in peripheral cells
- zona pellucid still intact (division occurs within the ZP)

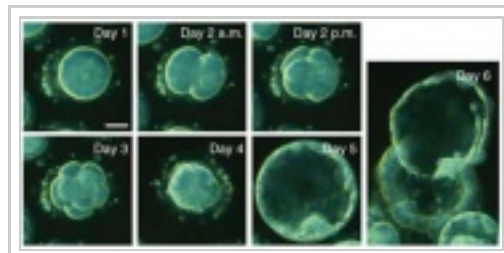




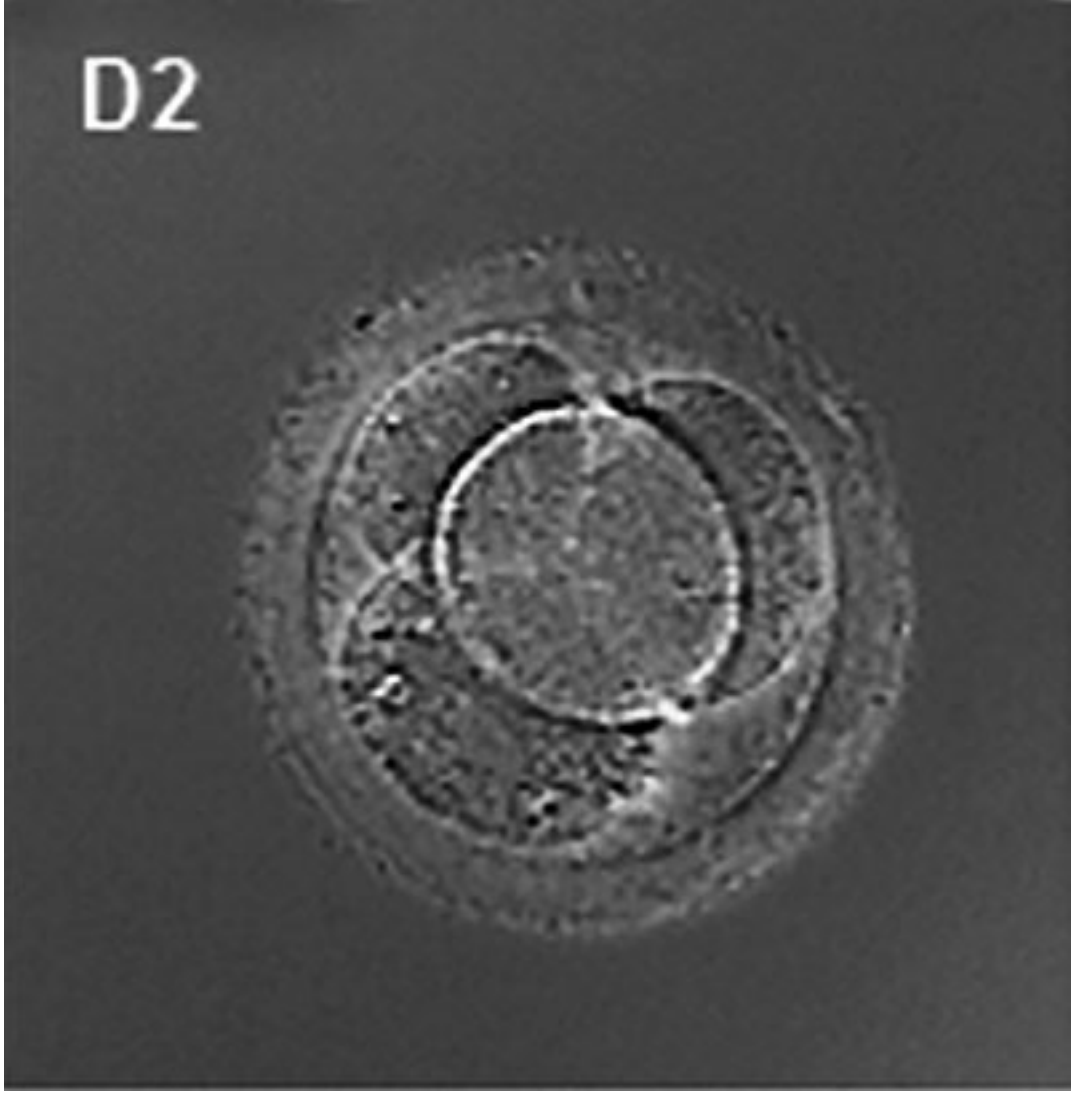
Human Zygote to Blastocyst Development (day 1 to 6)

Links: Carnegie stage 2 | Movie - Early Cell Division

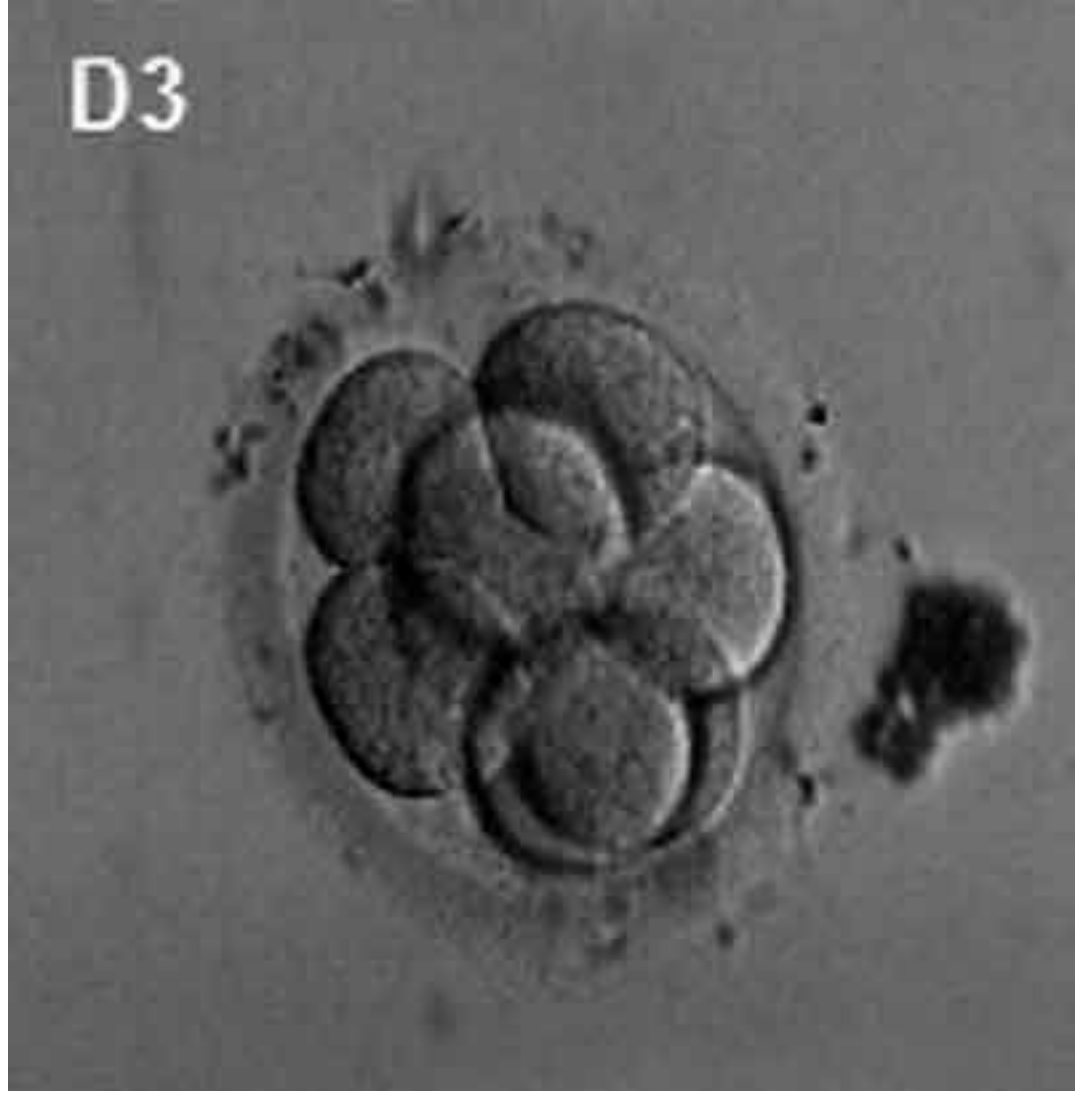
Morula



Human Zygote to Blastocyst Development (day 1 to 6)



Human Embryo (day 2)



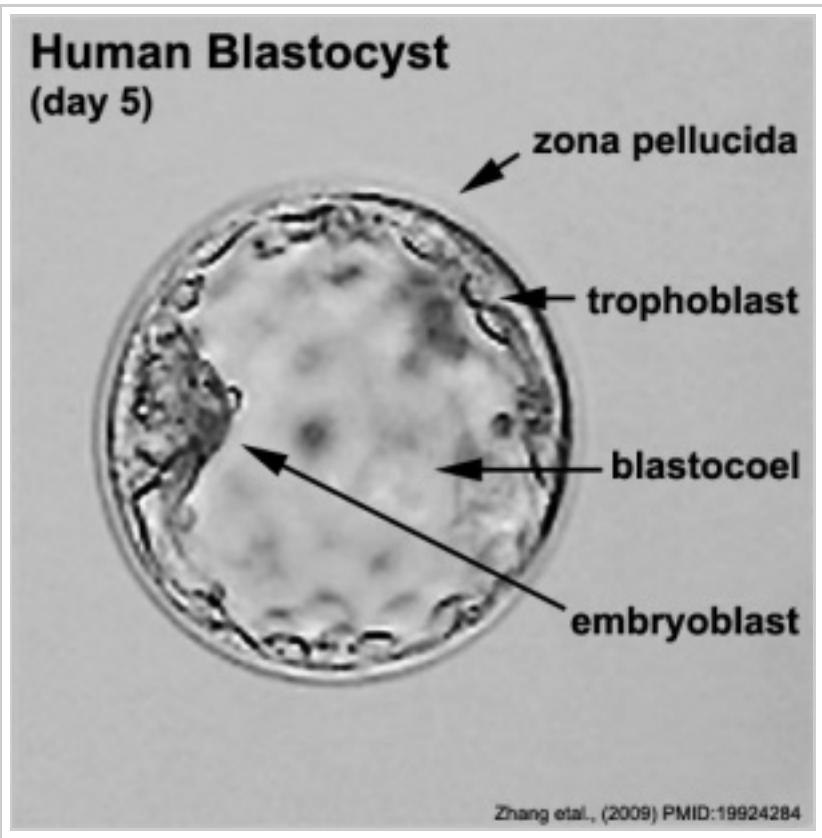
Human Embryo (day 3)

- about **day 4** is a solid ball of 16-20 cells with peripheral cells flattened against zona pellucida
- compaction occurs forming a cavity and leading to the next blastocyst stage

Links: Figure 8.19. Changes in DNA methylation during mammalian development (http://www.ncbi.nlm.nih.gov/books/bv.fcgi?&rid=hmg.figgrp.928)

Blastocyst

- about **day 5** have 2 identifiable cell types and a fluid-filled cavity (blastoceol)
  - outer cell layer - **trophoblast**, peripheral flattened cells, forms the placenta and placental membranes
  - inner cell mass - **embryoblast**, mass of rounder cells located on one wall of the blastocoel, forms entire embryo

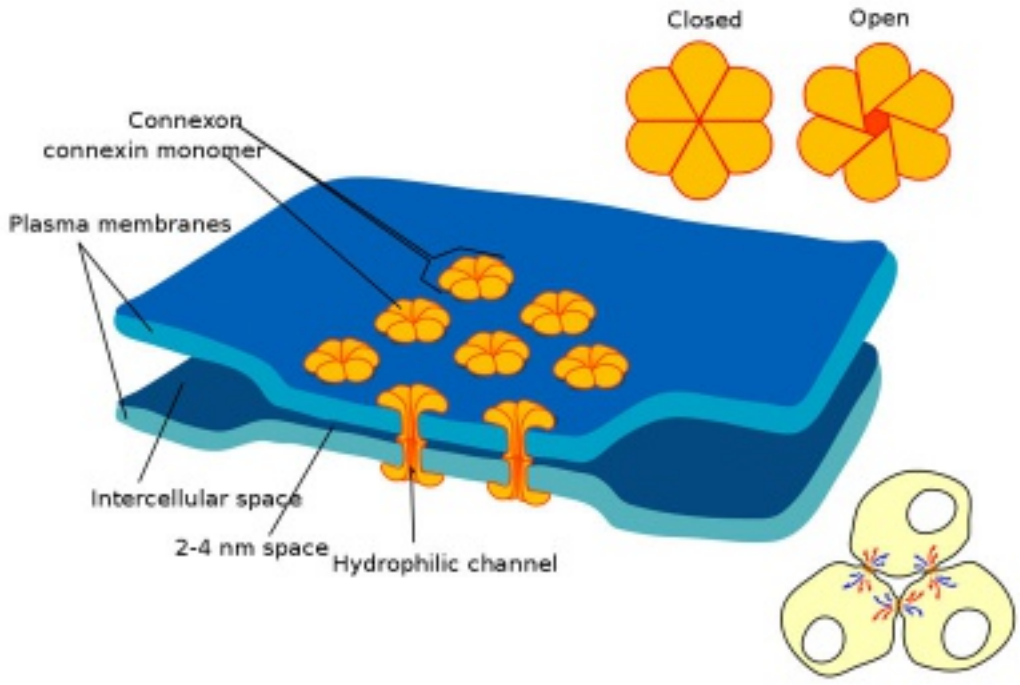


Blastocyst (day 5)

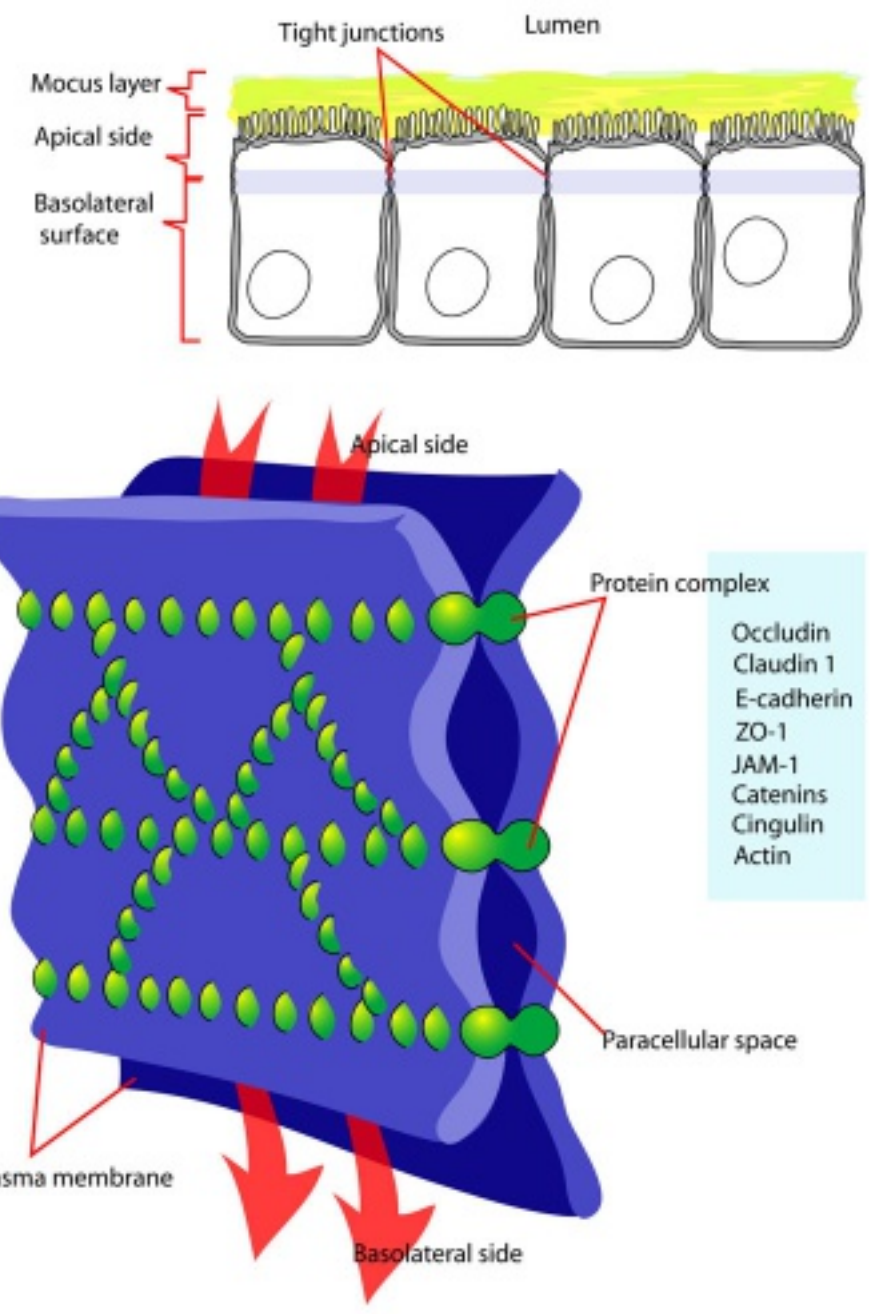
Blastula Cell Communication

Two forms of cellular junctions

- **gap junctions**, allow electrically couple cells of epithelium surrounding a fluid-filled cavity
- **tight junctions**, close to outer surface create a seal, isolates interior of embryo from external medium

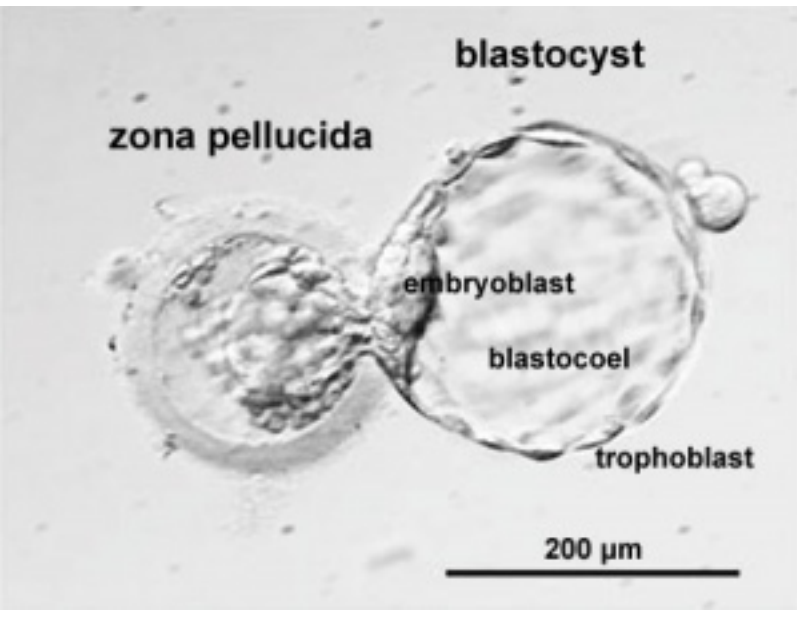


Gap junctions

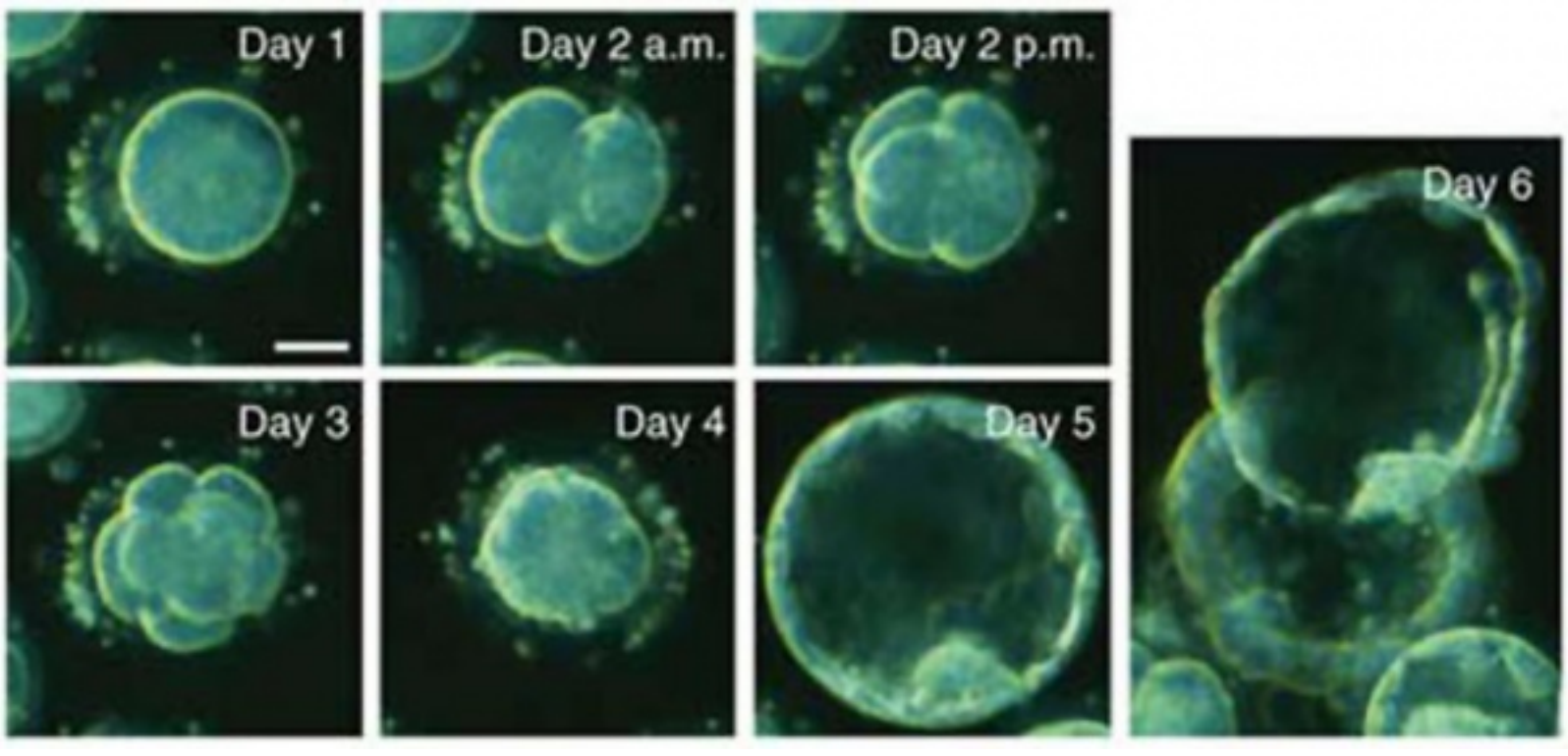


Tight junctions

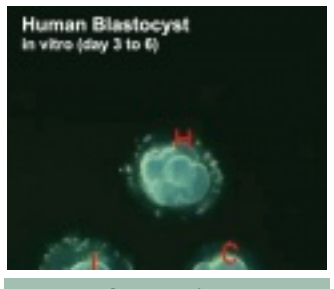
Blastocyst Hatching



Blastocyst Hatching - zona pellucida lost, ZP has sperm entry site, and entire ZP broken down by uterine secretions and possibly blastula secretions. **Uterine Glands** - secretions required for blastocyst motility and nutrition



Human Blastocyst (day 3 to 6)



Day 3 to 6

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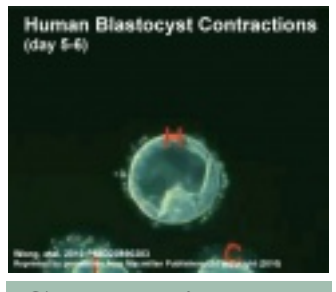

Contractions

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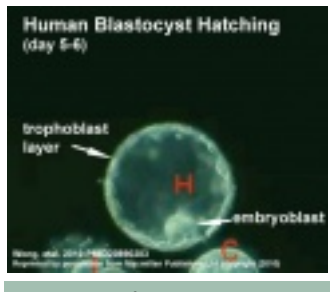

Hatching

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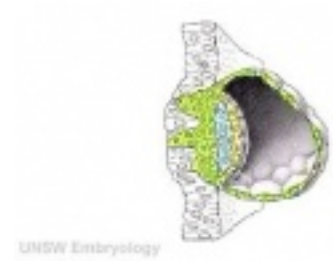
Links: Carnegie stage 3 | Figure 21-69. The blastula (http://www.ncbi.nlm.nih.gov/books/NBK26863/figure/A3927)

Week 2 - Implantation

The second week of human development is concerned with the process of implantation and the differentiation of the blastocyst into early embryonic and placental forming structures.

- implantation commences about **day 6 to 7**
- **Adplantation** - begins with initial adhesion to the uterine epithelium
  - blastocyst then slows in motility, "rolls" on surface, aligns with the inner cell mass closest to the epithelium and stops
- **Implantation** - migration of the blastocyst into the uterine epithelium, process complete by about **day 9**
  - interaction between trophoblast cells and endometrial epithelium (apoptosis and decidualization)
- **coagulation plug** - left where the blastocyst has entered the uterine wall **day 12**

Normal Implantation Sites - in uterine wall superior, posterior, lateral



Week 2 - Implant

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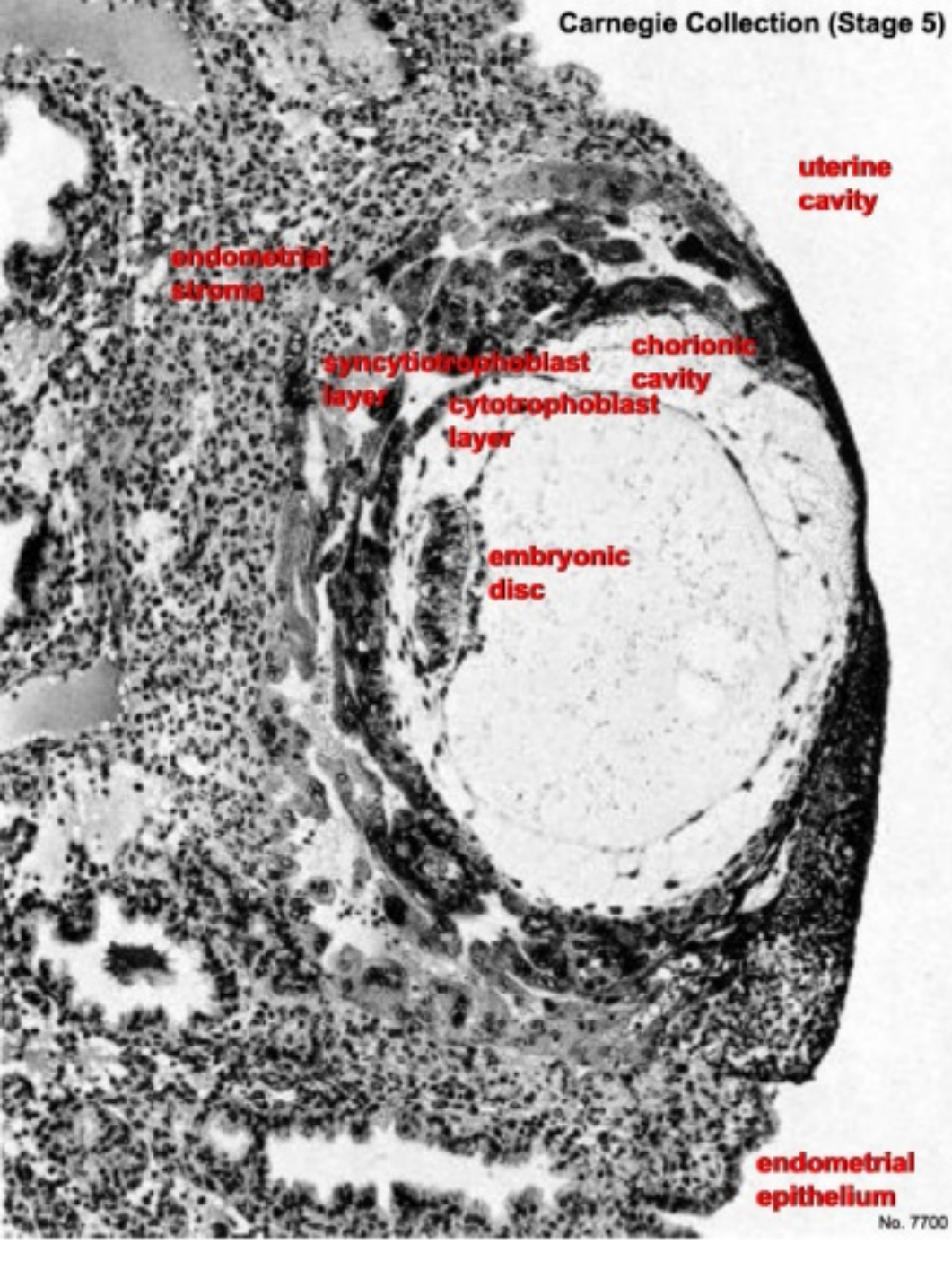


Endometrial Receptivity

- In humans, receptivity occurs 6 days after the post-ovulatory progesterone surge and lasts about 2 to 4 days.
  - Similar "receptivity window" in other species (rat day 5 and mouse day 4.5).
- Many studies have looked into identifying markers for this receptivity period both to optimise and to block this process.

Abnormal Implantation

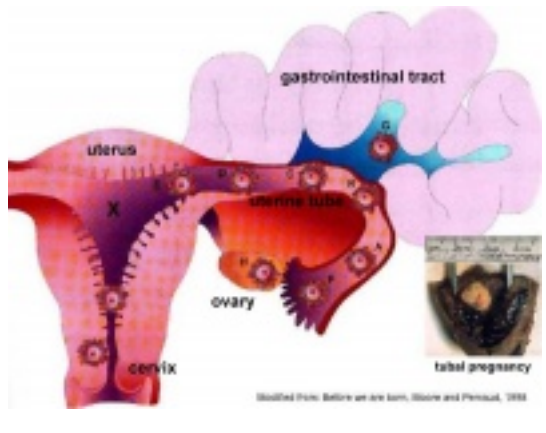
Abnormal implantation sites or Ectopic Pregnancy occurs if implantation is in uterine tube or outside the uterus.

Ectopic tubal pregnancy

- sites - external surface of uterus, ovary, bowel, gastrointestinal tract, mesentry, peritoneal wall
- If not spontaneous then, embryo has to be removed surgically

Tubal pregnancy - 94% of ectopic pregnancies

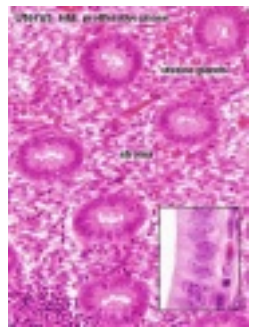
- if uterine epithelium is damaged (scarring, pelvic inflammatory disease)
- if zona pellucida is lost too early, allows premature tubal implantation
- embryo may develop through early stages, can erode through the uterine horn and reattach within the peritoneal cavity



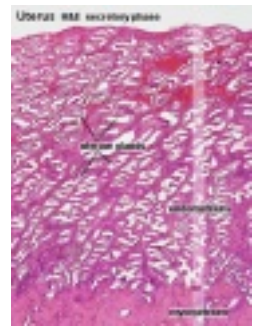
Links: Implantation | Ectopic Pregnancy | Movie - Ectopic pregnancy ultrasound

Uterus

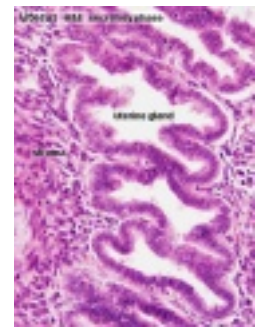
Uterus proliferative phase



Uterine gland proliferative phase



Uterus secretory phase



Uterine gland secretory phase

- Endometrium - 3 layers in secretory phase of menstrual cycle: compact, spongy, basal
- Myometrium - muscular layer outside endometrium, contracts in parturition
- Perimetrium - tunica serosa of the uterus continuous with the peritoneal wall

Endometrial Layers

- Compact - implantation occurs in this layer, dense stromal cells, uterine gland necks, capillaries of spiral arteries
- Spongy - swollen stromal cells, uterine gland bodies, spiral arteries
- Basal - not lost during menstruation or childbirth, own blood supply

Decidual Reaction

- transformation of endometrial stromal cells
- occurs initially at site of implantation and includes both cellular and matrix changes
- reaction spreads throughout entire uterus, not at cervix
- deposition of fibrinoid and glycogen and epithelial plaque formation (at anchoring villi)
- presence of decidual cells are indicative of pregnancy

Other Uterine Changes

- **Cervix** - at mouth of uterus, secretes mucus (CMP), forms a plug/barrier, mechanical and antibacterial
- **Vascular** - increased number of blood vessels

Decidua

The endometrium becomes the decidua and forms 3 distinct anatomical regions (at approx 3 weeks)

- Decidua Basalis at implantation site
- Decidua Capsularis enclosing the conceptus
- Decidua Parietalis the remainder of uterus
    - Decidua Capsularis and Parietalis fuse eventually fuse and uterine cavity is lost by 12 weeks

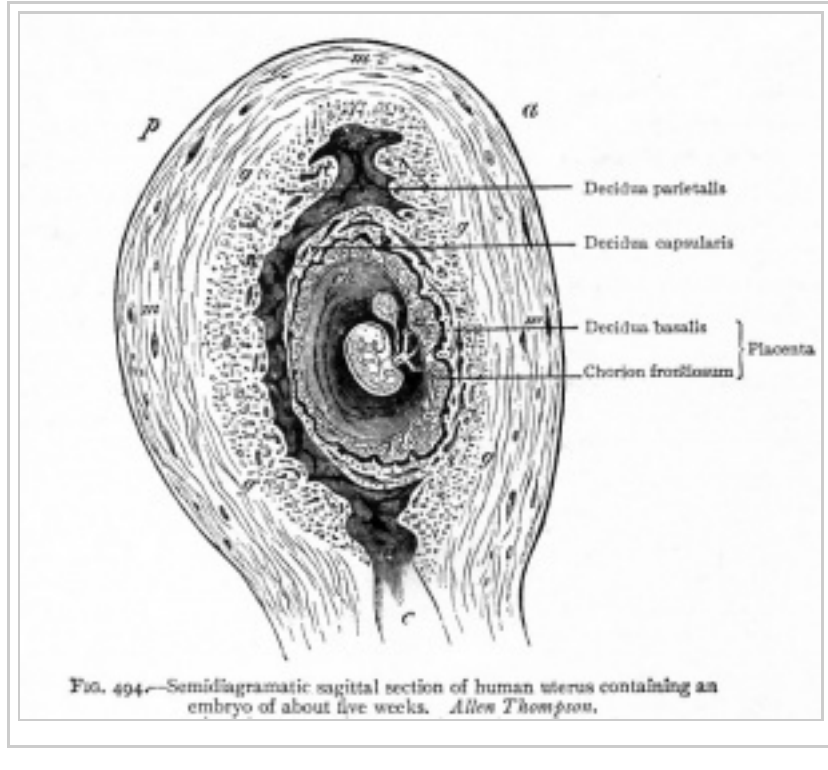


Fig. 494.—Semidiagramatic sagittal section of human uterus containing an embryo of about five weeks. *Allen Thompson.*

Uterus Abnormalities

Endometriosis endometrial tissue located in other regions of the uterus or other tissues. This misplaced tissue develops into growths or lesions which respond to the menstrual cycle hormonal changes in the same way that the tissue of the uterine lining does; each month the tissue builds up, breaks down, and sheds.

Conceptus

Bilaminar Embryoblast

- about **day 8 to 9**
- The outer trophoblast and inner embryoblast layers now both differentiate to form two distinct cellular layers.
- The trophoblast layer forms the **syncitotrophoblast** and **cytotrophoblast** layers.
- The embryoblast (inner cell mass) forms the **epiblast** and **hypoblast** layers.
  - **Epiblast** - will form the 3 germ layers.
  - **Hypoblast** - transient layer replaced by endoderm.
- This early stage of embryo development is referred to as the **bilaminar embryo**.

Movie - Week 2 Bilaminar Embryo

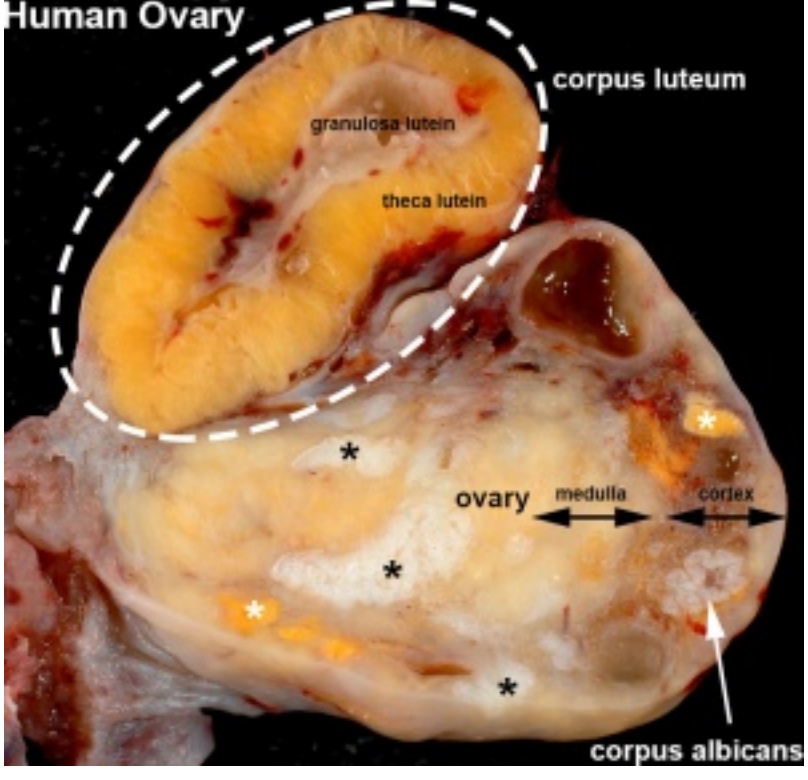
Bilaminar Trophoblast

Two trophoblast layers Cytotrophoblast and Syncitiotrophoblast.

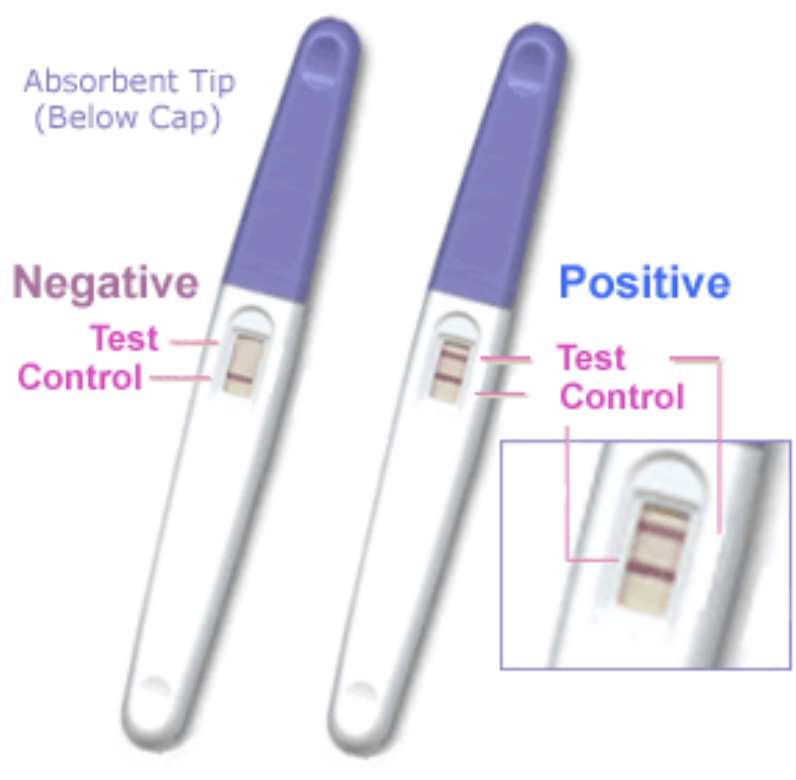
Cytotrophoblasts - form a continuous cellular layer that covers the developing placental villi.

Syncitiotrophoblasts

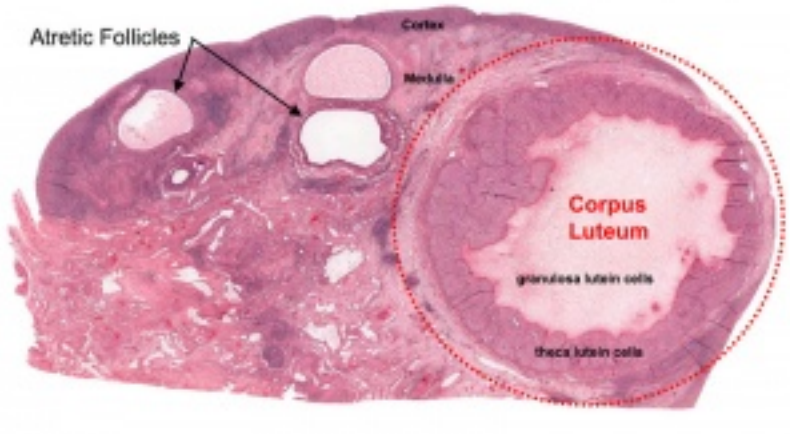
- **secrete proteolytic enzymes**, enzymes break down extracellular matrix around cells
- Allow passage of blastocyst into endometrial wall, totally surround the blastocyst
- generate spaces that fill with maternal blood- lacunae
- **secrete Human Chorionic Gonadotropin** (hCG), hormone, maintains decidua and Corpus Luteum, basis of pregnancy diagnostic test, present in urine is diagnostic of pregnancy
  - levels peak at 8 to 10 weeks of pregnancy, then decline and are lower for rest of pregnancy
  - 1-2 months: 5,000-200,000 mIU/ml; Non-pregnant females: <5.0 mIU/ml; Postmenopausal females: <9.5 mIU/ml)
  - Later in development placenta will secrete hCG



Human ovary corpus luteum



Pregnancy Test Kit



Twinning

Twinning can be due to two separate fertilization events (dizygotic twins) or as an abnormality of a single fertilization (monozygotic twins) event during the early weeks of development.

Dizygotic Twinning

Dizygotic twins (fraternal, non-identical) arise from separate fertilization events involving two separate oocyte (egg, ova) and spermatozoa (sperm).

- In **dizygotic twinning** the genetic material is different and implantation and placentation is also different.

Monoygotic Twinning

- In **monozygotic twinning** the genetic material is initially identical and degree of twinning will depend upon the timing (early to late) from separate fetal membranes and placenta to conjoined twins.
  - morula stage (diamniotic dichorionic), early blastocyst (diamniotic monochorionic), late blastocyst to bilaminar (monoamniotic monochorionic), bilaminar to trilaminar embryo (conjoined)
- Monozygotic twins are a unique research resource for comparing environmental effects on development and health.
- Congenital abnormality statistics for twins is generally increased in various conditions.

Monoygotic twins (identical) produced from a single fertilization event (one fertilised egg and a single spermatazoa, form a single zygote), these twins therefore share the same genetic makeup. Occurs in approximately 3-5 per 1000 pregnancies, more commonly with aged mothers. The later the twinning event, the less common are initially separate placental membranes and finally resulting in conjoined twins.

Week		Week 1							Week 2					
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Cell Number	1	1	2	16	32	128				bilaminar					
						Late									

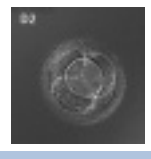
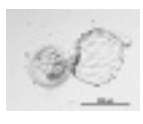
Event	Ovulation fertilization	First cell division	Morula	Early blastocyst	blastocyst Hatching	Implantation starts	X inactivation	
								
Monoygotic Twin Type		Diamniotic Dichorionic		Diamniotic Monochorionic		Monoamniotic Monochorionic		Conjoined

Table based upon recent Twinning Review.[1]

1. ↑ Judith G Hall **Twinning.** Lancet: 2003, 362(9385);735-43 PMID:12957099

Links: Twinning | Australian Twin Registry (http://www.twins.org.au/index.php?page=31)

Now watch the Week 1 overview.

Week 1 Movie [Expand]

2014 Course: **Week 2** Lecture 1 Lecture 2 Lab 1 | **Week 3 Lecture 3** Lecture 4 Lab 2 | **Week 4** Lecture 5 Lecture 6 Lab 3 | **Week 5** Lecture 7 Lecture 8 Lab 4 | **Week 6** Lecture 9 Lecture 10 Lab 5 | **Week 7** Lecture 11 Lecture 12 Lab 6 | **Week 8** Lecture 13 Lecture 14 | Lab 7 | **Week 9** Lecture 15 Lecture 16 Lab 8 | **Week 10** Lecture 17 Lecture 18 Lab 9 | **Week 11** Lecture 19 Lecture 20 Lab 10 | **Week 12** Lecture 21 Lecture 22 Lab 11 | **Week 13** Lecture 23 Lecture 24 Lab 12 | Moodle (http://moodle.telt.unsw.edu.au/course/view.php?id=9262)

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