

Lecture - Placenta Development

Introduction

This lecture is an introduction to the development and functions of the placenta.

The placenta (Greek, *plakuos* = flat cake) named on the basis of this organs appearance. The placenta a materno-fetal organ which begins developing at implantation of the blastocyst and is delivered with the fetus at birth. Only recently have we begun to understand the many different functions this organ carries out in addition to its role in embryonic nutrition.

If you have time after working through this online lecture page, have a look at the [Medicine practical class](#), 7 pages the students work through in 2 hours.

The placenta and placental blood at birth has recently been seen as a new source for [stem cells](#) in bone marrow replacement therapy in many diseases. The topic of stem cells will be covered later in this current course.

Lecture Objectives

- Understanding of placental villi development
- Understanding of placental structure
- Understanding of placental functions
- Brief understanding of placental abnormalities



Spiegel and Casseri: De formato foetu liber singularis (Dedication dated 1626).

Lecture Resources

References [\[Expand\]](#)

Movies [\[Expand\]](#)

2016 Lecture Video Recording [\[Expand\]](#)

Nutrition

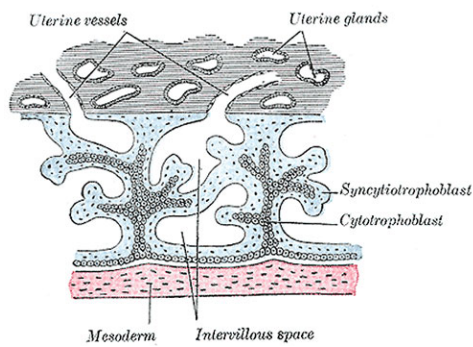
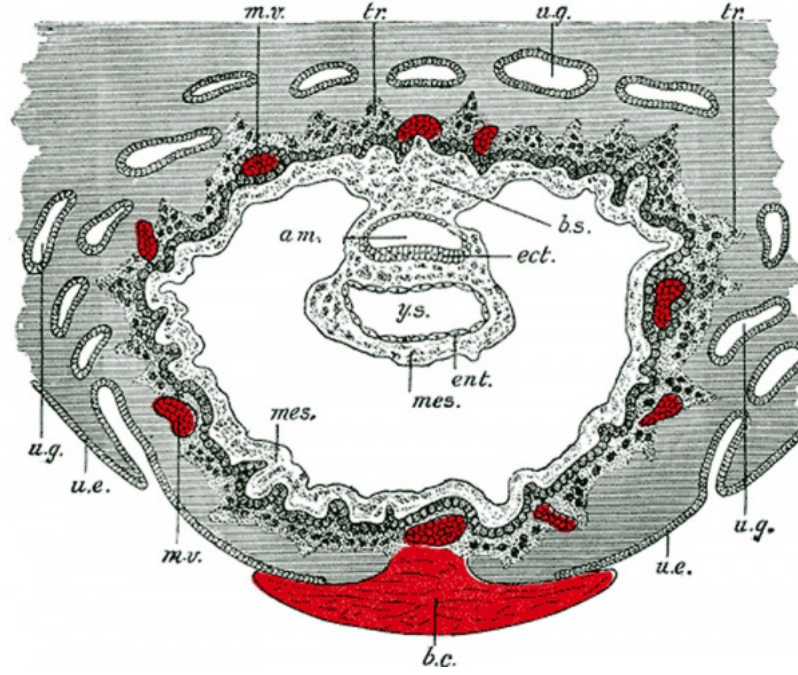
- **Histiotrophic** - describes the initial transfer of nutrition from maternal to embryo.
 - occurs before implantation and during early implantation mainly from uterine glands.
- **Haemotrophic** - describes the later blood-borne nutrition.
 - occurs in the embryonic and fetal period after placenta development.

Fetal Membranes

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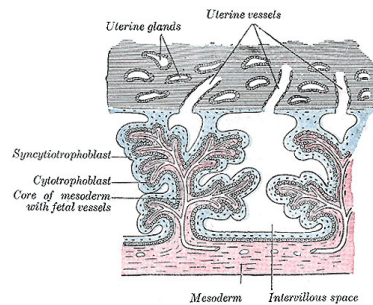
Villi Stages





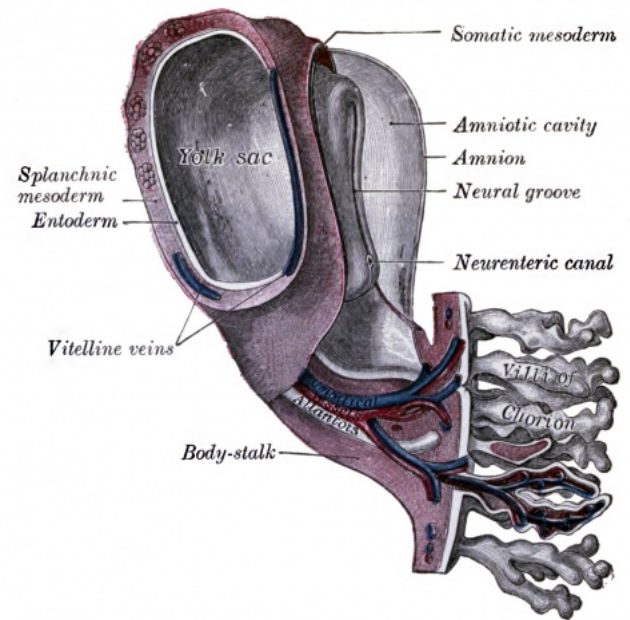
Primary villi

Week 2 - first stage of chorionic villi development, trophoblastic shell cells (syncytiotrophoblasts and cytotrophoblasts) form finger-like extensions into maternal decidua.



Secondary villi

Week 3 - second stage of chorionic villi development, extraembryonic mesoderm grows into villi, covers entire surface of chorionic sac.

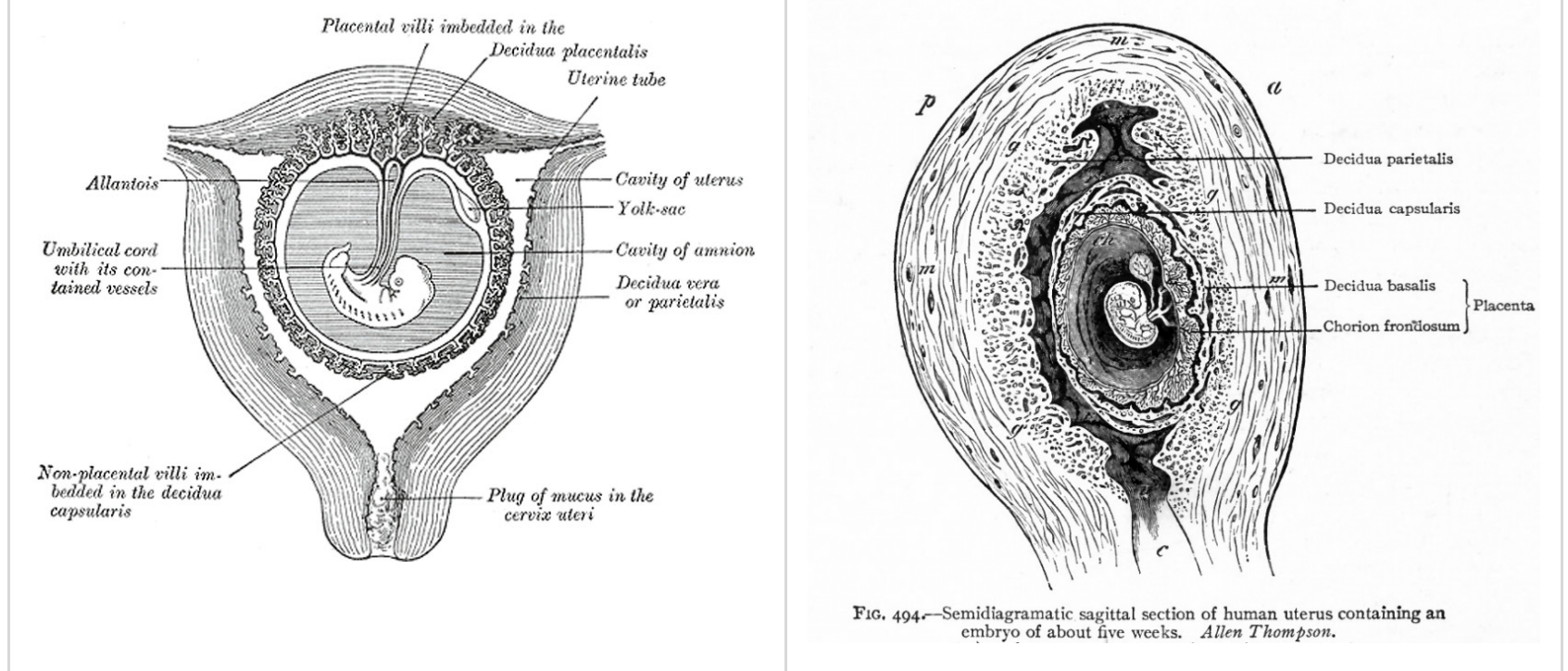


Tertiary villi

Week 4 - third stage of chorionic villi development, mesenchyme differentiates into blood vessels and cells, forms arteriocapillary network, fuse with placental vessels, developing in connecting stalk. Basal region will form chorionic plate.

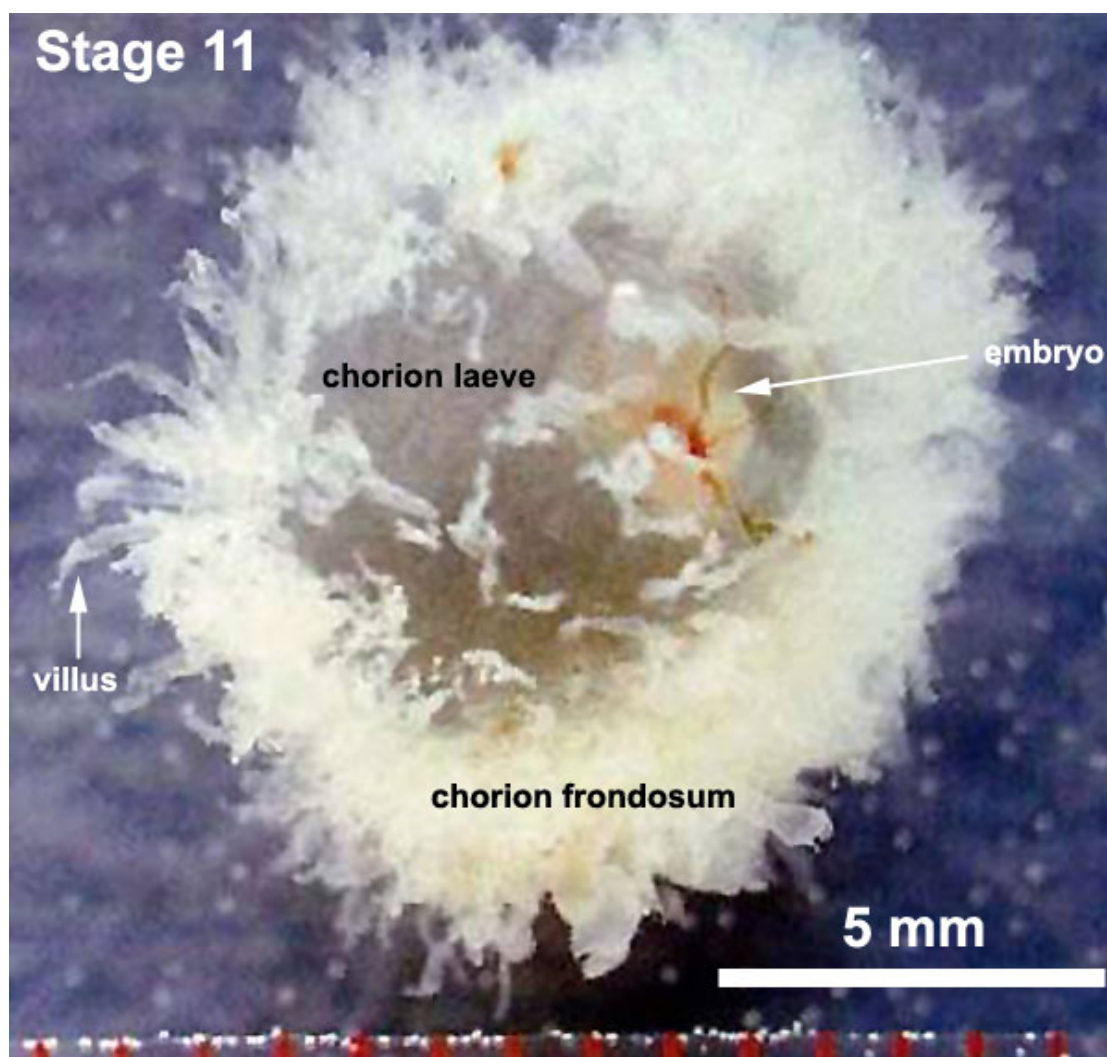
Chorionioic Villi Location

Historic - Semi-diagrammatic sagittal section of human uterus containing an embryo. Note the villi locations and the names for different maternal decidual regions.



Originally cover entire chorionic surface and become restricted to decidua basalis region forming 2 regions:

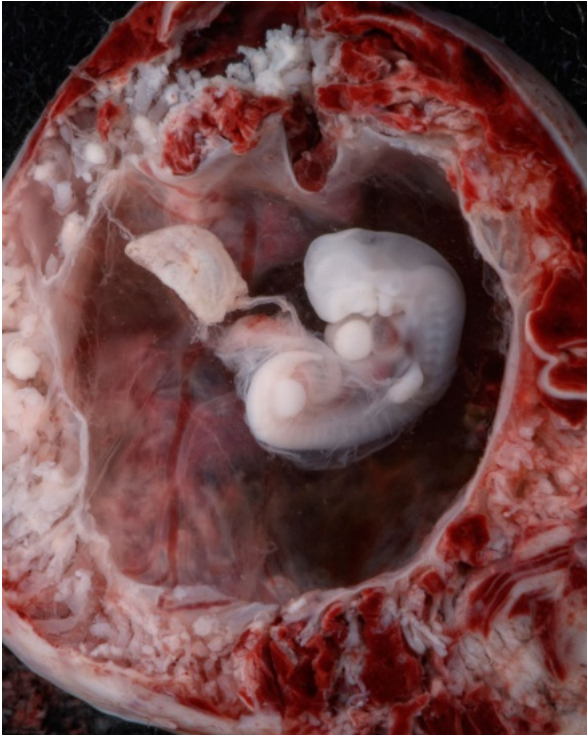
Week 4 - Carnegie stage 11



- **Frondosum** - "leafy" where villi are mainly located
- **Capsularis** - smooth chorion, where villi are absent or not abundant

Week 5 - Carnegie stage 14

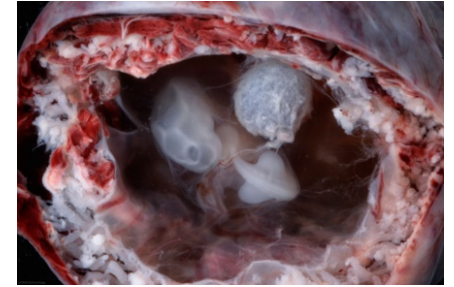
Stage 14 - Lateral View



[Mobile](#) | [Desktop](#) | [Original](#)

[Stage 14](#) | [Embryo Slides](#)

Stage 14 - Ventral View



[Mobile](#) | [Desktop](#) | [Original](#)

[Stage 14](#) | [Embryo Slides](#)

Week 7 - [Carnegie stage 18](#))

Human Embryo
(Week 7, Carnegie Stage 18)



Villi Terms

- **primary villi** - week 2, first stage of chorionic villi development, trophoblastic shell cells (syncytiotrophoblasts and cytotrophoblasts) form finger-like extensions into maternal decidua.
- **secondary villi** - week 3, second stage of chorionic villi development, extraembryonic mesoderm grows into villi, covers

entire surface of chorionic sac.

- **tertiary villi** third stage of chorionic villi development, mesenchyme differentiates into blood vessels and cells, forms arteriocardillary network, fuse with placental vessels, developing in connecting stalk
- **stem villi** - or anchoring villi, cytotrophoblast cells attached to maternal tissue.
- **branched villi** - or terminal villi, grow from sides of stem villi, region of main exchange, surrounded by maternal blood in intervillous spaces.
- **terminal villi** - not active outgrowths caused by proliferation of the trophoblast. Passive protrusions induced by capillary coiling due to growth of the fetal capillaries within the mature intermediate villi (third trimester).
- **chorionic plate** - region of membrane at the base of the villi through which placental arteries and vein passes.
- Placenta anchoring villi
- Villi first trimester
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-

Placenta at Birth

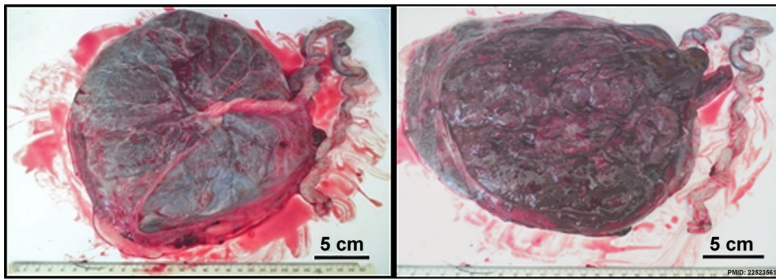
- **Placenta** (Greek, *plakuos* = flat cake)
- embryonic/maternal organ
- villous chorion/decidua basalis
- continuous with amniotic and chorionic sacks

Dimensions

- at birth - discoid up to 20cm diameter and 3 cm thick (term) and weighs 500-600 gm
- Shapes - accessory placenta, bidiscoid, diffuse, horseshoe
- maternal and embryonic surface, both delivered at parturition

- retention may cause uterine hemorrhage

Term Placenta



Fetal side

Maternal side

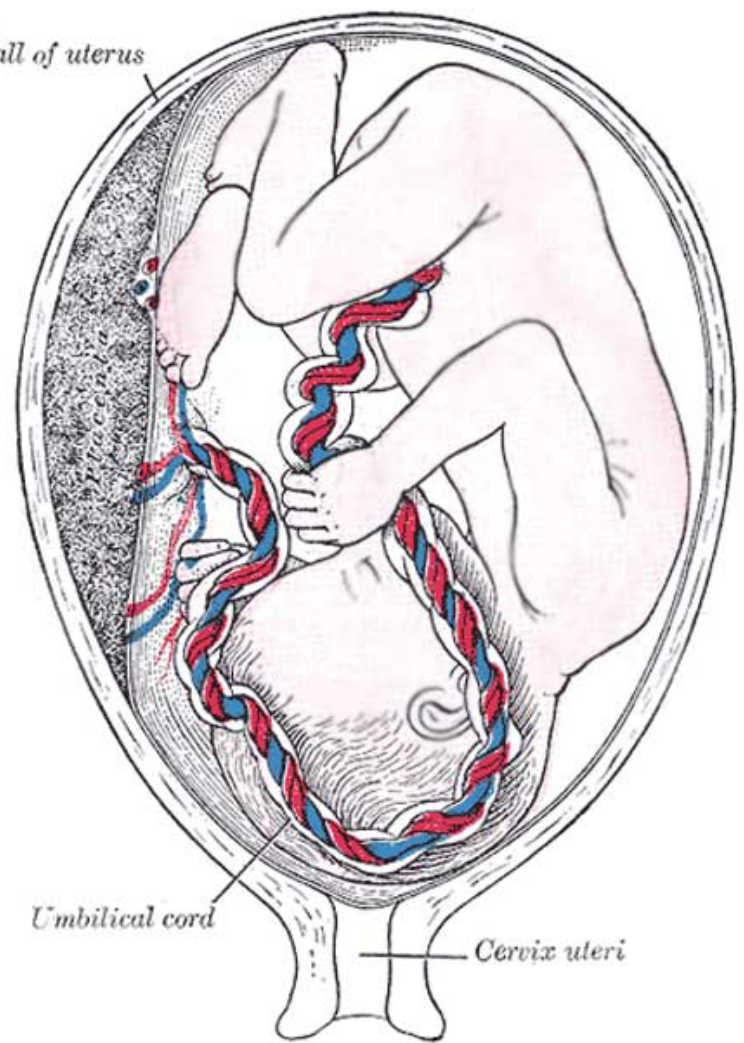
Fetal Surface

- umbilical cord attachment - cord 1-2 cm diameter, 30-90cm long
- covered with **amniotic membrane** and attached to **chorionic plate**
- umbilical vessels branch into chorionic vessels which anastomose

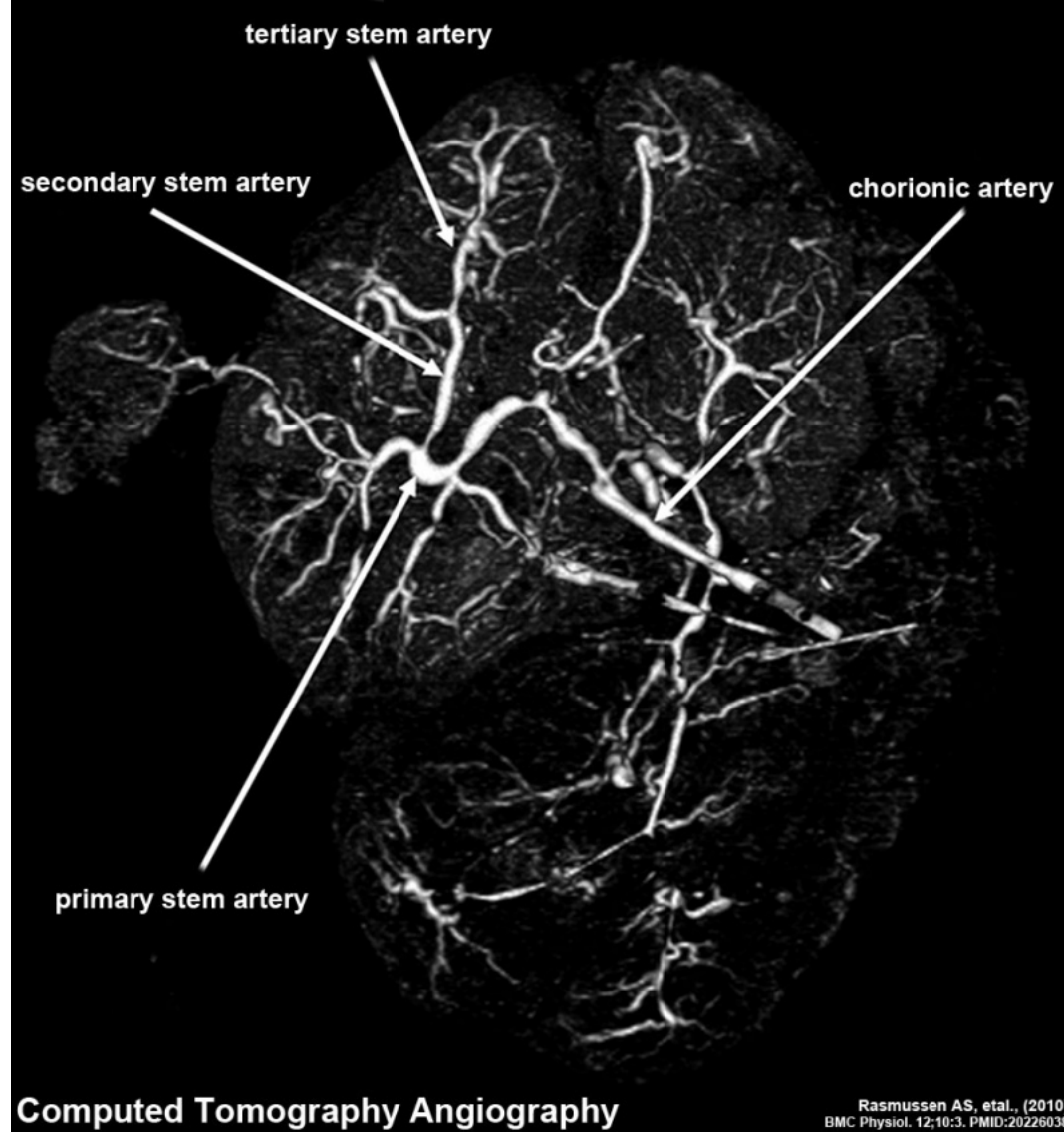
Maternal Surface

- **Cotyledons** - form cobblestone appearance, originally placental septa formed grooves.
- covered with maternal decidua basalis

Wall of uterus



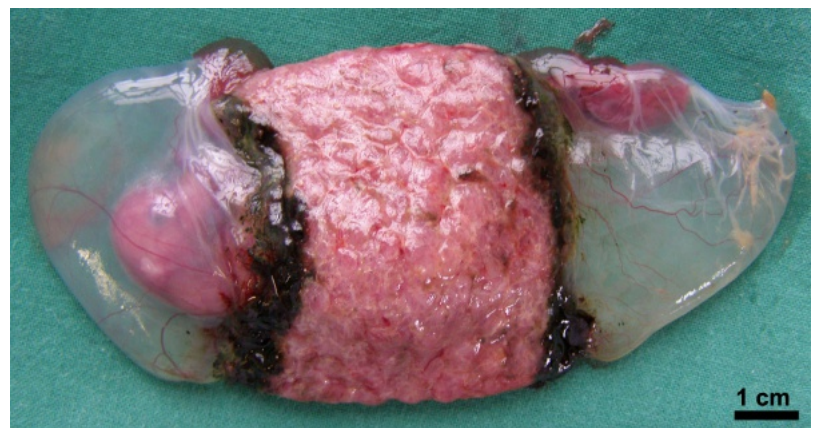
Fetus in utero, between fifth and sixth months



CT term placental blood vessels showing branching pattern of placental artery.

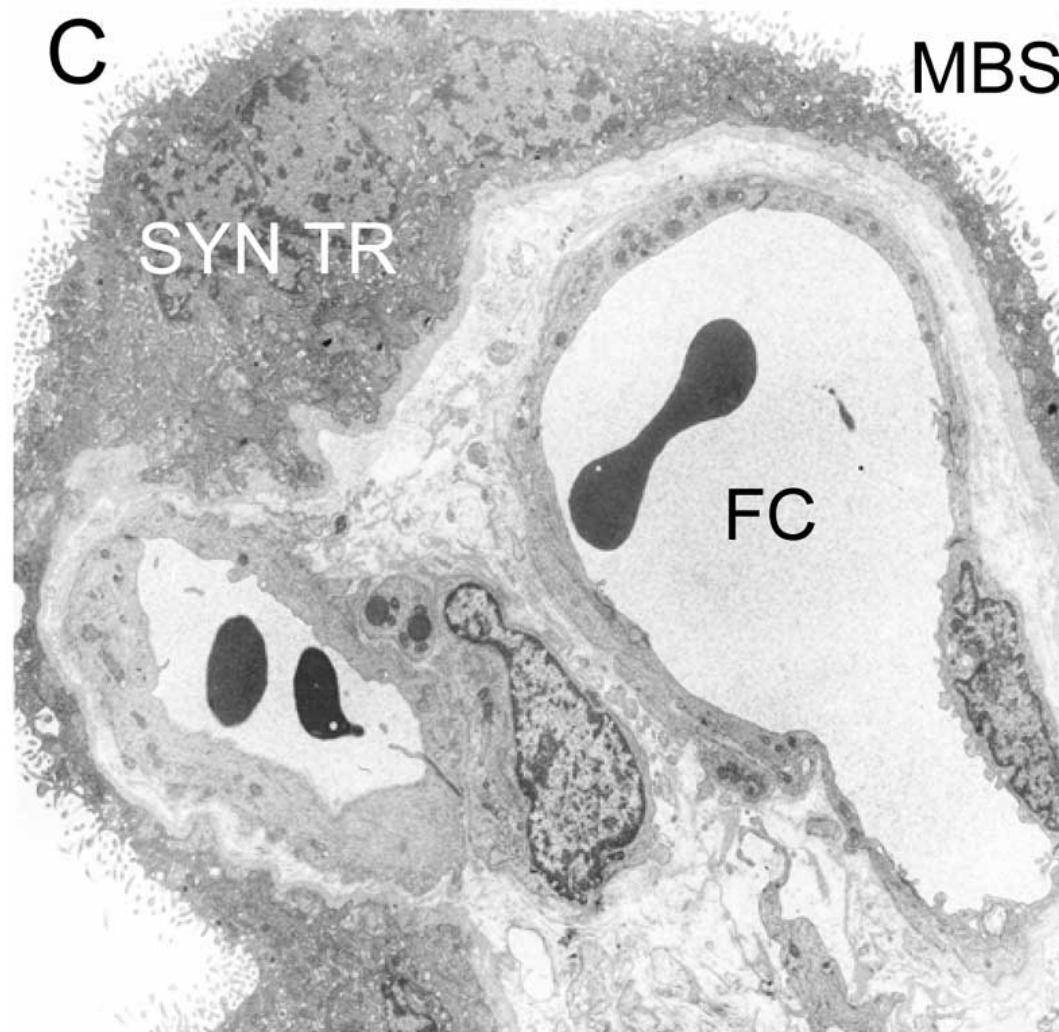
Placental Classification

Classification of placenta is on the basis of histological (microscopic) structural organization and layers between fetal and maternal circulation, giving 3 main groups:



- **Haemochorial** - placenta where the chorion comes in direct contact with maternal blood (human)
- **Endotheliochorial** - maternal endometrial blood vessels are bare to their endothelium and these comes in contact with the chorion. (dogs, cats)
- **Epitheliochorial** - maternal epithelium of the uterus comes in contact with the chorion. considered as primitive (pigs, cows)

The presence of these three differing types of placenta have also been used to describe the pattern mammalian evolution. See also Placental Layers

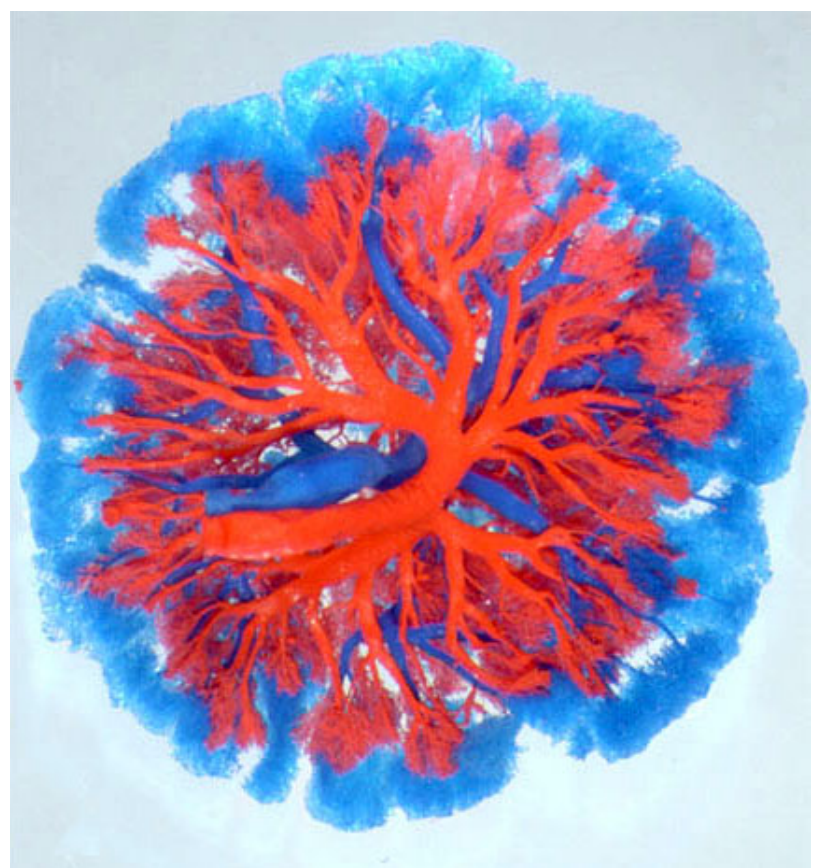


Haemochorial human placenta

Placental Types

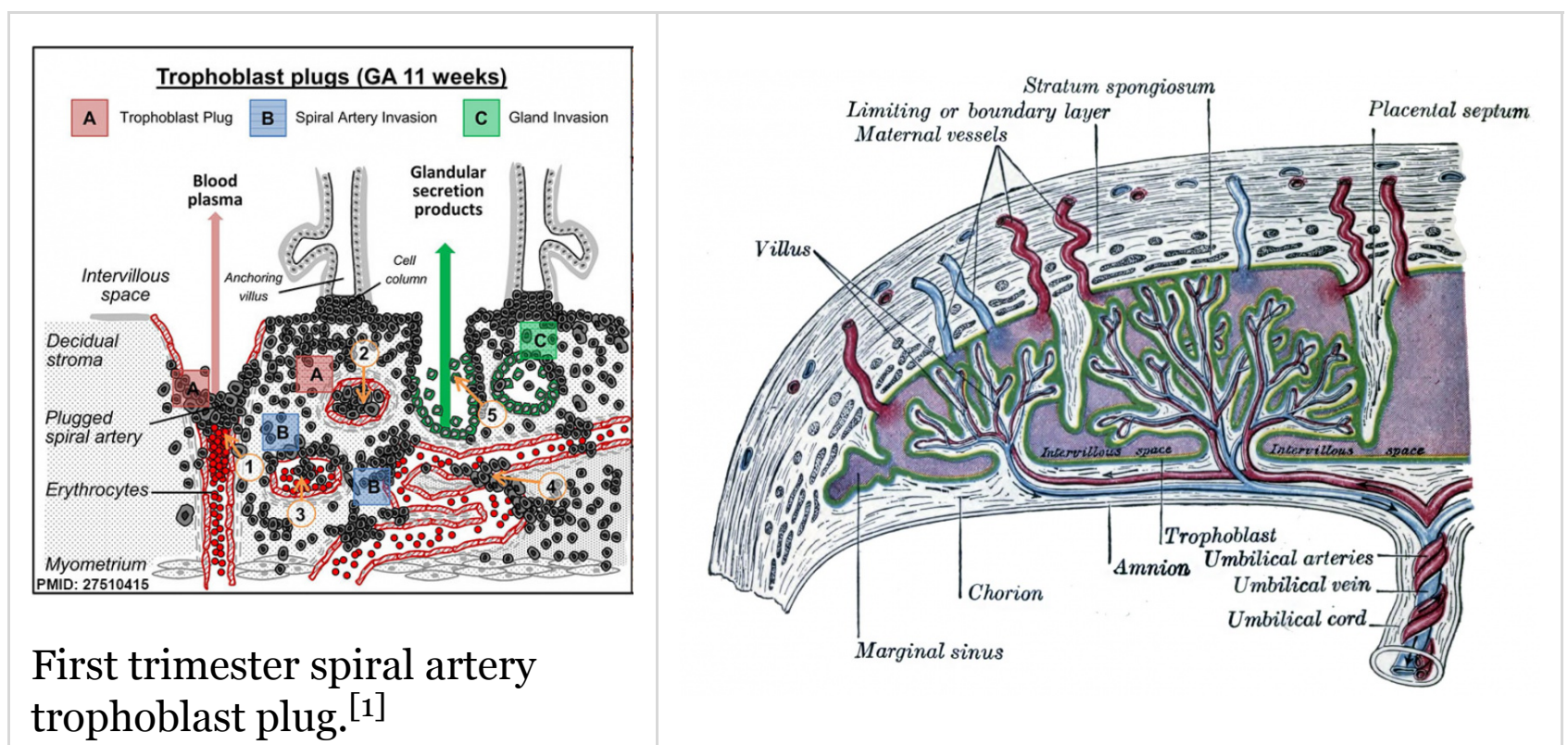
- Discoid in humans, mice, insectivores, rabbits, rats, and monkeys.
- Zonary in dogs, cats, bears and seals.
- Cotyledenary in cows, deer, goat, and giraffe.
- Diffuse in horses, pigs, camels, lemurs, opossums, kangaroos, and whales

Links: [Comparative Placentation](#)

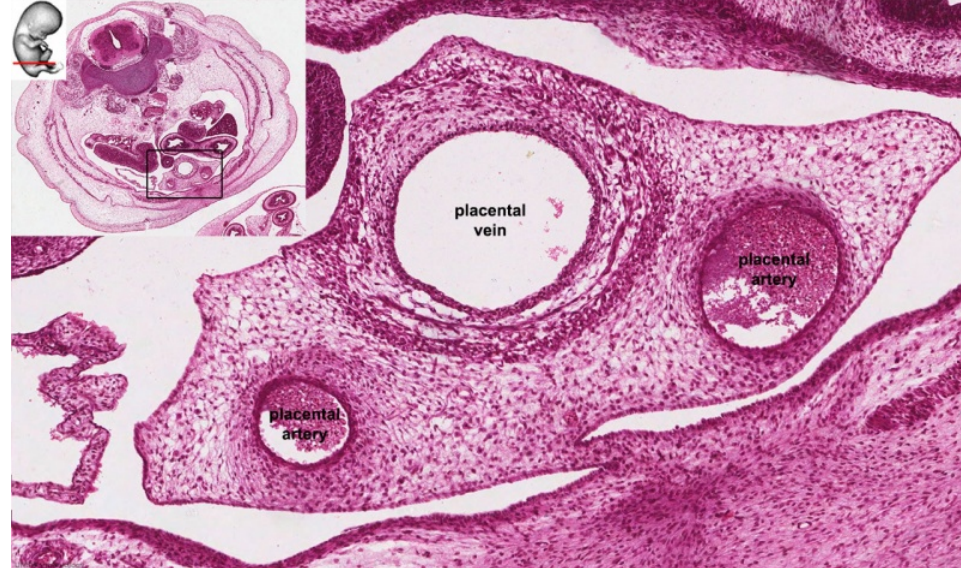
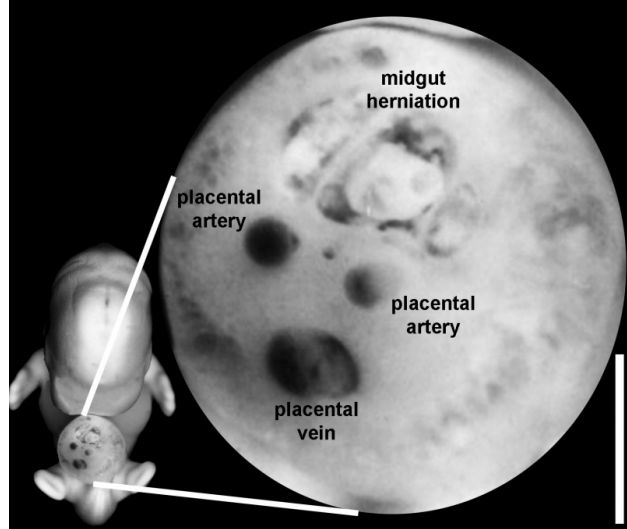


Chorionoic Villi Trimester Development

- **Trimester 1 and 2** - immature intermediate villi, developmental steps towards the stem villi.
- **Trimester 3** - mature intermediate villi develop during the last trimester, produce numerous terminal villi.
 - Terminal villi are not active outgrowths caused by trophoblast proliferation, passive protrusions induced by capillary coiling due to excessive longitudinal growth of the fetal capillaries within the mature intermediate villi.
 - Capillary bed arrangement in the terminal villi can vary from simple U-like loops to branched network, due to capillary elongation and sprouting.(Data from PMID 2327595)

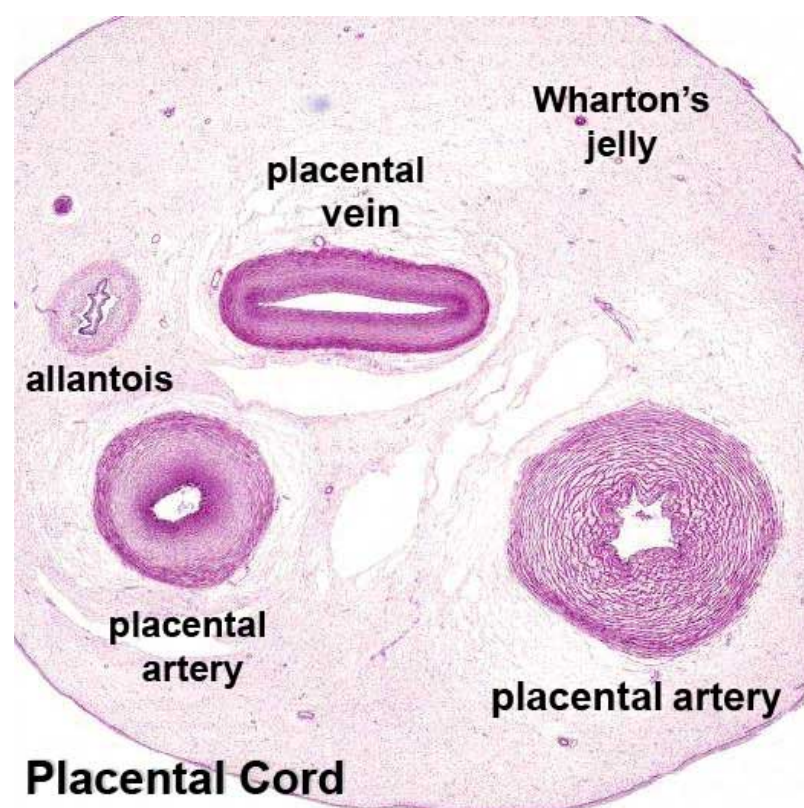
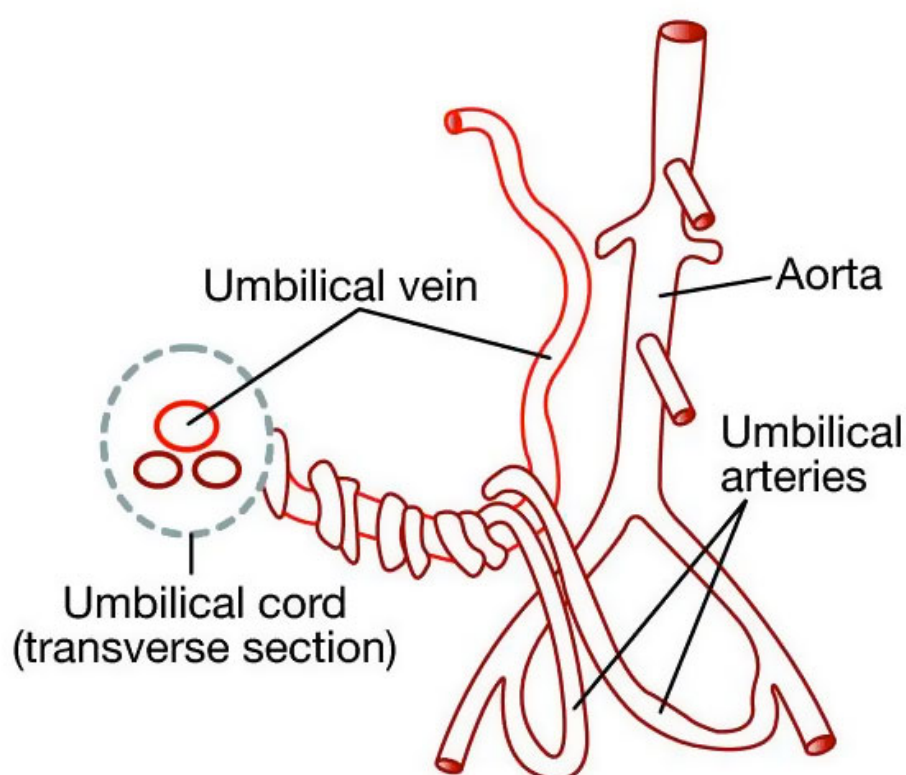


Placental Cord Blood Vessels



Week 6 Umbilicus containing initial placental cord.

Week 8 Embryo showing the placental blood vessels within the ventral body wall.



Placental Cord

- initially in the connecting stalk (then umbilical cord) anastomose in chorion
 - extend maternally - toward chorionic villi
 - extend embryonically - to the sinus venosus and dorsal aorta
- **Arteries** - paired, carry deoxygenated blood (from dorsal aorta) and waste products to the placental villi
- **Veins** - paired initially then **only left** at end of embryonic period, carry oxygenated blood to the embryo (sinus venosus)

Placental Function

- 4 layers separate maternal and fetal blood: syncytiotrophoblast, cytotrophoblast, villi connective tissue and fetal capillary endothelium
- 3 main functions: metabolism, transport and endocrine

Placental Metabolism

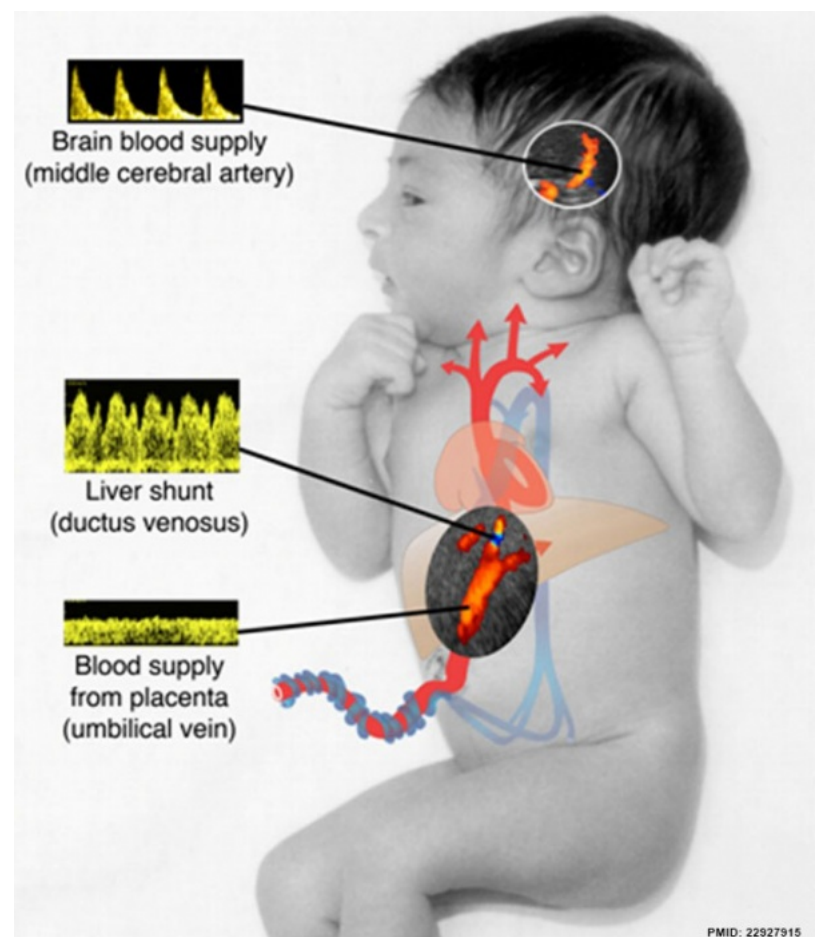
Synthesizes: glycogen, cholesterol, fatty acids

- provides nutrient and energy

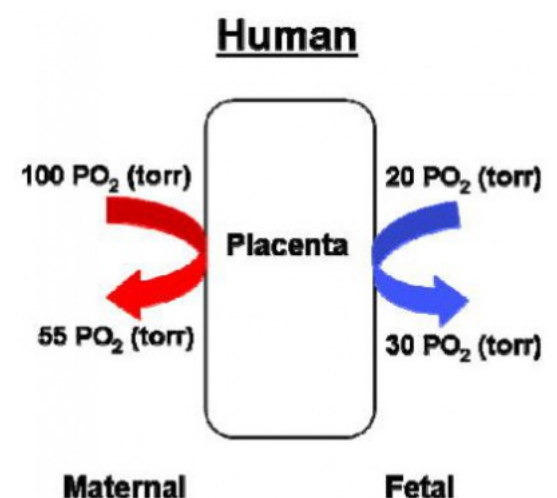
Placental Transport

gases and nutrition

- oxygen, carbon dioxide, carbon monoxide
- water, glucose, vitamins
- hormones, mainly steroid not protein
- electrolytes
- maternal antibodies



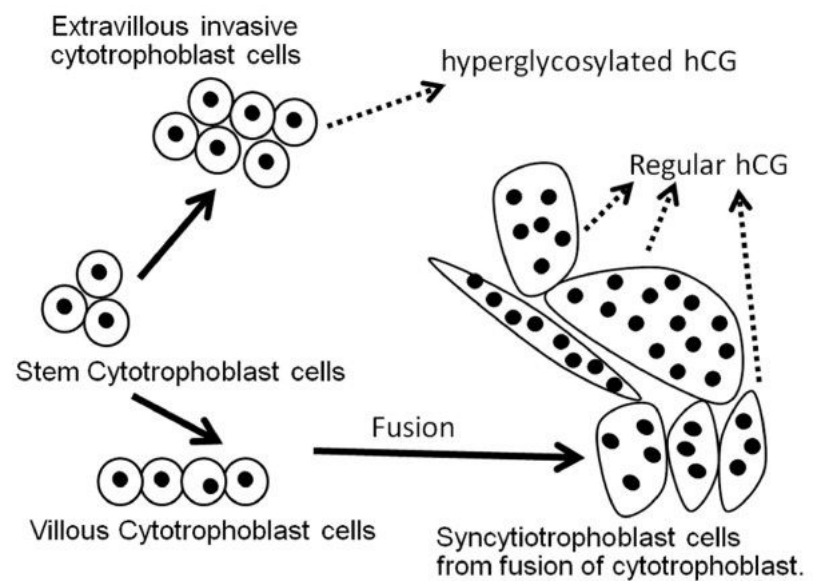
Fetal blood flow liver and brain



- waste products - urea, uric acid, bilirubin
- drugs and their metabolites (fetal drug addiction)
- infectious agents (cytomegalovirus, rubella, measles, microorganisms)

Placental Endocrine

- Human chorionic gonadotrophin (hCG) - like leutenizing hormone, supports corpus luteum
- Human chorionic somatomotropin (hCS) (or placental lactogen) - hormone level increases in maternal blood through pregnancy, decreases maternal insulin sensitivity (raising maternal blood glucose levels and decreasing maternal glucose utilization) aiding fetal nutrition ("anti-insulin" function)
- Human chorionic thyrotropin (hCT) - Peptide placental hormone, similar to anterior pituitary released thyroid stimulating hormone (TSH), which along with human chorionic gonadotrophin (hCG) is thought to act on maternal thyroid. There is little recent research published on this hormone, its level and activities.
- Human chorionic corticotropin (hCACTH) - placental hormone thought to have corticotropin (ACTH)-like activity, increasing maternal cortisol levels.
- Steroid Hormones
 - progestins - progesterone, support of the endometrium and suppress uterine smooth muscle contractility.
 - estrogens - estriol, stimulate growth of the myometrium and mammary gland development.
 - both hormones support maternal endometrium
- Relaxin - Humans high levels early in pregnancy than at birth promotes angiogenesis probably plays a role in development of the uterus/ placenta than in the birth process



Fetal Placenta

Trophoblast cells are the major source of placental hormones.

Placental growth hormone

(PGH) is mainly expressed in the syncytiotrophoblast cells (PGH differs from pituitary derived growth hormone by 13 amino acids).

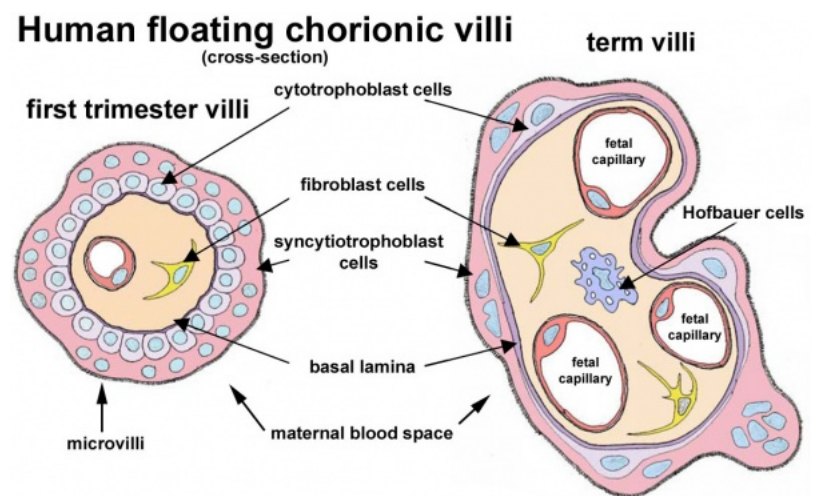
extravillous cytotrophoblast - arise from anchoring villi invade the uterine spiral arteries, generating fibrinoid material and endovascular trophoblastic cells. syncytiotrophoblast

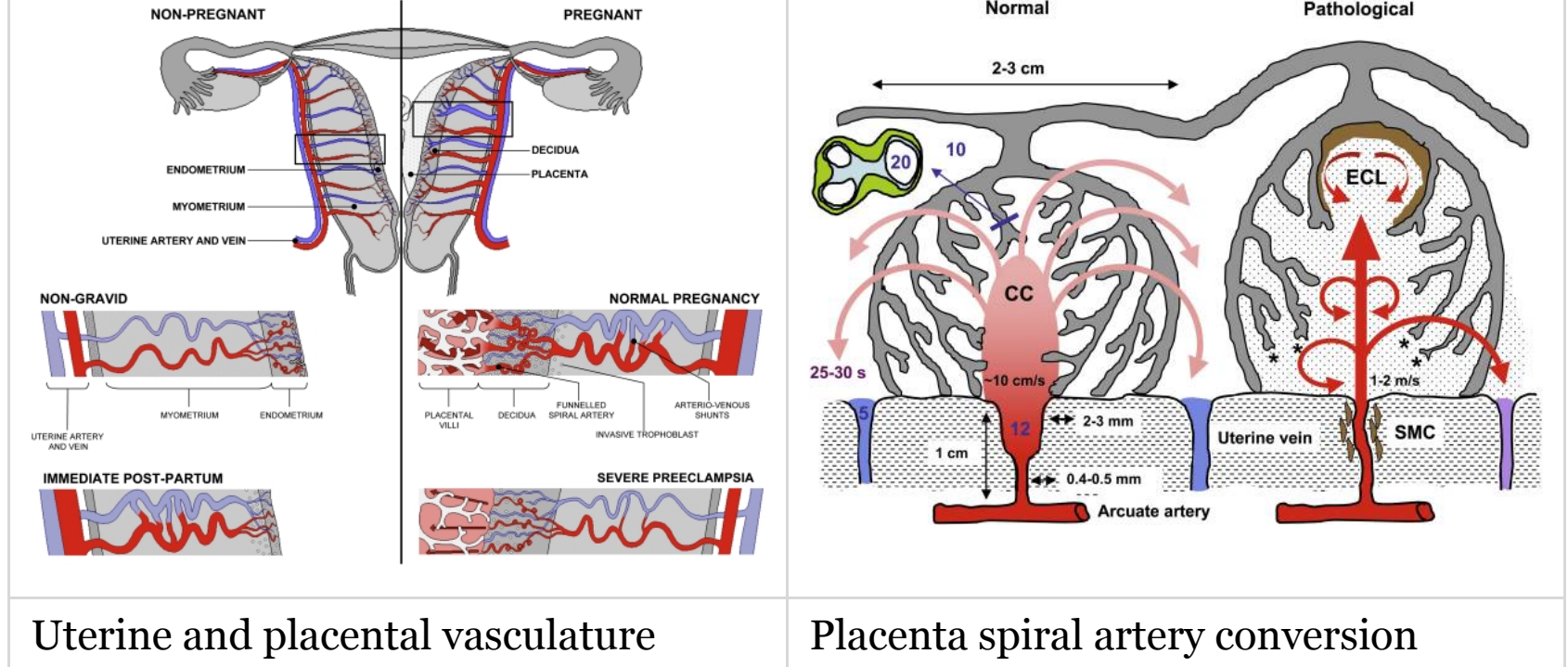
Fetal Blood Vessels At least 2 phases of development during pregnancy driven by vascular endothelial growth factor (VEGF):

1. Initially cytotrophoblasts are the cellular stimulus to vasculogenesis and angiogenesis.
2. Later Hofbauer (lacental villi macrophages of mesenchymal origin) and stromal cells take over the stimulation of blood vessel development.

Placenta Human chorionic gonadotrophin (hCG) After implantation cells within the developing placenta (syncytiotrophoblasts) synthesize and secrete Human chorionic gonadotrophin (hCG) into the maternal bloodstream. The main function of serum hCG is to maintain the corpus luteum in the maternal ovary and therefore maintain the early pregnancy, that is block the menstrual cycle. Later the placenta itself supports the pregnancy.

Maternal Placenta





Fibrinoid - said to exist as 2 forms of extracellular matrix:

1. Fibrin-type fibrinoid is a maternal blood-clot product which replaces degenerative syncytiotrophoblast
2. Matrix-type fibrinoid is secreted by invasive extravillous trophoblast cells.

Fibrinoid layer (Nitabuch's layer) is thought to act to prevent excessively deep implantation.

Decidualization - process of endometrial stromal cells (fibroblast-like) change in morphology (polygonal cells) and protein expression and secretion (specific decidual proteins: prolactin, insulin-like growth factor binding protein-1, tissue factor, interleukin-15, and VEGF).

1. Estrogen and progesterone - receptive phase, luminal and glandular epithelial cells change in preparation for blastocyst adplantation.
2. Human Chorionic gonadotropin - luminal epithelium endoreplication leading to epithelial plaque formation.
3. Human Chorionic gonadotropin - trophoblast invasion and decidualization of human stromal fibroblasts.

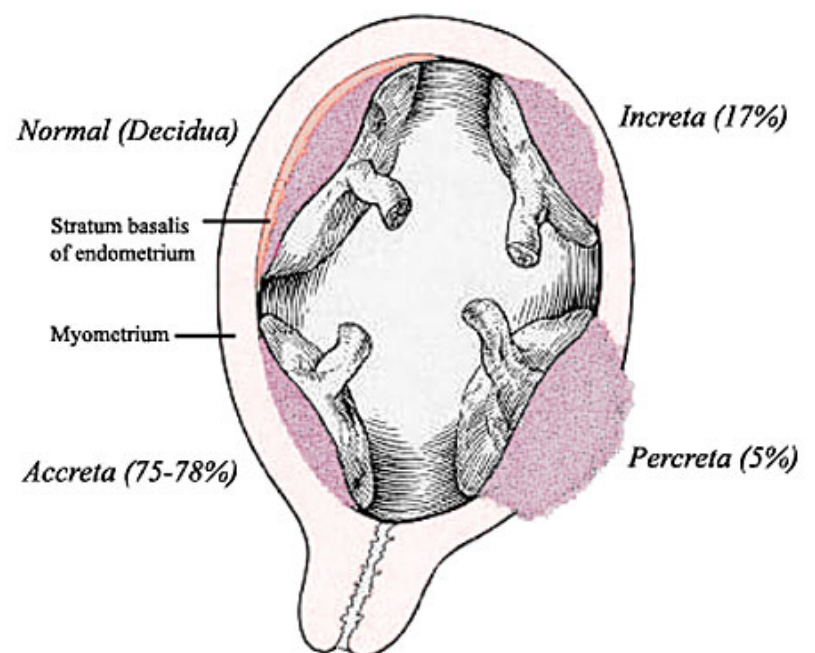
Artery Dilatation - due to extravillous trophoblast cells invading uterine wall and maternal spiral arteries replacing both smooth muscle with fibrinoid material and part of vessel endothelium. There is also a proliferation of maternal blood vessels.

Other changes

- Endoreplication - rounds of nuclear DNA replication without intervening cell or nuclear division (mitosis).
 - Cytokines - of maternal origin also act on placental development.
 - Natural Killer (NK) cells - 30% of all the decidual cells towards the end of the first trimester of pregnancy. These lymphocytes are present in the maternal decidua in large numbers (70%, normal circulating blood lymphocytes 15%) close to the extravillous trophoblast cells. Have a cytolytic potential against virus-infected and tumor-transformed cells.
1. ↑ Gregor Weiss, Monika Sundl, Andreas Glasner, Berthold Huppertz, Gerit Moser **The trophoblast plug during early pregnancy: a deeper insight.** Histochem. Cell Biol.: 2016; [PubMed 27510415](#)

Placental Abnormalities

- **Placenta Accreta** - abnormal adherence, with absence of decidua basalis. The incidence of placenta accreta also significantly increases in women with previous cesarean section compared to those without a prior surgical delivery.
- **Placenta Increta** - occurs when the placenta attaches deep into the uterine wall and penetrates into the uterine muscle, but does not penetrate the uterine serosa. Placenta increta accounts for approximately 15-17% of all cases.
- **Placenta Percreta** - placental villi penetrate myometrium and through to uterine serosa.
- **Placenta Previa** - In this placental abnormality, the placenta overlies internal os of uterus, essentially covering the birth canal. This



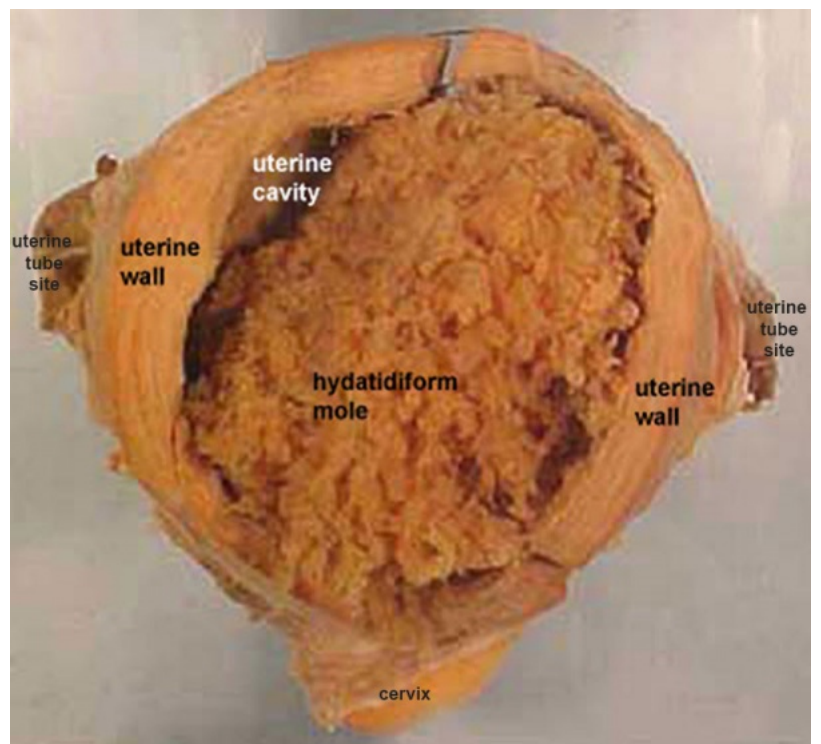
condition occurs in approximately 1 in 200 to 250 pregnancies. In the third trimester and at term, abnormal bleeding can require cesarian delivery and can also lead to Abruption Placenta. Ultrasound screening programs during 1st and early 2nd trimester pregnancies now include placental localization. Diagnosis can also be made by transvaginal ultrasound.

- Vasa Previa** - (vasa praevia) placental abnormality where the fetal vessels lie within the membranes close too or crossing the inner cervical os (opening). This occurs normally in 1:2500-5000 pregnancies and leads to complications similar too those for Placenta Previa. Type II is defined as the condition where the fetal vessels are found crossing over the internal os connecting either a bilobed placenta or a succenturiate lobe with the main placental mass. Some recent evidence of successful in utero laser ablation of type II vasa previa at 22.5 weeks of gestation.
- Abruption Placenta** - a retroplacental blood clot formation, abnormal hemorrhage prior to delivery.
- Chronic Intervillositis** - (massive chronicintervillositis, chronic histiocytic intervillositis) Rare placental abnormality and pathology defined by inflammatory placental lesions, mainly in the intervillous space (IVS), with a maternal infiltrate of mononuclear cells

Placenta previa



Historic model of placenta previa



Hydatidiform mole pathology

(monocytes, lymphocytes, histiocytes) and intervillous fibrinoid deposition.

- **Hydatidiform mole** - placental tumor with no embryo development. Several forms of hydatidiform mole: partial mole, complete mole and persistent gestational trophoblastic tumor. Many of these tumours arise from a haploid sperm fertilizing an egg without a female pronucleus (the alternative form, an embryo without sperm contribution, is called parthenogenesis). The tumour has a "grape-like" placental appearance without enclosed embryo formation. Following a first molar pregnancy, there is approximately a 1% risk of a second molar pregnancy.

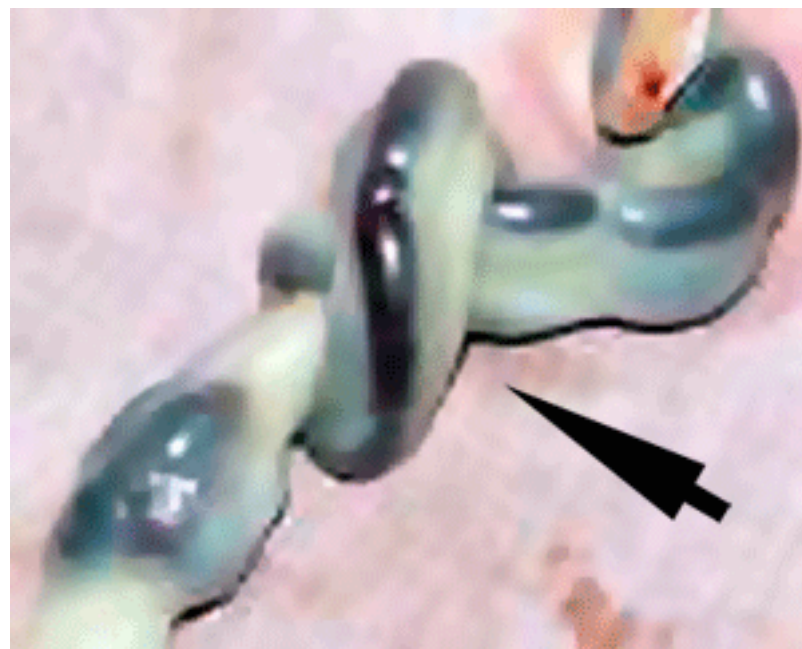
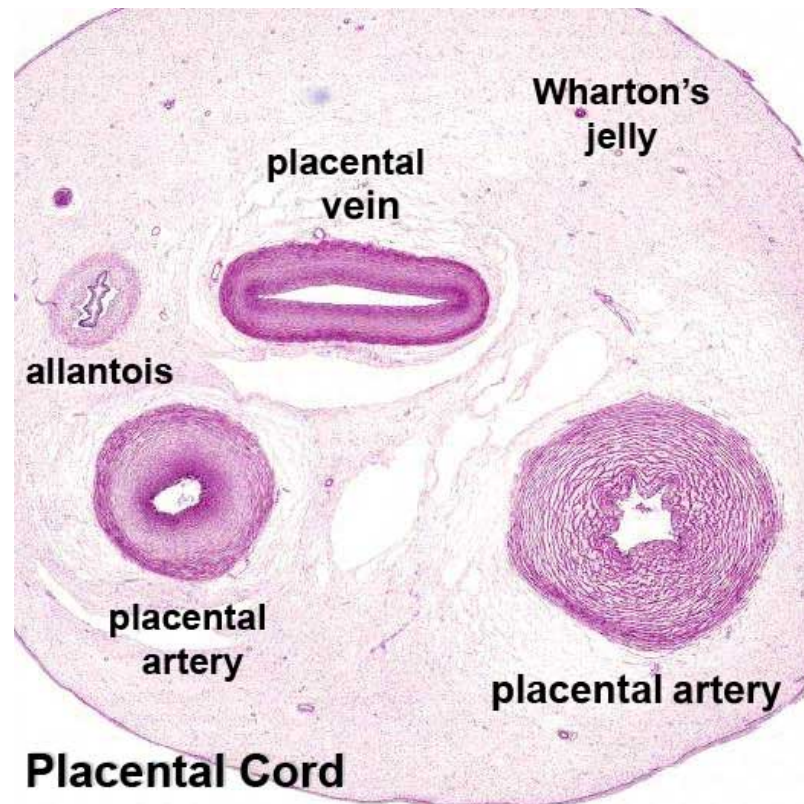
- **Placenta Abnormalities**

- Placenta abnormalities
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- Placenta percreta MRI
- Placenta previa and increta
- Bilobed placenta and velamentous cord
- Placenta velamentous cord
- Multilobed placenta MRI
- Circumvallate placenta
- Monochorionic twin placenta
- Placental chorioangioma
-
-

Links: [Placenta - Abnormalities](#)

Placental Cord Abnormalities

There are few abnormalities associated with umbilical cord development, other than abnormally short or long cords, which in most cases do not cause difficulties. In some cases though, long cords can wrap around limbs or the fetus neck, which can then restrict blood flow or lead to tissue or nerve damage, and therefore affect development.



- **Cord knotting** - can also occur (1%) in most cases these knots have no effect, in some cases of severe knotting this can prevent the passage of placental blood.
- **Cord torsion** - Rare event where even without knot formation can also affect placental blood flow, even leading to fetal demise.

Placental Infections

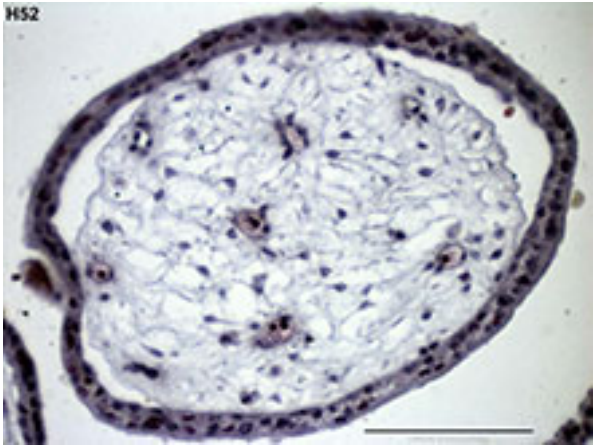
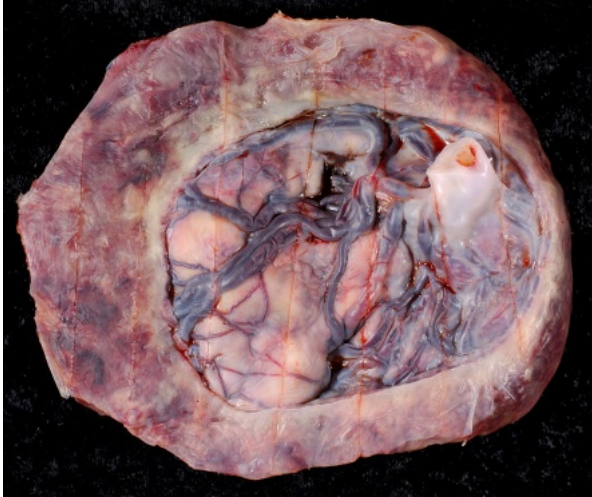
- Several infective agents may cross into the placenta from the maternal circulation, as well as enter the embryo/fetal circulation. The variety of bacterial infections that can occur during pregnancy is as variable as the potential developmental effects, from virtually insignificant to a major developmental, abortive or fatal in outcome.
- Pregnant women have an increased susceptibility to malaria infection. Malarial infection of the placenta by sequestration of the infected red blood cells leading to low birth weight and other effects. There are four types of malaria caused by the protozoan parasite *Plasmodium falciparum* (main), *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*). This condition is common in regions where malaria is endemic with women carrying their first pregnancy (primigravida).

Placental Pathology

MH - content in this section is not examinable.

- Chronic Villitis - can occur following placental infection leading to maternal inflammation of the villous stroma, often with associated intervillitis. The inflammation can lead to disruption of blood flow and necrotic cell death.
- Massive Chronic Intervillitis (MCI) - maternal blood-filled space is filled with CD68-positive histiocytes and an increase in fibrin, occurring more commonly in the first trimester.
- Meconium Myonecrosis - prolonged meconium exposure leads to toxic death of myocytes of placental vessels (umbilical cord or chorionic plate).
- Neuroblastoma - a fetal malignancy that leads to an enlarged placenta, with tumor cells in the fetal circulation and rarely in the chorionic villi.
- Thrombophilias - (protein C or S deficiency, factor V Leiden, sickle cell disease, antiphospholipid antibody) can generate an increased fibrin/fibrinoid deposition in the maternal or intervillous space, this can trap and kill villi.

Additional Images

Virtual Slides	
<div>Placental Villi</div> <div></div> <div>Mobile Desktop Original</div> <div>Placenta Embryo Slides</div> <div>Tertiary Villi cross-section</div>	<div>Human Circumvallate Placenta</div> <div></div> <div>Mobile Desktop Original</div> <div>Placenta Abnormal Embryo Slides</div> <div>Abnormal placenta</div>

[Historic - Fetal Membranes Images](#)

- Isolated villi from chorion frondosum of a human embryo of eight weeks
- Section of chorion of human embryo of one month (9 mm)
- Histology of the placenta - diagrammatic representations of the minute structure of the placenta

External Links

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- [Comparative Placentation](#)
- [University of Ottawa - Histology - Placenta](#)
- Virtual Microscopy Histology

Placenta Terms

[Placenta Terms](#) (expand to view) [Expand]

Other Terms Lists [Expand]

[2018 ANAT2341](#) - [Timetable](#) | [Course Outline](#) | **[Moodle](#)** | [Tutorial 1](#) | [Tutorial 2](#) | [Tutorial 3](#)

Labs: [1 Preimplantation and Implantation](#) | [2 Reproductive Technology Revolution](#) | [3 Group Projects](#) | [4 GM manipulation mouse embryos](#) | [5 Early chicken eggs](#) | [6 Female reproductive tract](#) | [7 Skin regeneration](#) | [8 Vertebral development](#) | [9 Organogenesis Lab](#) | [10 Cardiac development](#) | [11 Group projects](#) | [12 Stem Cell Journal Club](#)

Lectures: [1 Introduction](#) | [2 Fertilization](#) | [3 Week 1/2](#) | [4 Week 3](#) | [5 Ectoderm](#) | **[6 Placenta](#)** | [7 Mesoderm](#) | [8 Endoderm](#) | [9 Research Technology](#) | [10 Cardiovascular](#) | [11 Respiratory](#) | [12 Neural crest](#) | [13 Head](#) | [14 Musculoskeletal](#) | [15 Limb](#) | [16 Renal](#) | [17 Genital](#) | [18 Endocrine](#) | [19 Sensory](#) | [20 Fetal](#) | [21 Integumentary](#) | [22 Birth](#) | [23 Stem cells](#) | [24 Revision](#)

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