

Lecture 4

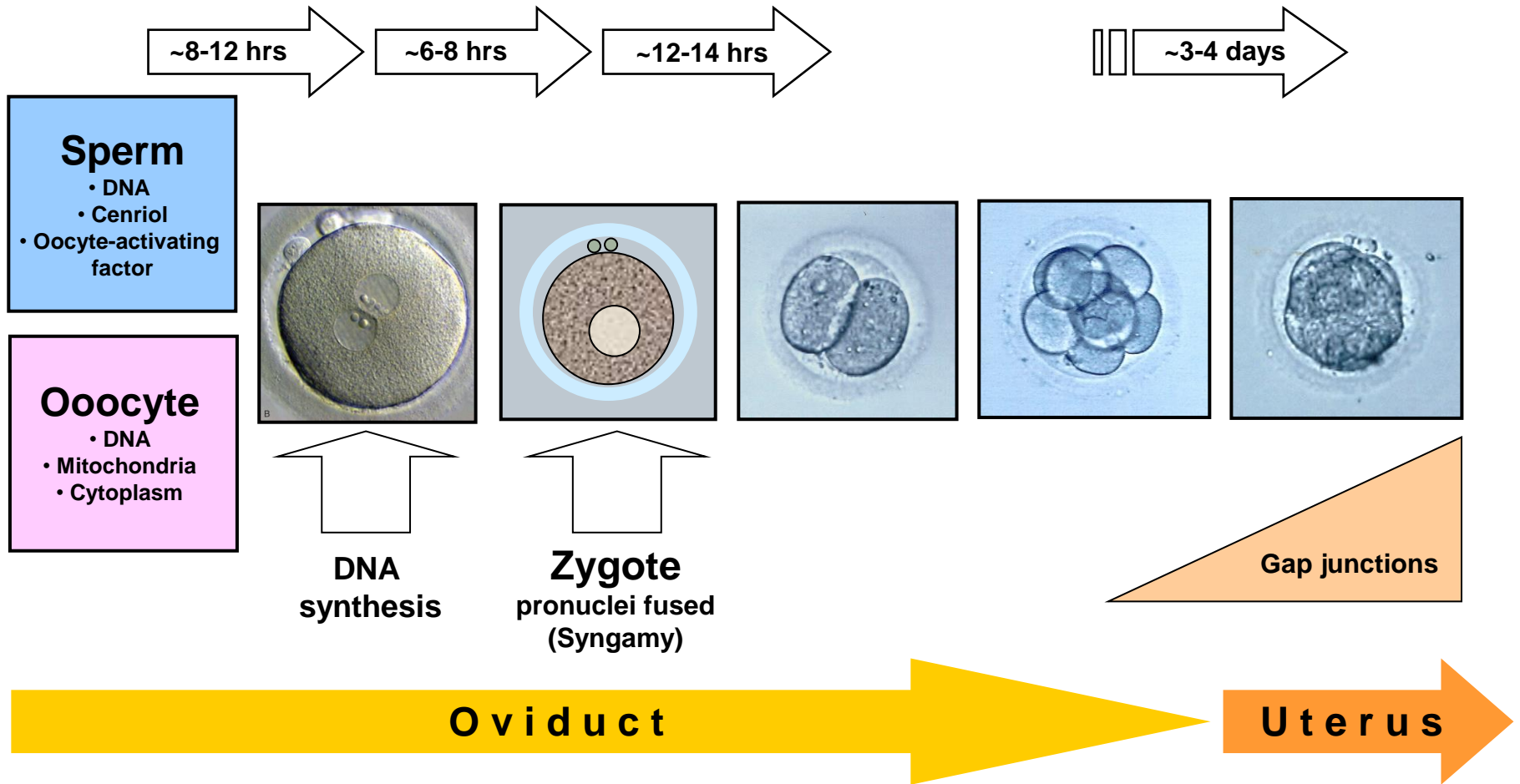
Reproductive biology and Embryology

- Early embryo cleavages
- Implantation
- Somatic nuclear transfer– cloning
- Gastrulation
- Extraembryonal structures
- Fetal membranes
- Placenta

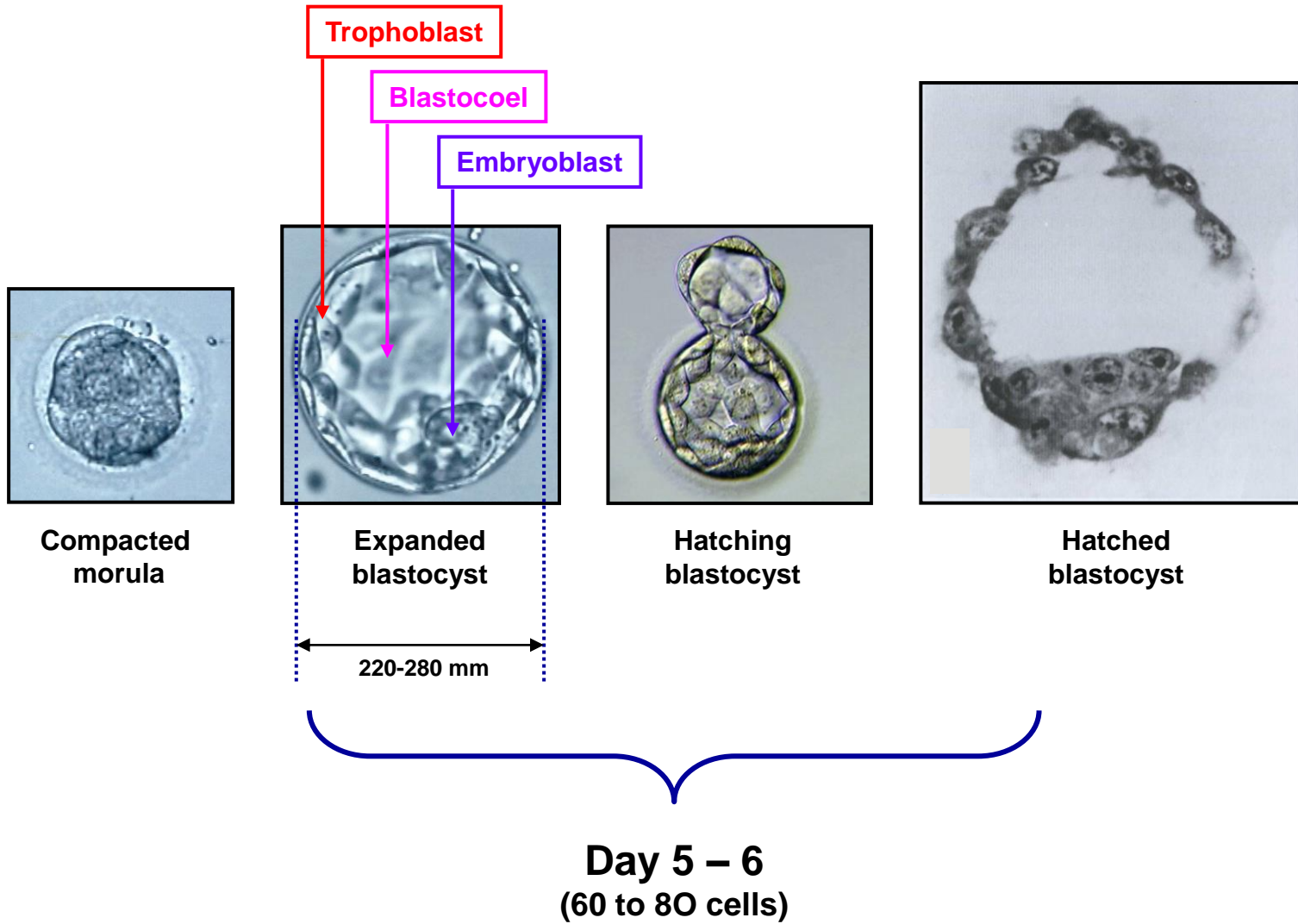
Brno, March 2024

Fertilization

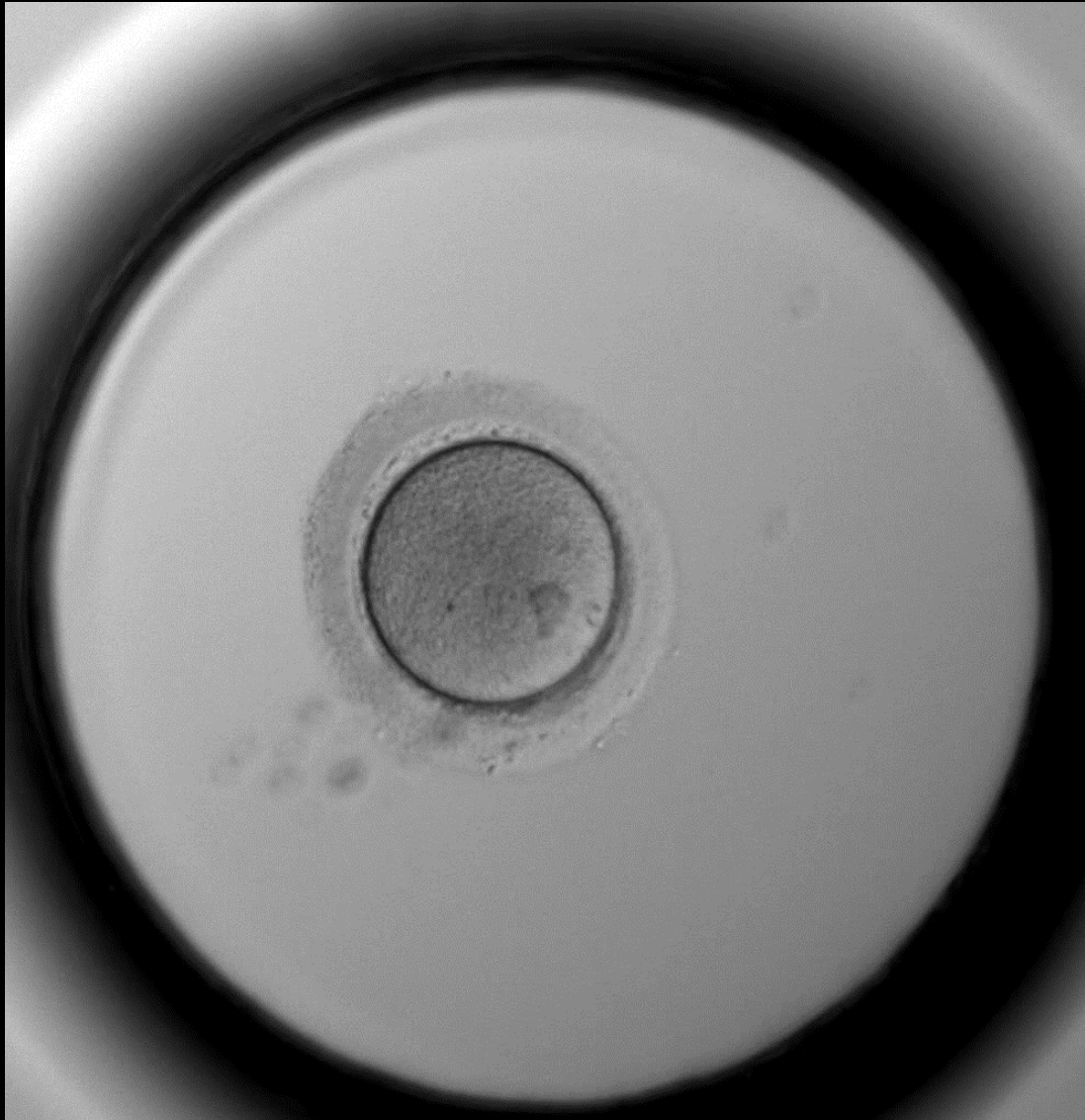
Zygote formation and the first cleavages



Blastocyst formation

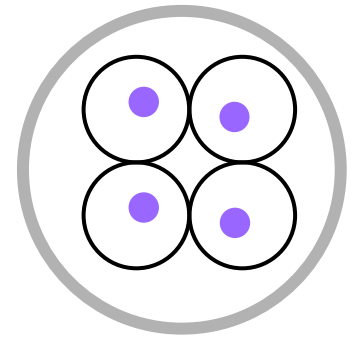
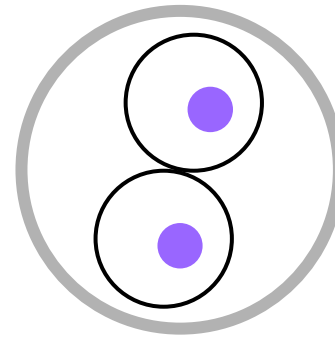
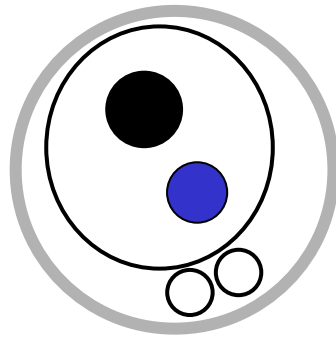
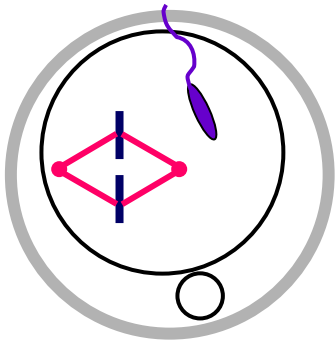
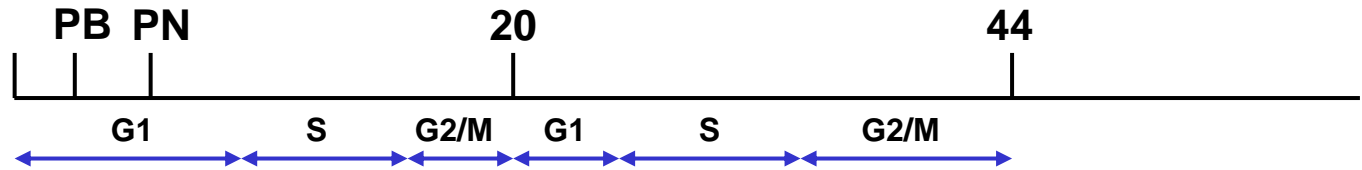


Early embryogenesis of human embryo



Dr. Zuzana Holubcová
Dept. Histology and Embryology + REPROFIT, Brno

A potency of oocyte cytoplasm



Translation of maternal mRNA

Translation of zygotic mRNA

Zygotic transcription

Activation of embryonal genome

Repression of transcription

Significance of „enhancers“

Activation of embryonal genome

It is not a single discrete event
(first signs occur in zygote, in man it reaches its maximum in 4- to 8-cell embryo)

Two types of transcripts

Transcripts that replace degraded maternal mRNAs

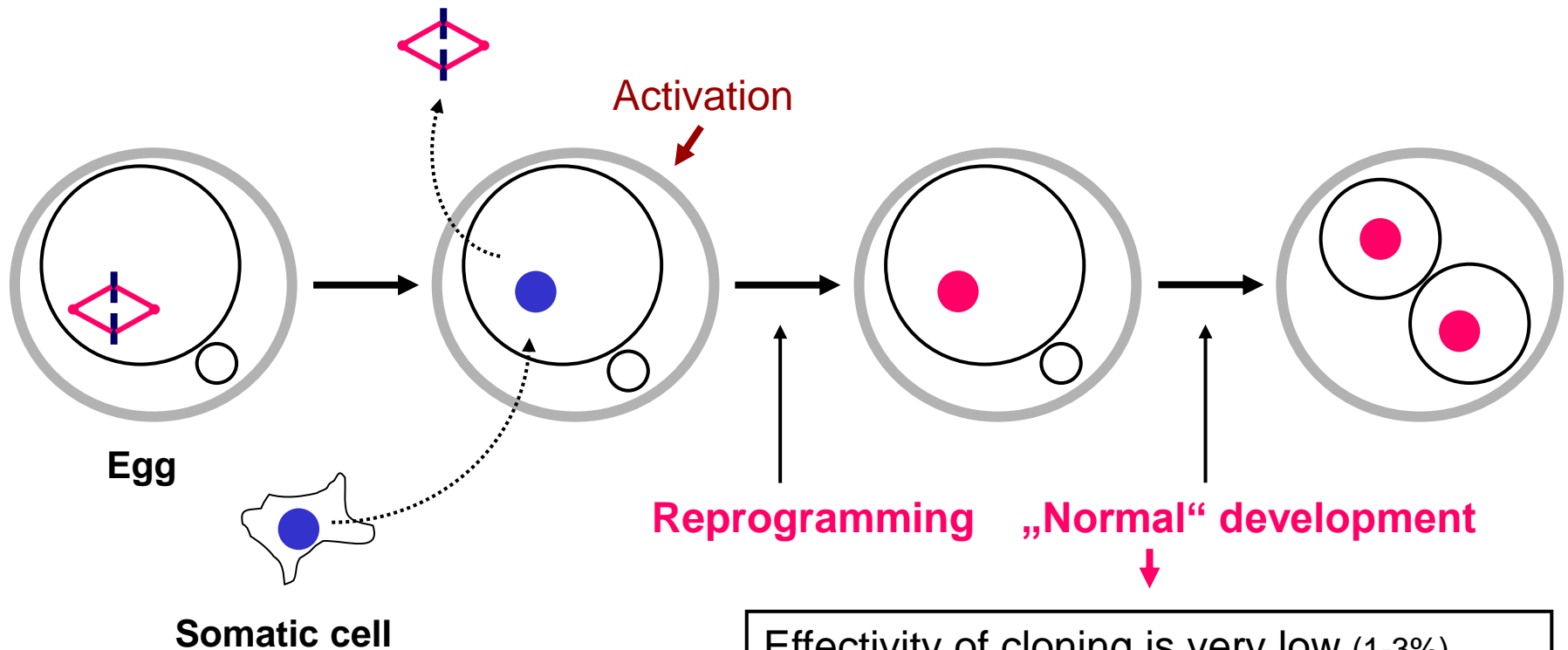
Novel transcripts that underlie **new pattern of gene expression**

It is „responsible“ for establishment of totipotency of blastomeres

&

It represents phenomenon known as genome REPROGRAMMING

Nuclear transfer (cloning) - principle



Effectivity of cloning is very low (1-3%)

Reprogramming is slow and most likely incomplete (as the result, gene expression is often abnormal)

Effectivity of reprogamming depends on many factors (type of somatic cells, position in cell cycle phase, ...)

Blastocyst implantation

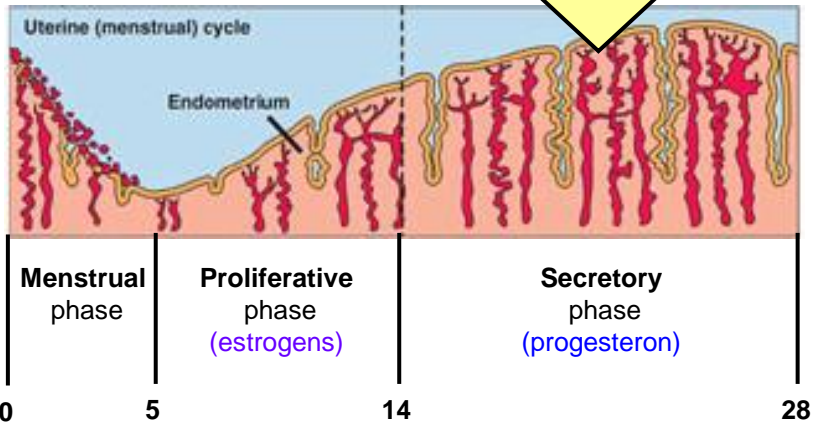


Molecular players

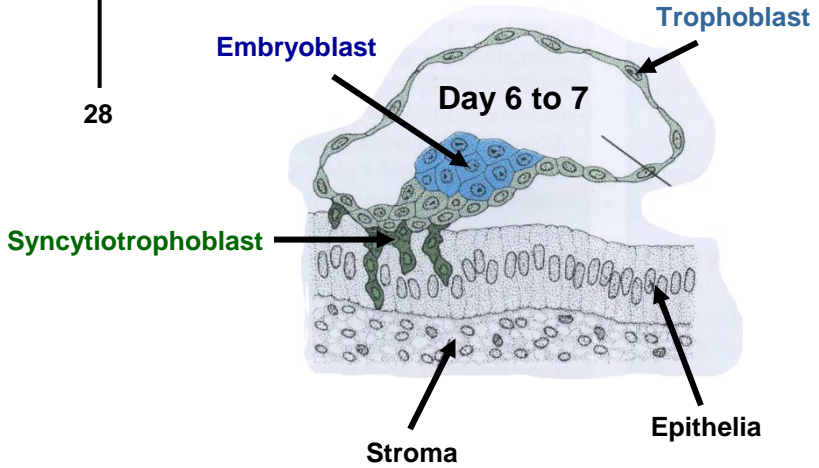
- Selectin on trophoblast + glycoproteins on epithelia
- Integrins + Laminin, Fibronectin
- IGF1, IGF2, VEGF
- Metalloproteinases + their tissue inhibitors
- Progesteron
- hCH
- Prostaglandins

Functional zone of endometrium

compact
+
spongius
+
basal



Ovulation followed by Fertilizaion



Blastocyst implantation

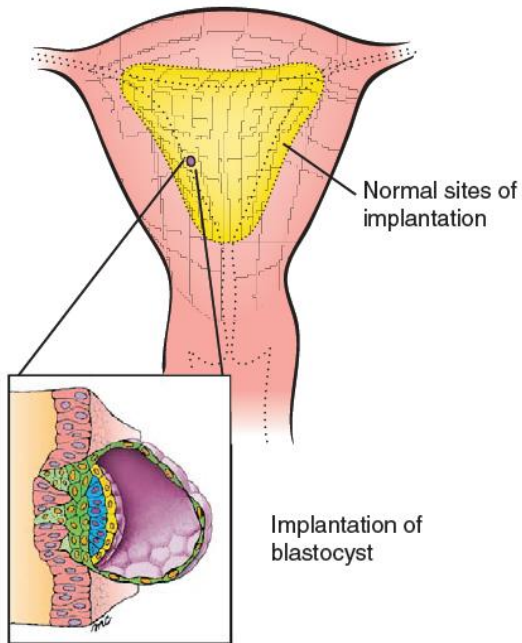


<http://myselfishgenes.blogspot.hu/2013/05/what-happens-to-my-embryos-if-they-do.html>

Blastocyst impantation – place of implantation

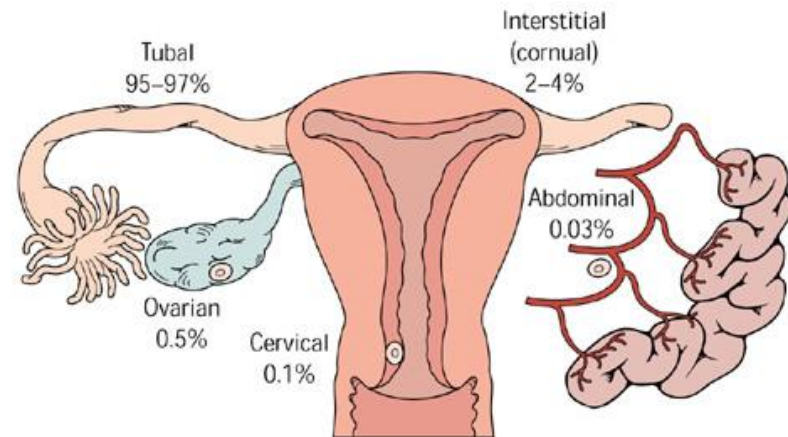
Normal

(posterior / anterior wall of uterus)



Abnormal

(0,25 až 1% of all implantations)



Early development – The second week (1)

Completion of implantation + Further embryo development

Trophoblast

- Furtner invasion into endometrium
- Damage to capillaries and glands
- Engulfment of apoptosing cells (Fas/Fas ligand)

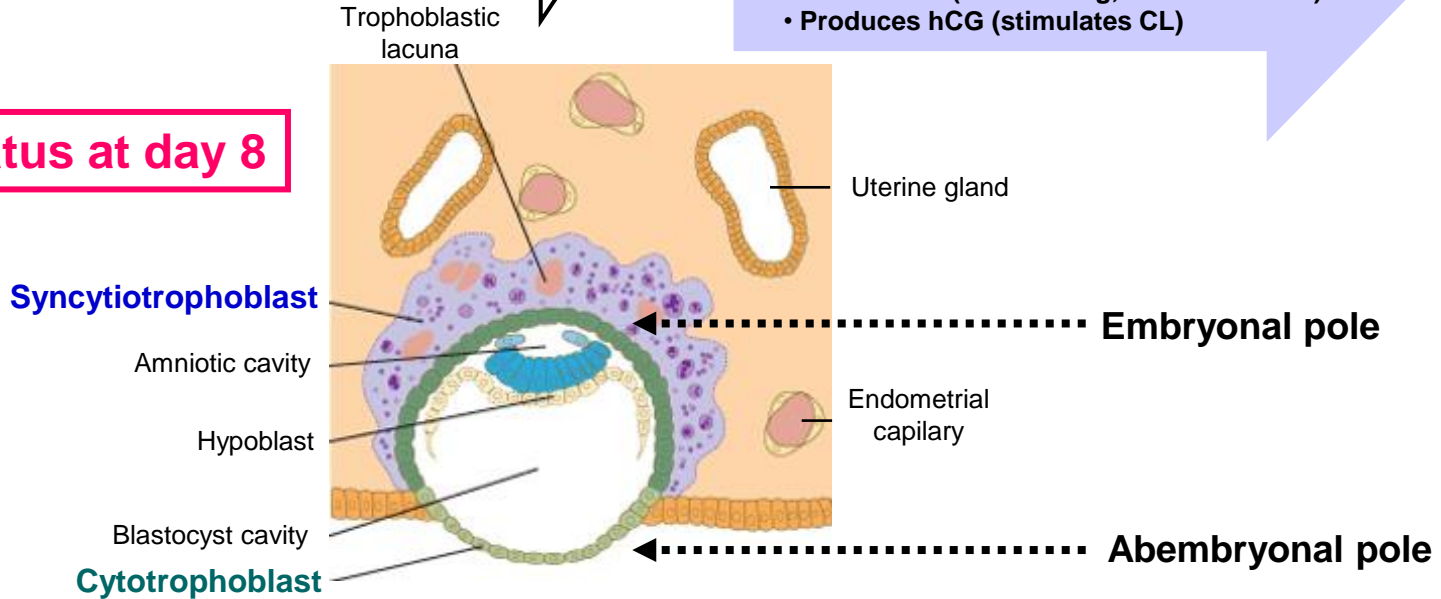
Cytotrophoblast

- Mitoticaly dividing cell (single layer)
- Supply for syncytiotrophoblast

Syncytiotrophoblast

- Fused cells (nondividing, multinucleated)
- Produces hCG (stimulates CL)

Status at day 8



Early development – The second week (2)

Decidual reaction of endometrium

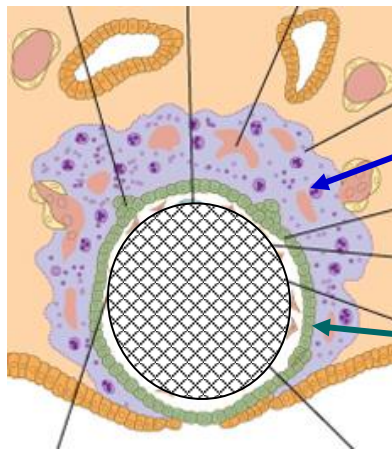
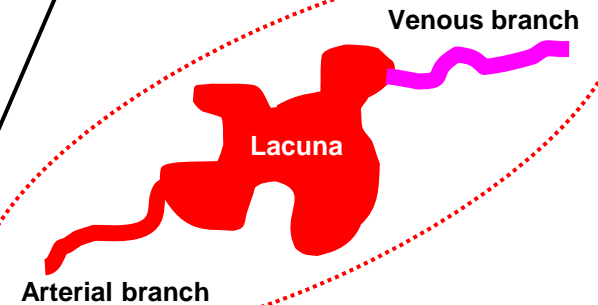
Vessel number/density increases

Fibroblasts differentiate into glycogen- and lipid-containing cells

Fused lacunae create a network

Uterine vessels erode

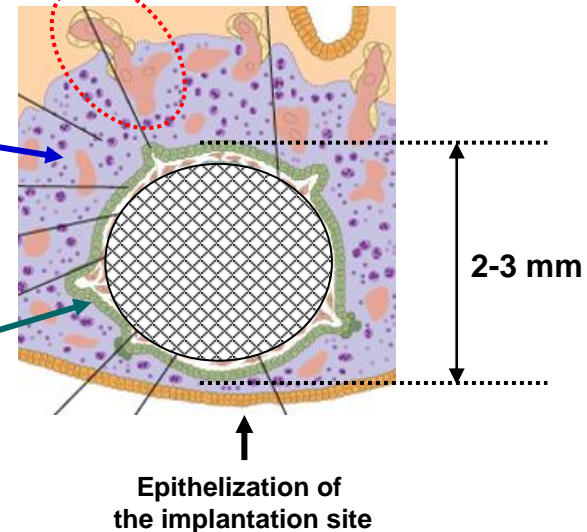
Uteroplacental circulation



Status at day 10

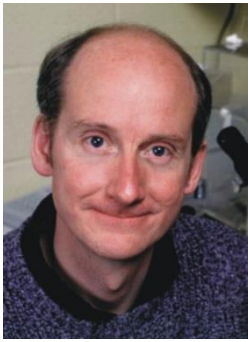
Syncytiotrophoblast
Sponge-like appearance

Cytotrophoblast



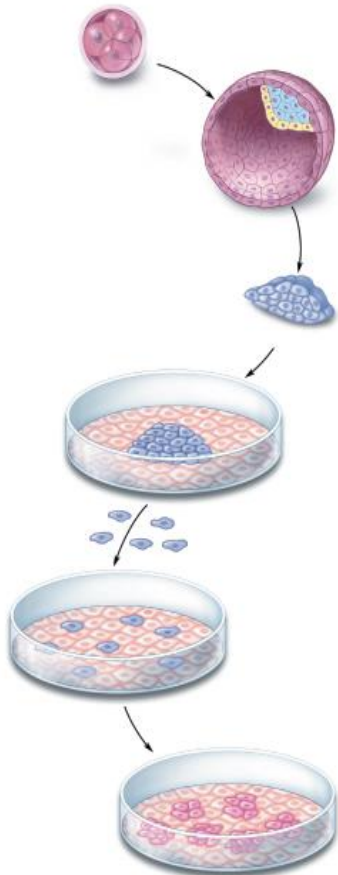
Status at day 12

Epithelization of the implantation site



Human Embryonic Stem (hES) Cells

(Thompson et al, 1998)

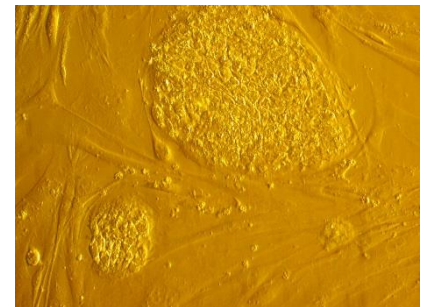
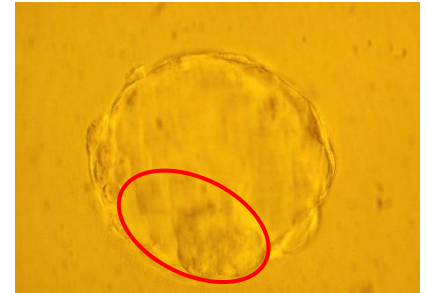


Early embryo at blastocyst stage

Isolated embryoblast (ICM - Inner Cell Mass)

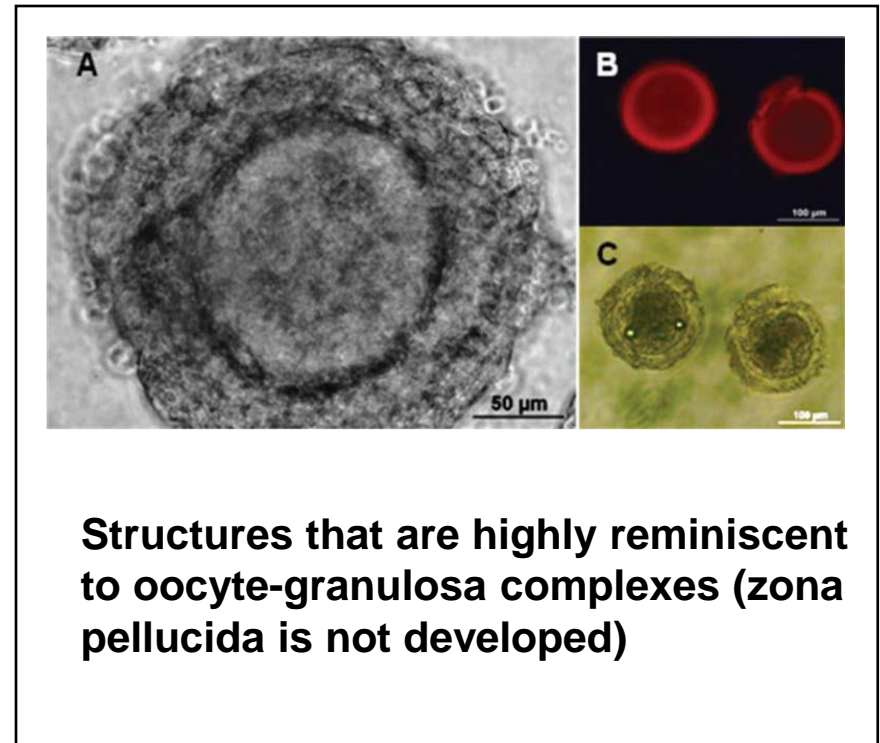
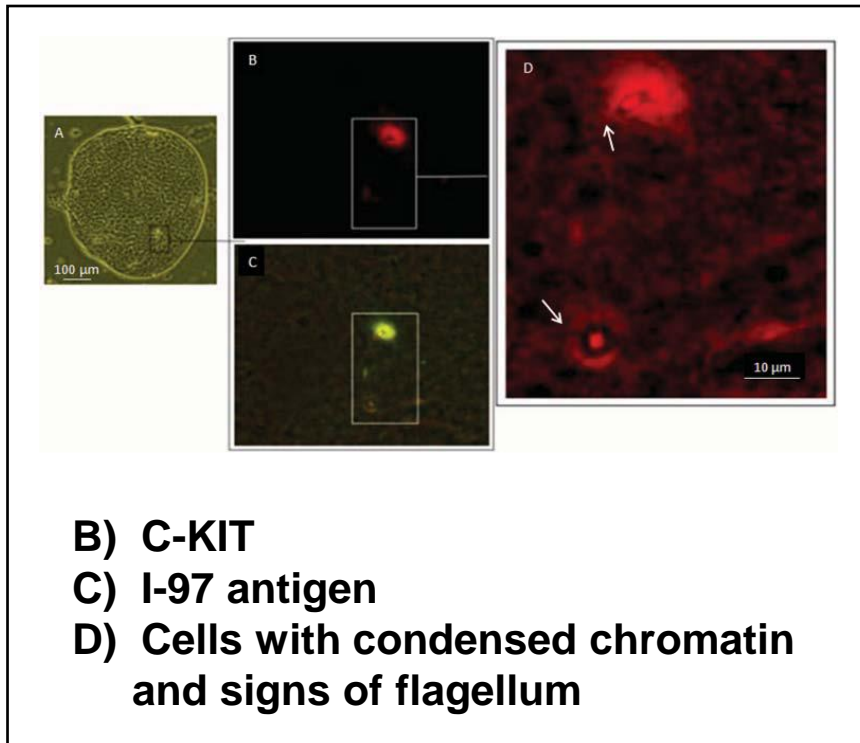
Isolated embryoblast after placing to *in vitro* conditions (+ feeder cells + FGF2)

Propagation in culture by enzymatic disaggregation (repeated passaging)



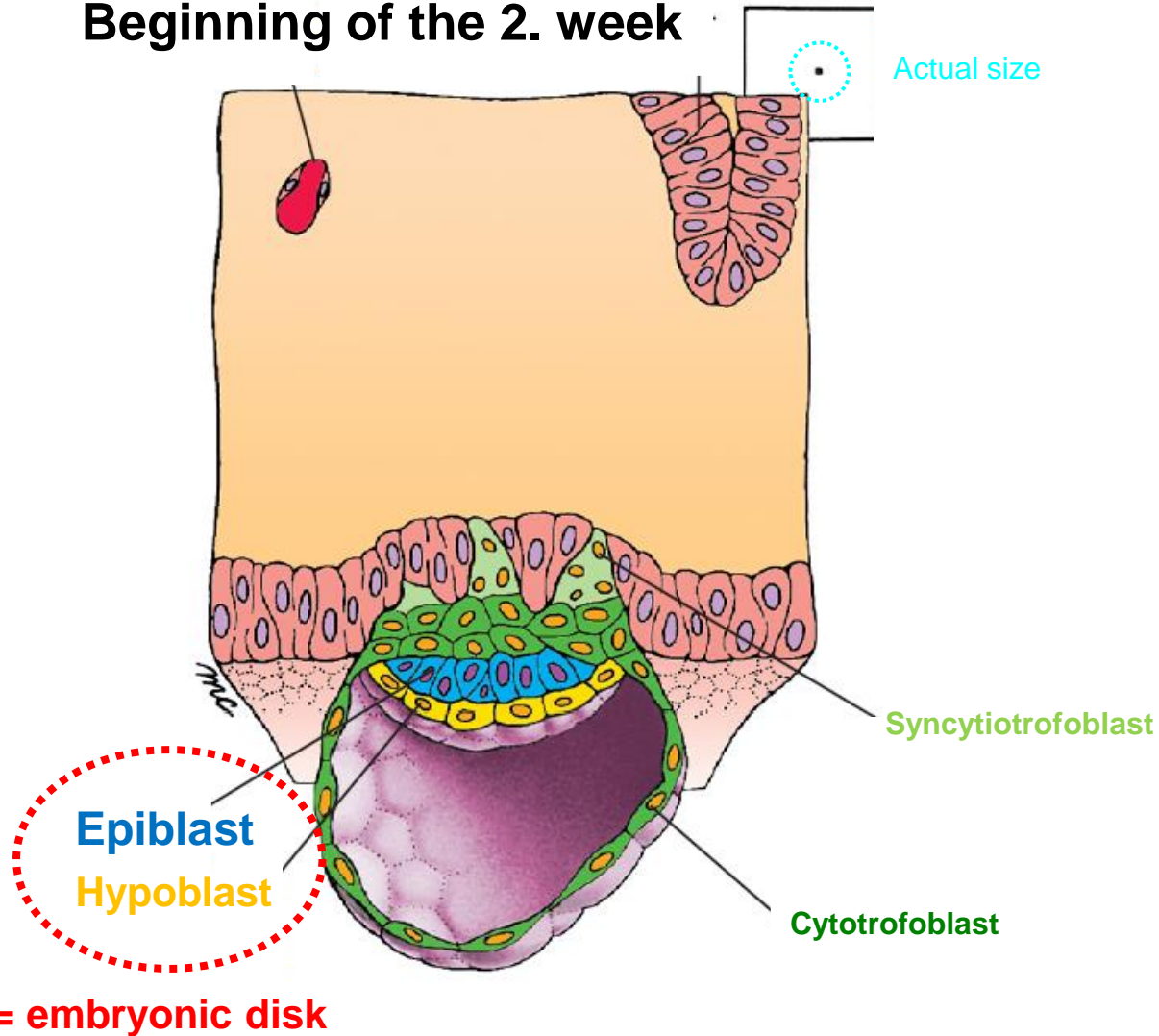
Derivation of postmeiotic germ cells from hESC

Prof. Harry Moore, University of Sheffield, 2009



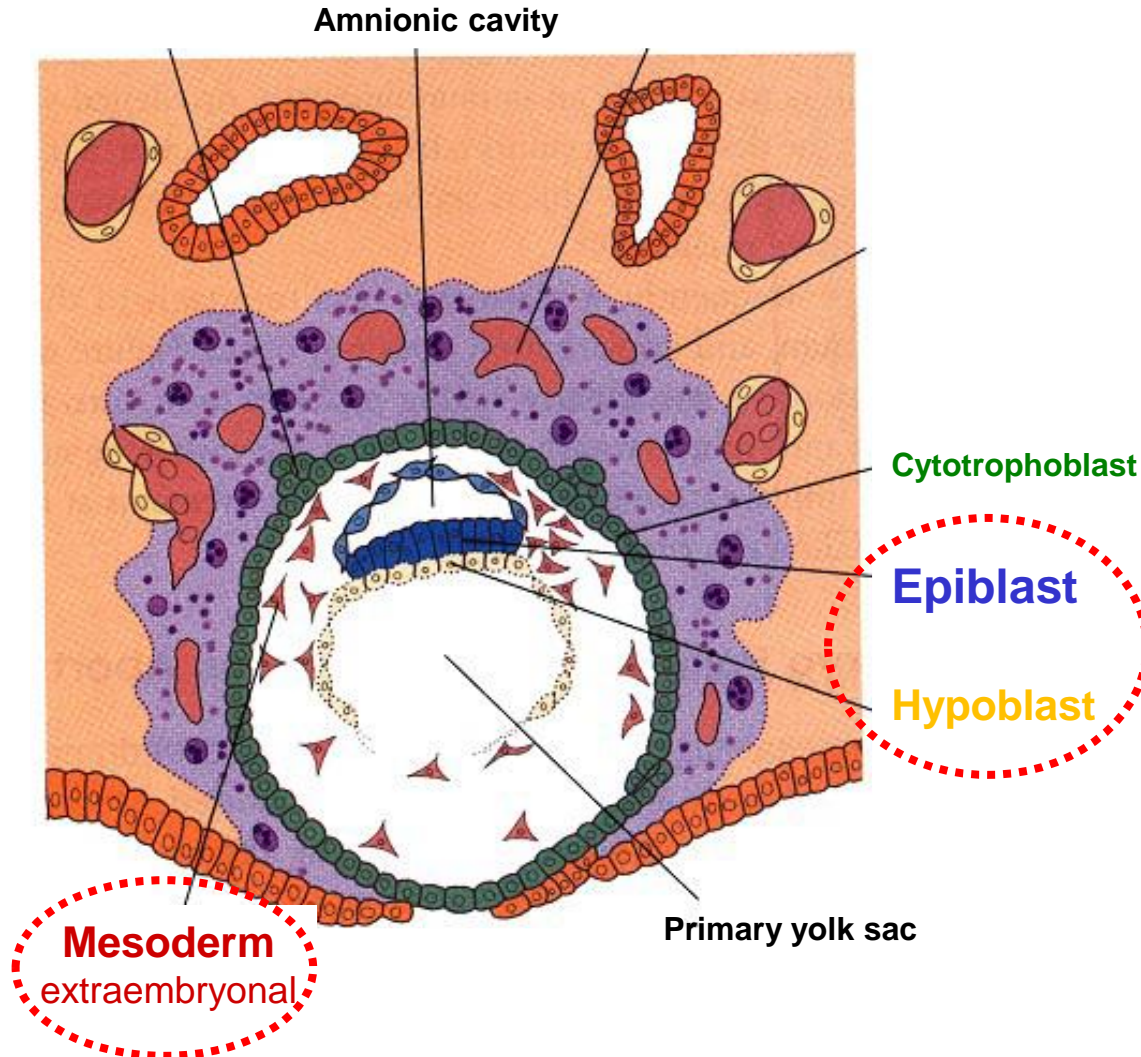
Gastrulation – establishment of three germ layers

Beginning of the 2. week



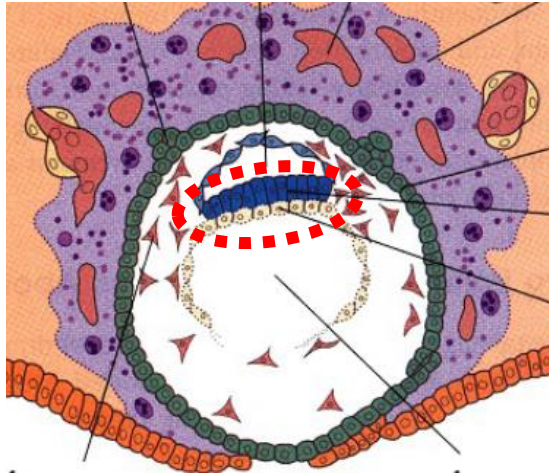
Gastrulation – establishment of three germ layers

Day 8 to 9



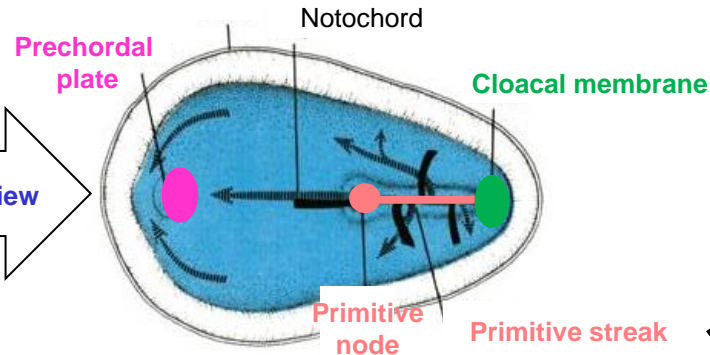
Gastrulation – establishment of three germ layers

Embryonic disk – first at day 6 to 7

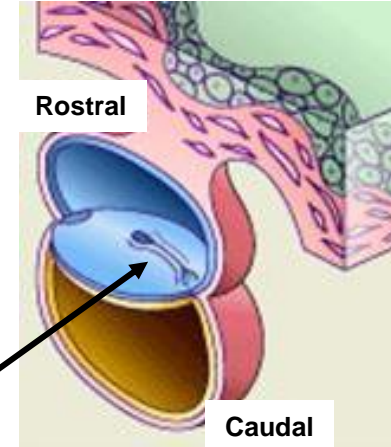


Dorsal view

Rostral ← → Caudal



Transversal section



Rostral

Caudal

Primitive streak (groove)

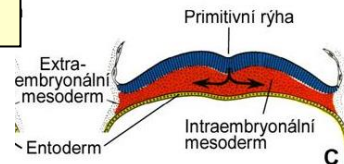
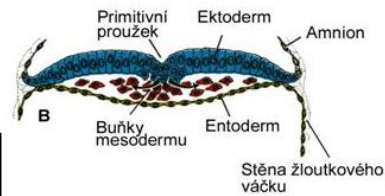
Ectodermal epithelial cells

Endodermal cells

Mesodermal cells

Hypoblast

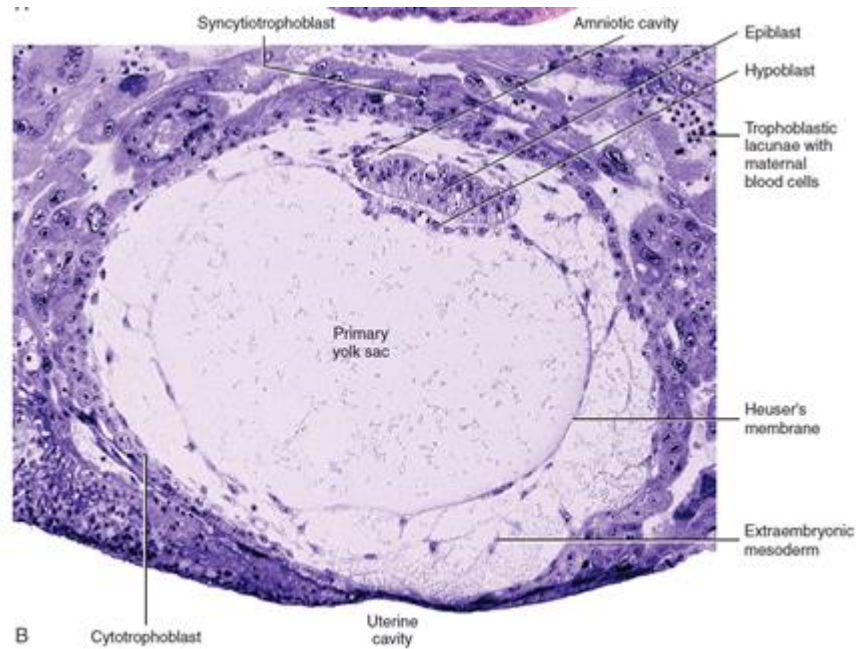
Specification of Mesoderm + Endoderm (expanded view)



= epithelio-mesenchymal transition

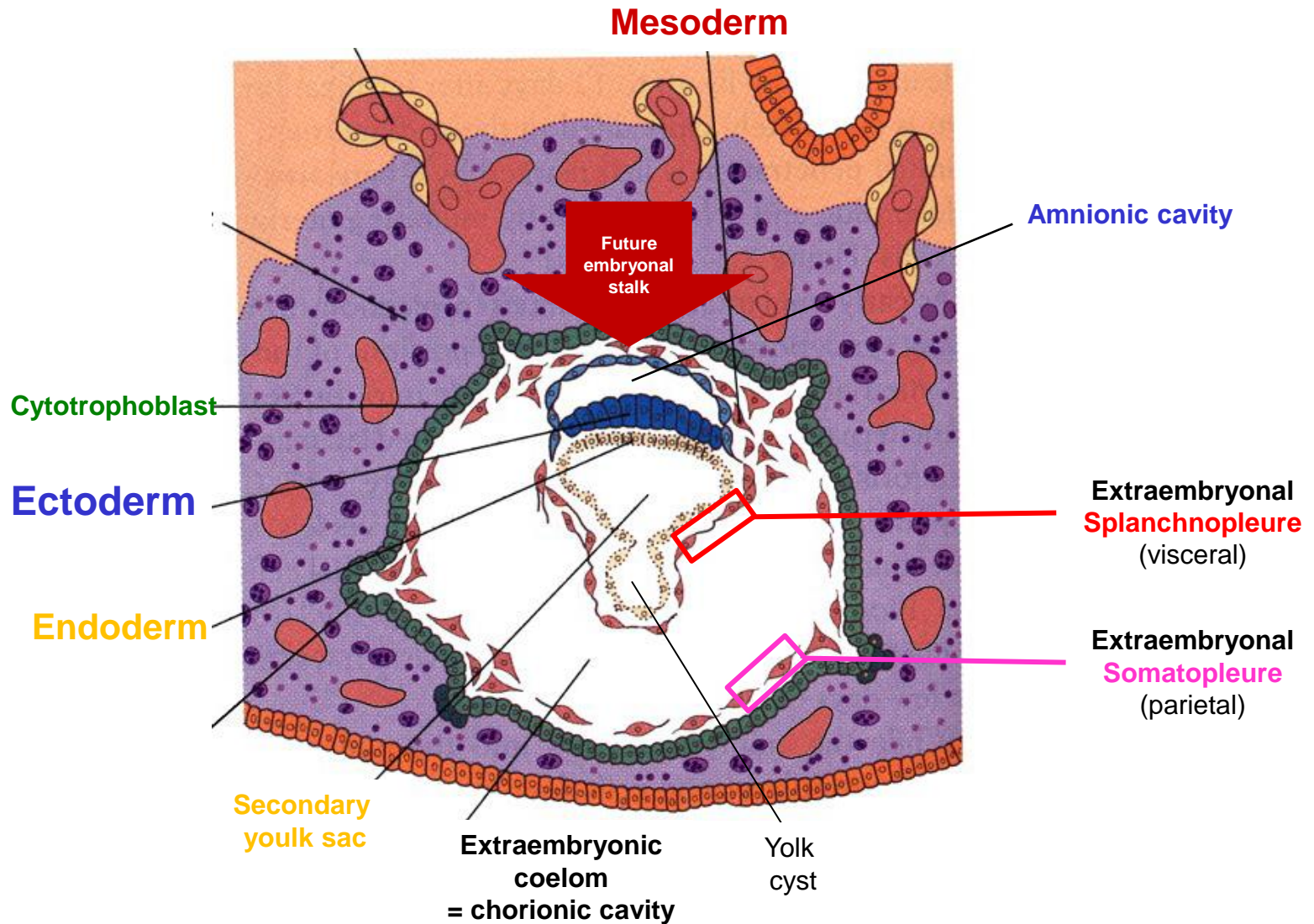
Gastrulation – establishment of three germ layers

Day 9 – primary yolk sac



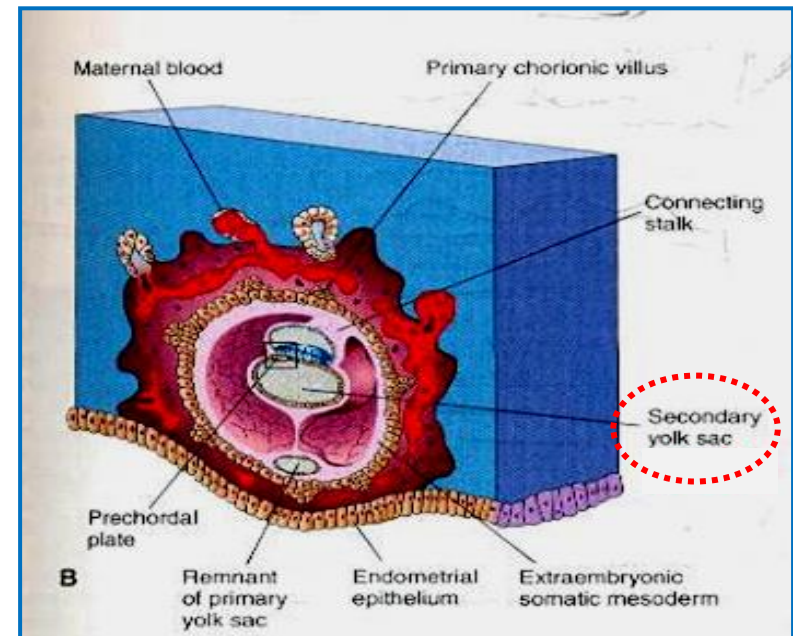
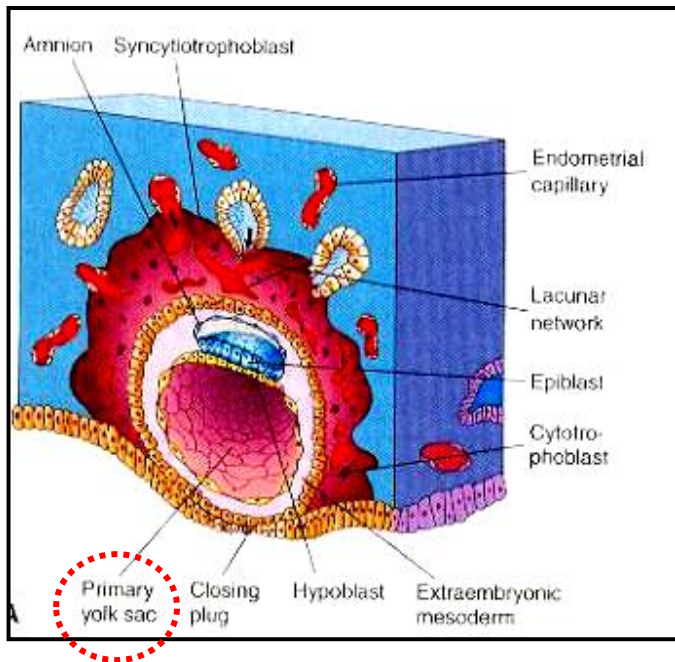
Gastrulation – establishment of three germ layers

Day 12 - 13



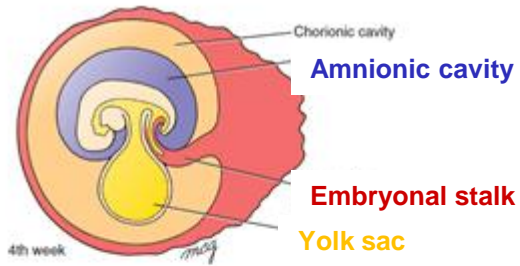
Extraembryonal structures – yolk sac 1

End of the 2. week



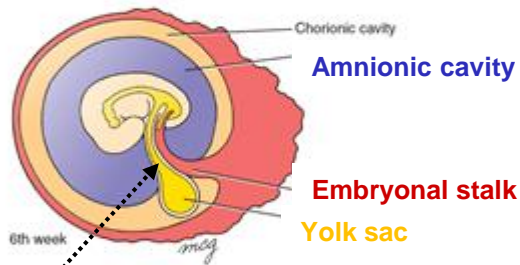
Wall of secondary yolk sac = endoderm + mesoderm

Extraembryonal structures – yolk sac 2

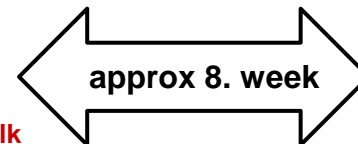
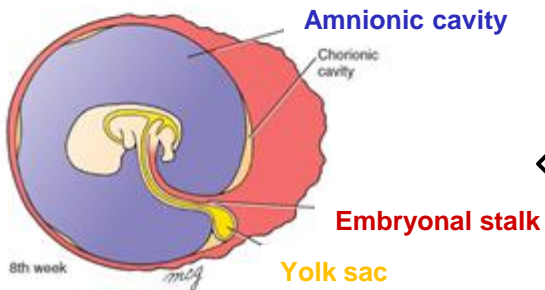
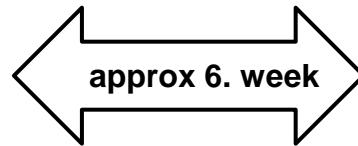


Functions of yolk sac:

- does not contain yolk (oligolecithal egg)
- 3. week – hematopoiesis (since 6. week in liver)
- 3.- 4. week – PGC
- 4. week – incorporation into primitive gut
- since 6. week – loss of link to gut – obliteration
- abnormal persistence - Meckel diverticle

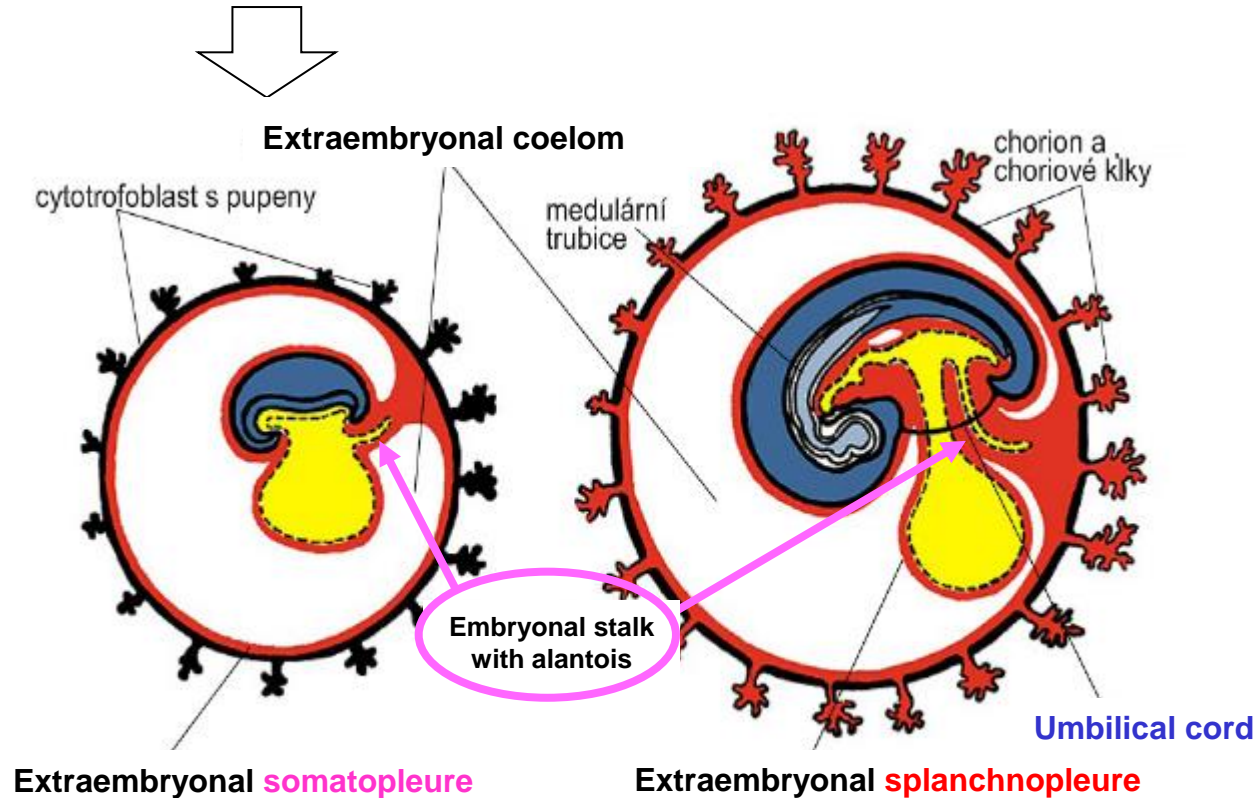


Ductus omphaloentericus



Extraembryonal structures – alantois

Beginning of the 3. week – diverticle of caudal wall of yolk sac

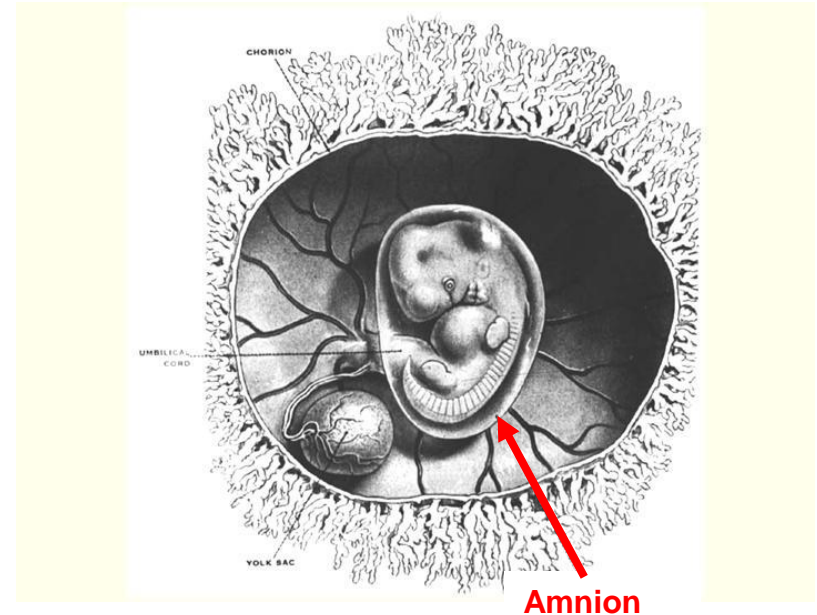
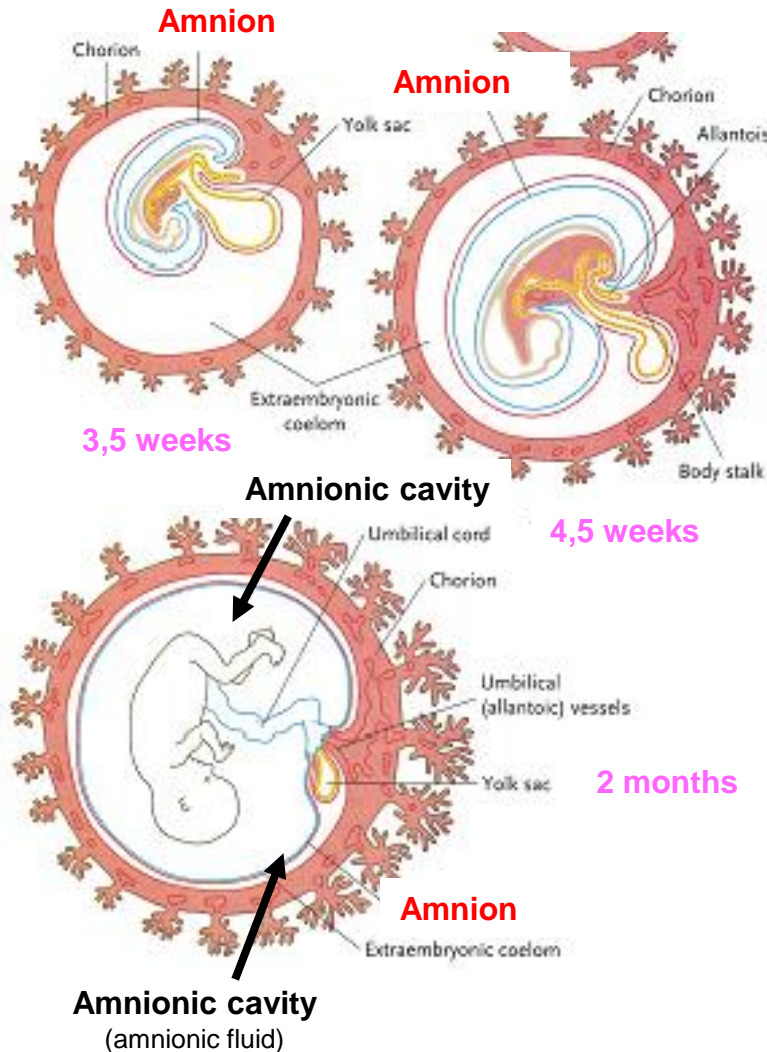


Functions:

- In humans rudimentary structure
- **vessels of alantois – umbilical vein and arteries**
- 2. month – extraembryonal part degenerates
- 3. month – intraembryonal part – urachus (link to urinary bladder)

Extraembryonal structures – amnion (internal fetal membrane)

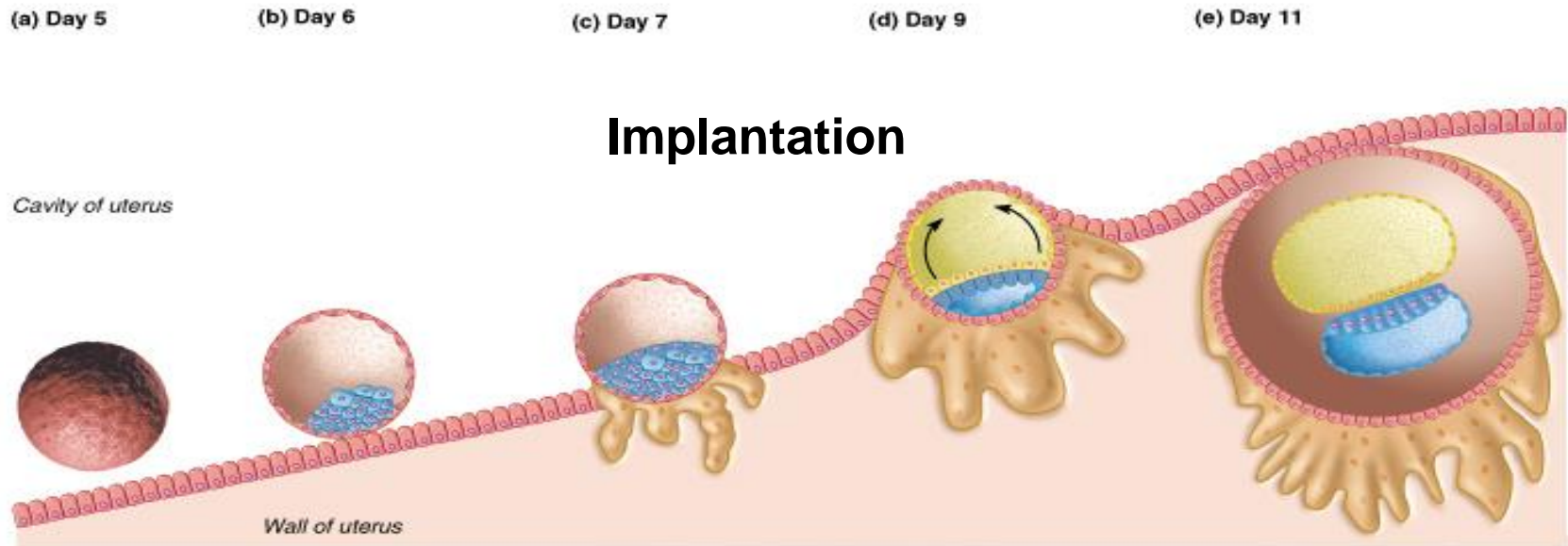
thin, transparent = flat simple ectodermal epithelium + extraembryonal mesoderm (somatopleure)



Amniotic fluid:

- 99% water; 800 až 1000 ml in the last month of pregnancy
- source = diffusion from endometrium through amniochorion
- source = transfer through placenta
- source = transfer through skin of fetus
- source = excretion by fetal kidneys (since 11. week)
- very fast turnover – passage via fetus (digestive + respiratory tracts)
- function – free movement without adhesion (space for symmetrical growth)
- function – barrier (temperature, mechanical damage, infection)
- function – chemical homeostasis

Extraembryonal structures – chorion (external fetal membrane)

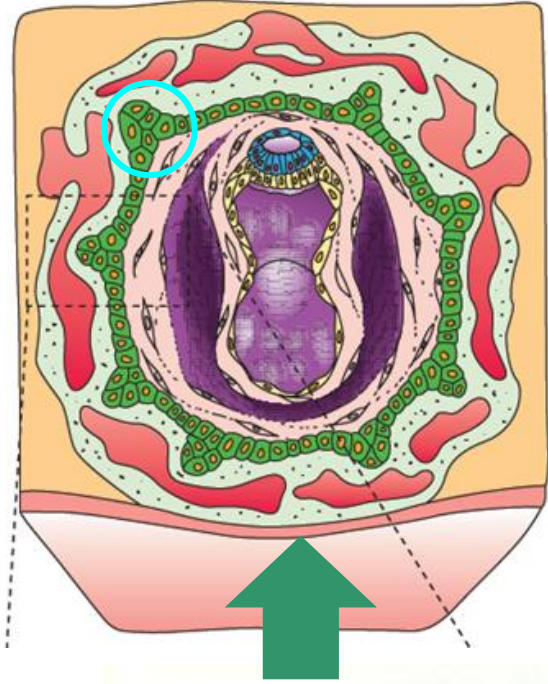


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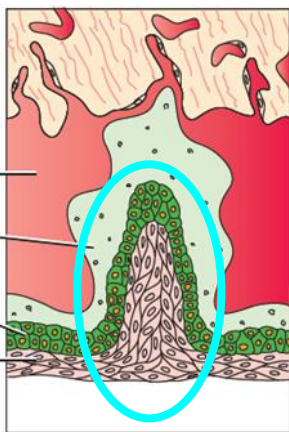
Syncytiotrophoblast invades into surrounding stroma

Extraembryonal structures – chorion – chorionic villi

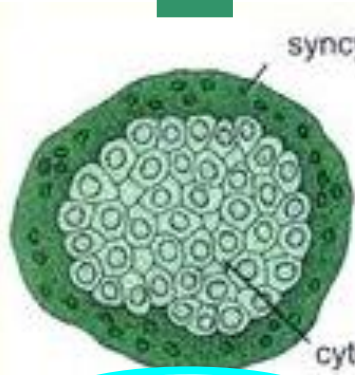
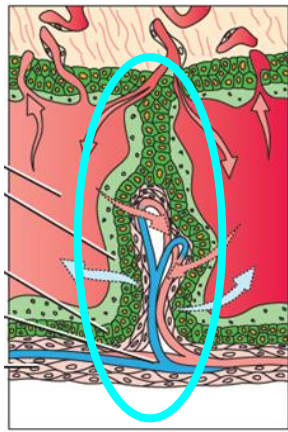
Day 11 až 13



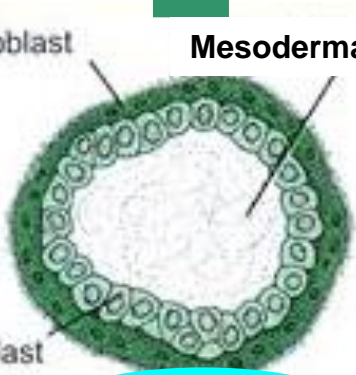
Day 16



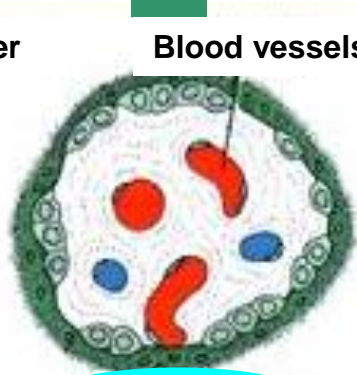
End of the 3. week



primary villus



secondary villus



tertiary villus

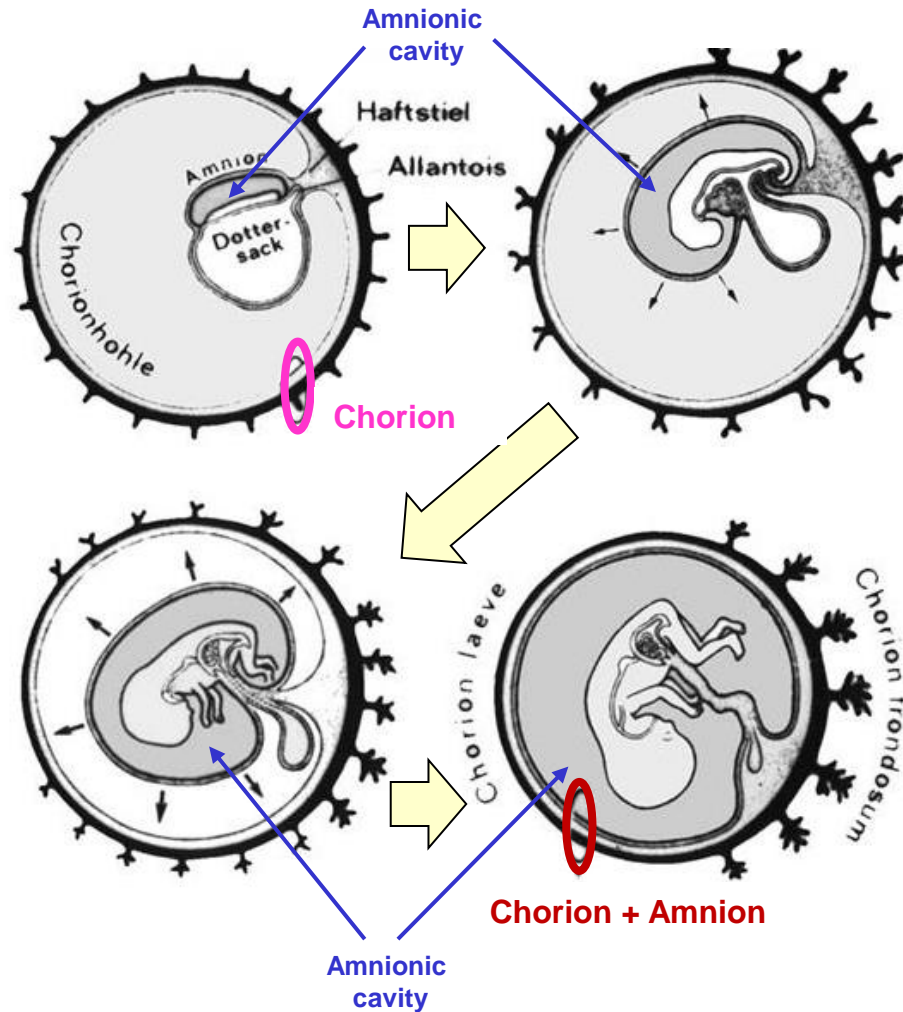
syncytiotrophoblast

Mesodermal center

Blood vessels

cytotrophoblast

Extraembryonal structures – chorion – expansion of amnion

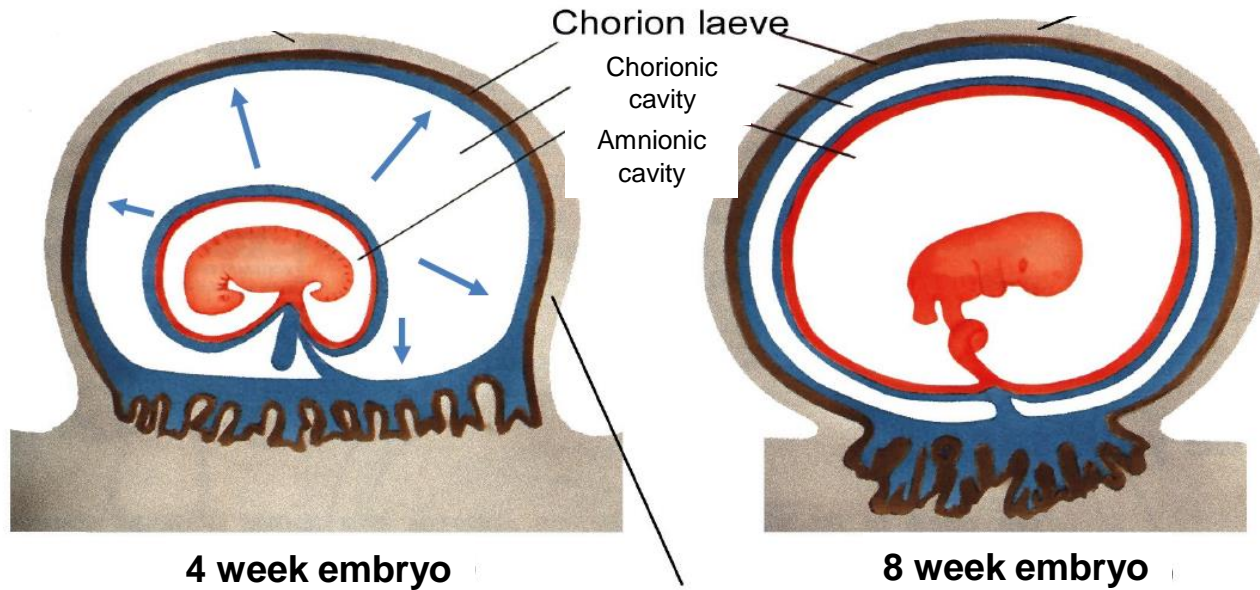


Extraembryonal structures – growth of amnion and chorion

CHORION = cytotrofoblast + mezoderm (ex.)

AMNION = mezoderm (ex.) + ektoderm

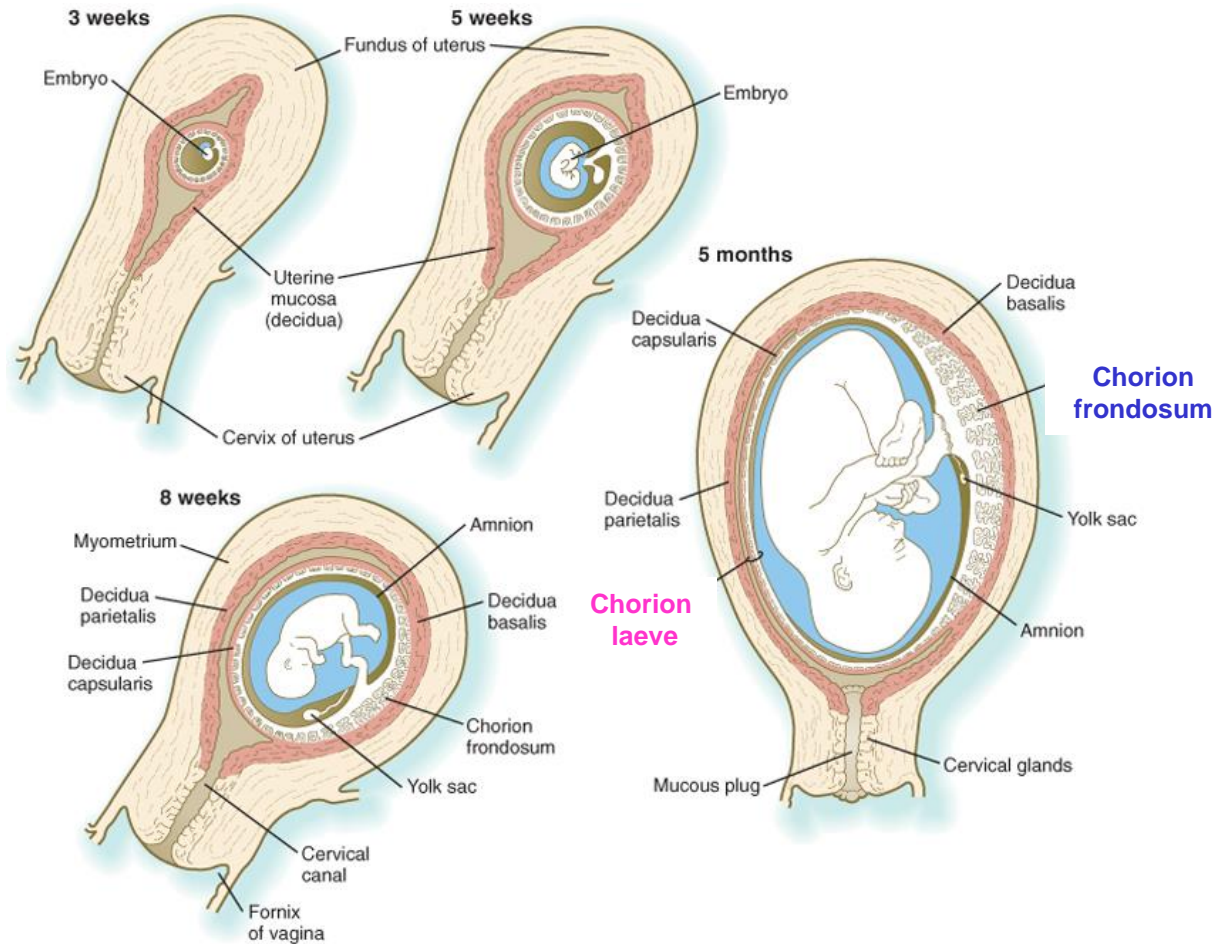
Growth of amnionic and chorionic cavities



Extraembryonal structures – chorion – *frondosum x laeve*

Ch. frondosum – vilous

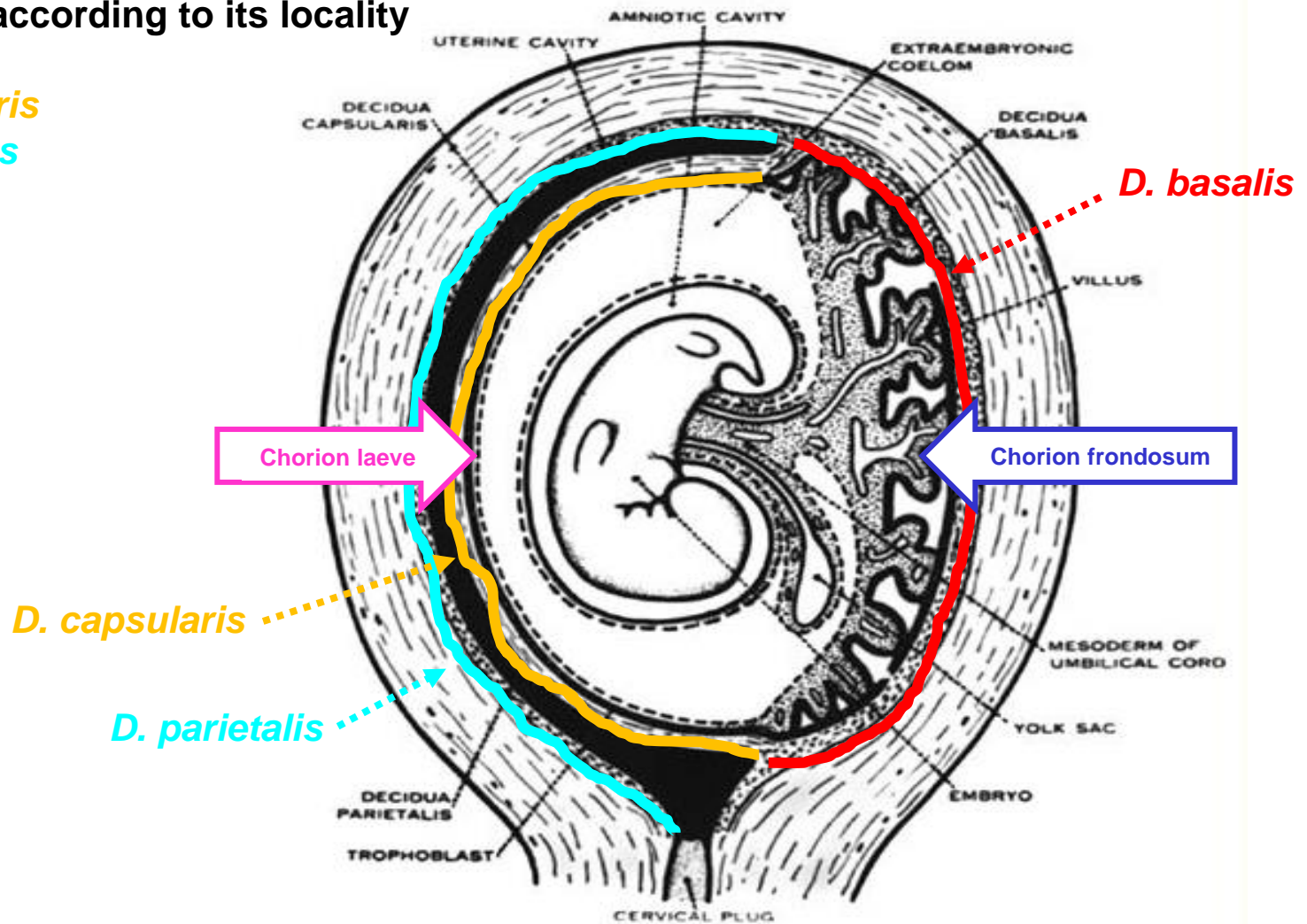
Ch. laeve - smooth



Extraembryonal structures – chorion – decidua

Decidua – according to its locality

- *basalis*
- *capsularis*
- *parietalis*



Decidua basalis – between embryo and myometrium

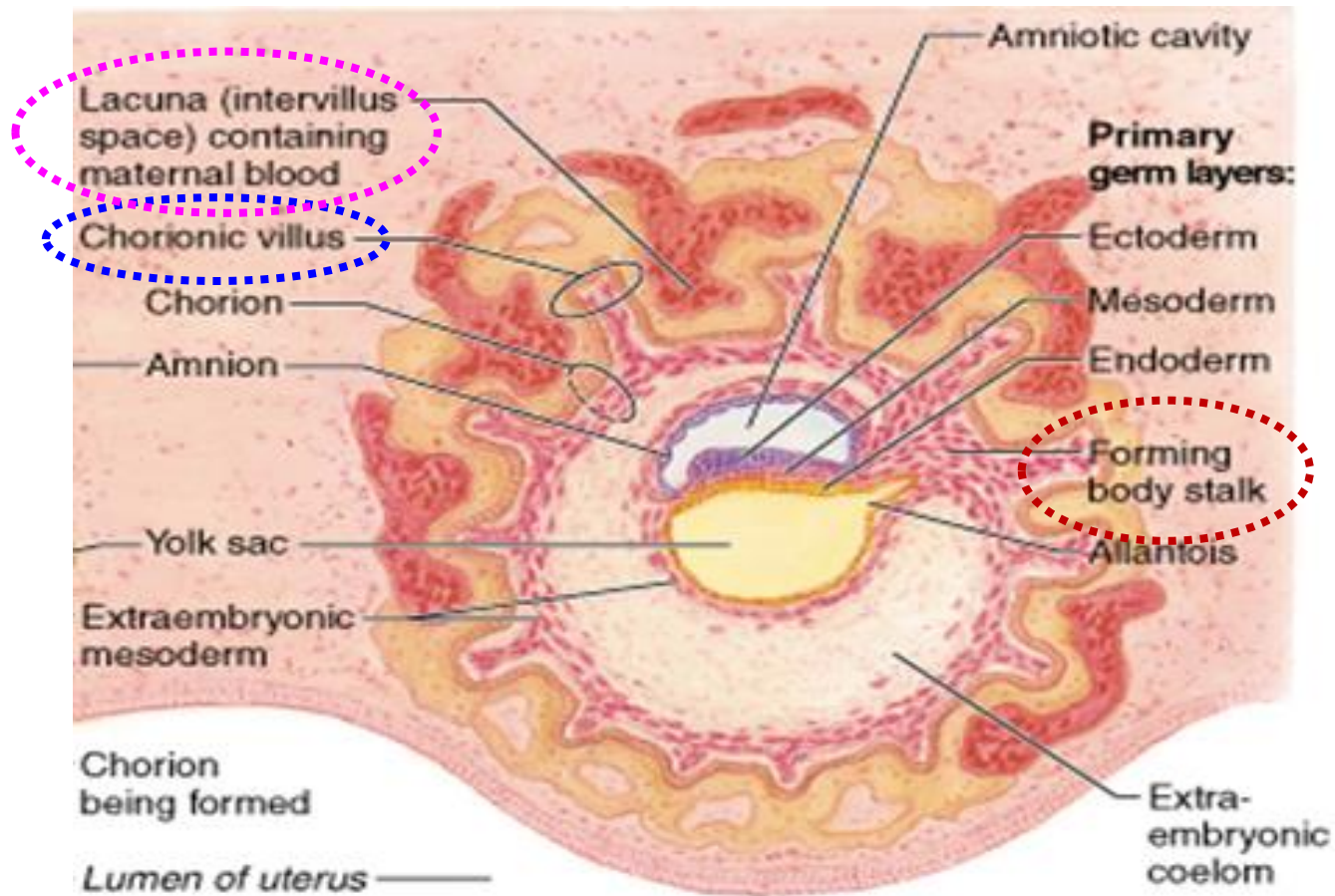
Decidua capsularis – between embryo and uterine cavity (becomes thinner)

Decidua parietalis – opposite wall of uterus

Extraembryonal structures – chorion – decidua



Extraembryonal structures – chorion – placenta



(c) 16-day embryo

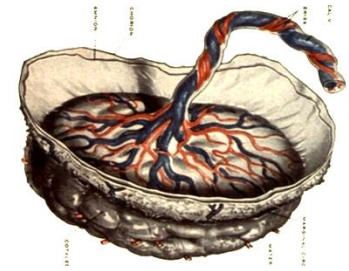
Chorionic villi - finger like projection of embryonic tissue that come in contact with bleeding endometrium

Decidual cells – fibroblast of endometrium (large, cuboidal, very active proteosynthesis)

Placenta – thick disk made by decidua and chorionic villi (formed at the start of month 4)

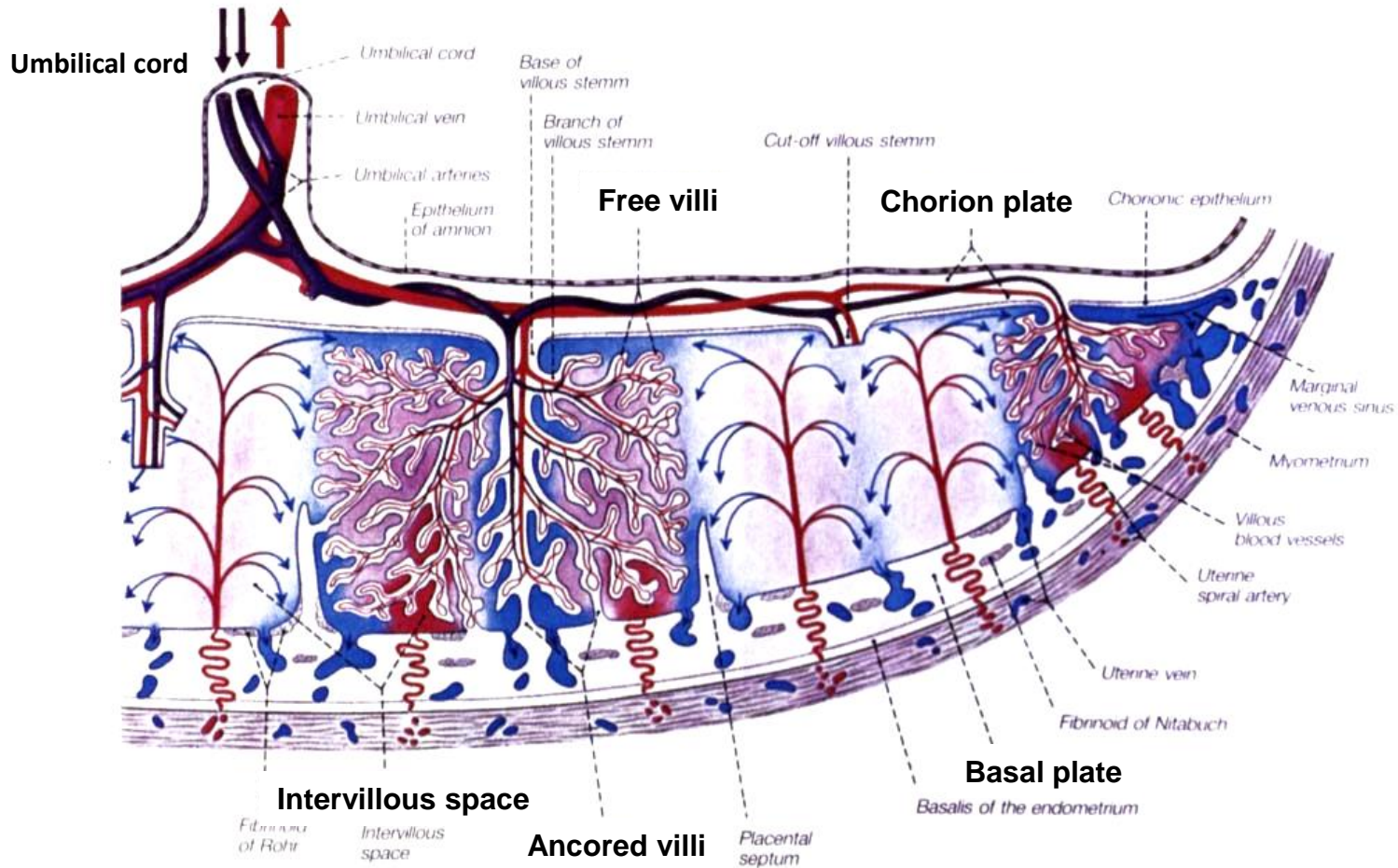
discoid
15 – 20 cm
400 – 600 g

Placenta

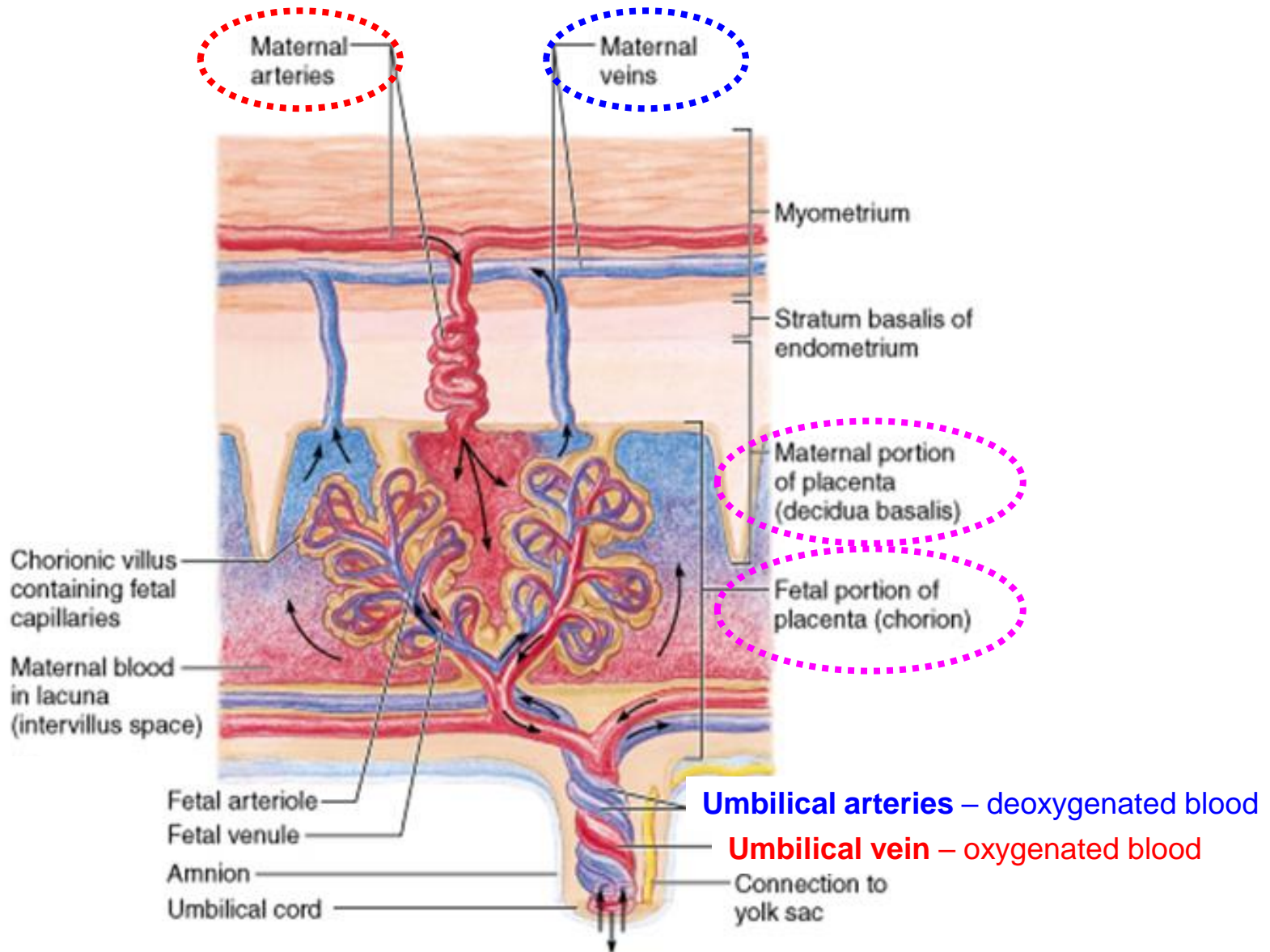


Discoidalis + Hemochorialis

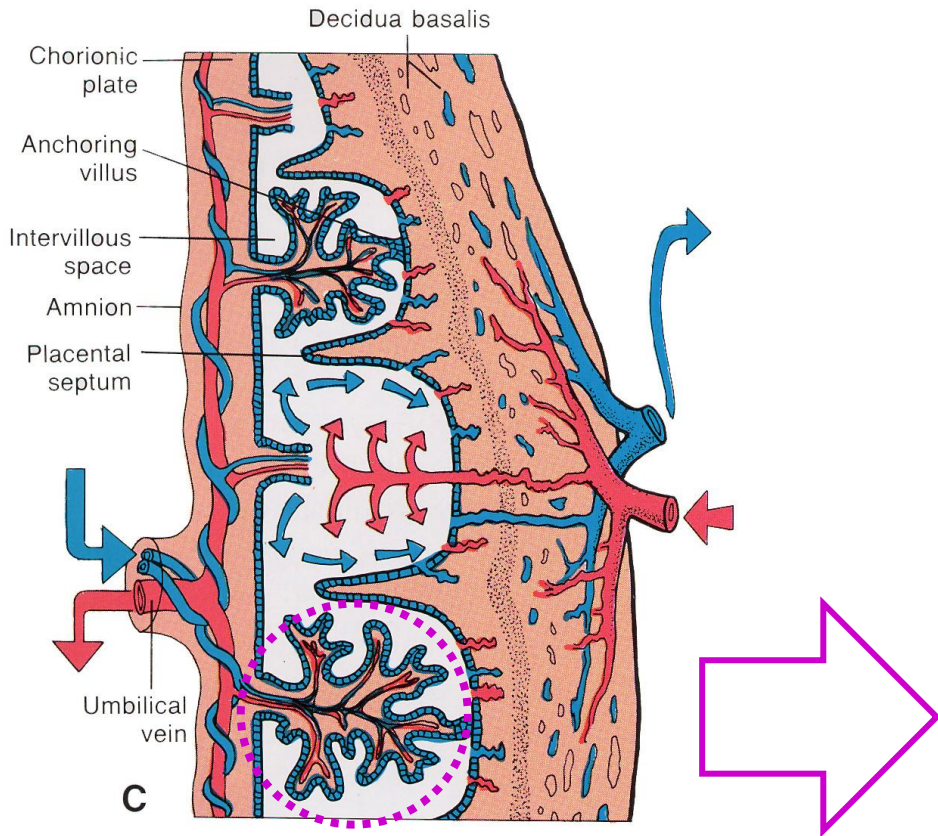
- **pars fetalis** – chorion plate, chorion villi (anchored, free = terminal)
- **pars materna** – decidua basalis
- **intervillous spaces** – develop from lacunes



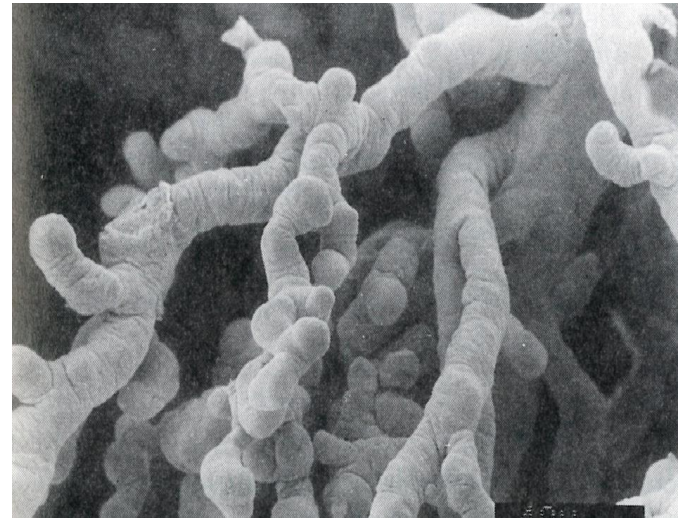
Placenta – blood circulation



Placenta – terminal villi

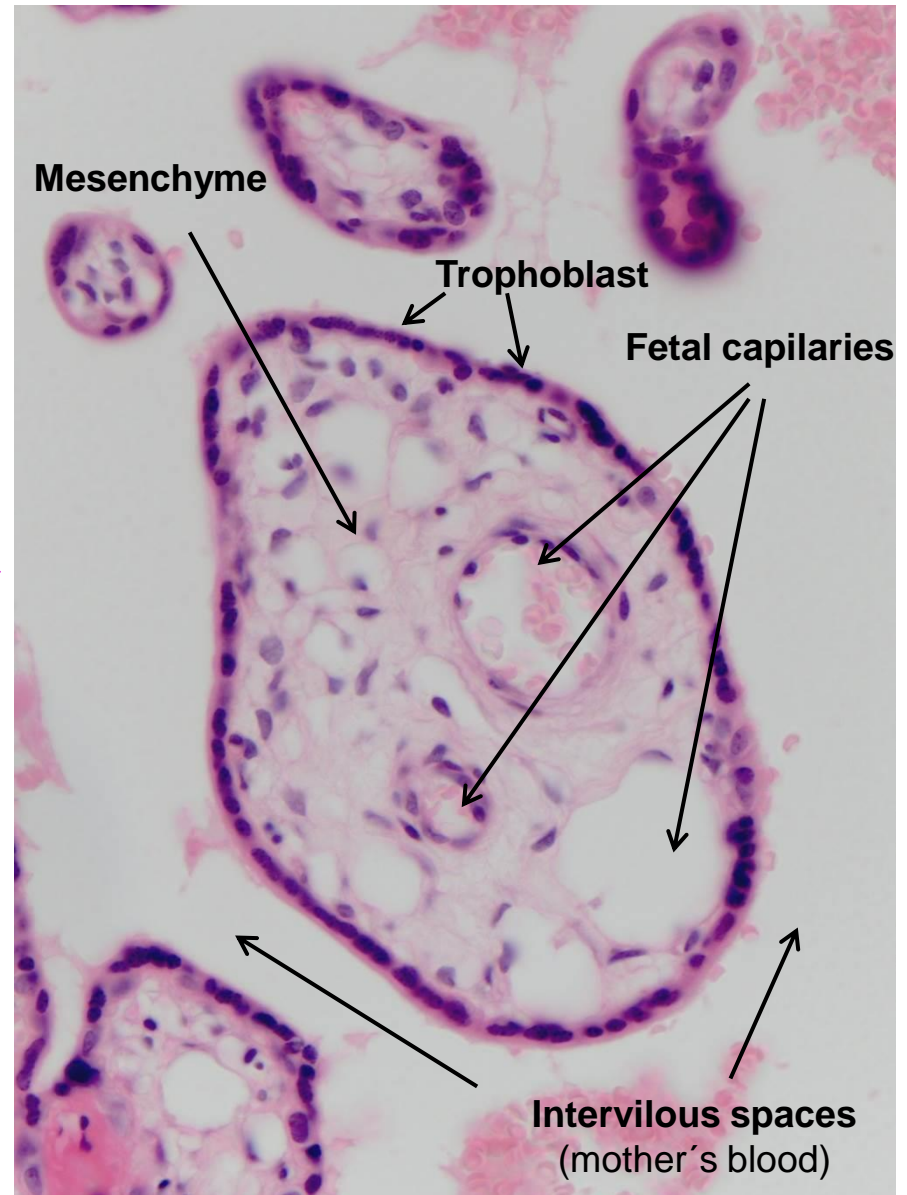
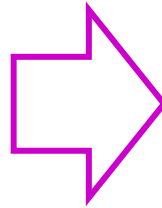
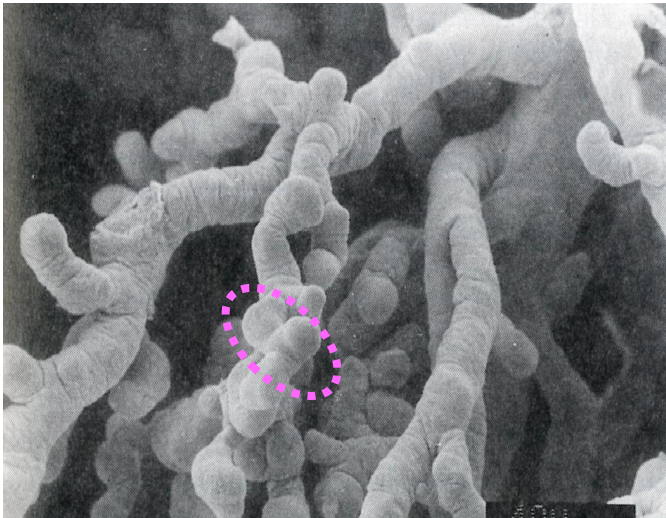


Terminal villi – human – end of pregnancy



Placenta - fetomaternal barrier 1

Terminal villi – human – end of pregnancy

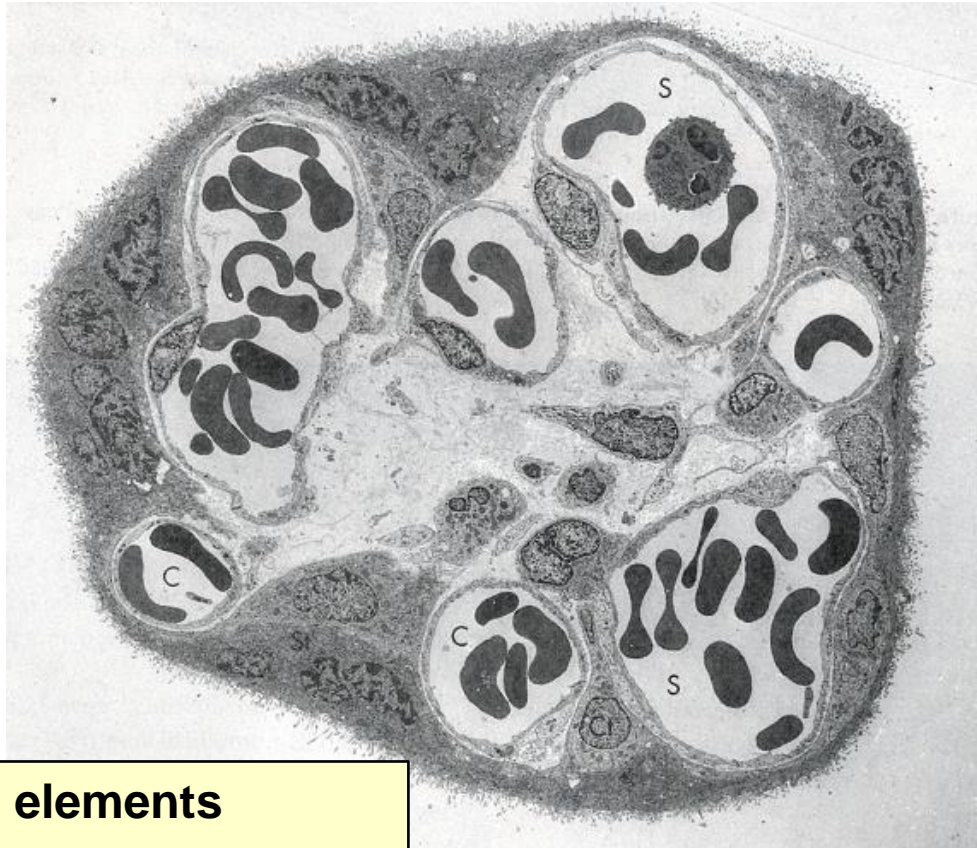


Barrier = 5 elements

- Endothelium of fetal capillaries
- Basal membrane of endothelium
- *Mesenchyme of villi* (*extraembr. mesoderm*)
- Basal membrane of trophoblast cells
- Cells of cyto- a syncytio-trophoblast

since month 5 cytotrophoblast loses its continuity

Placenta - fetomaternal barrier 2

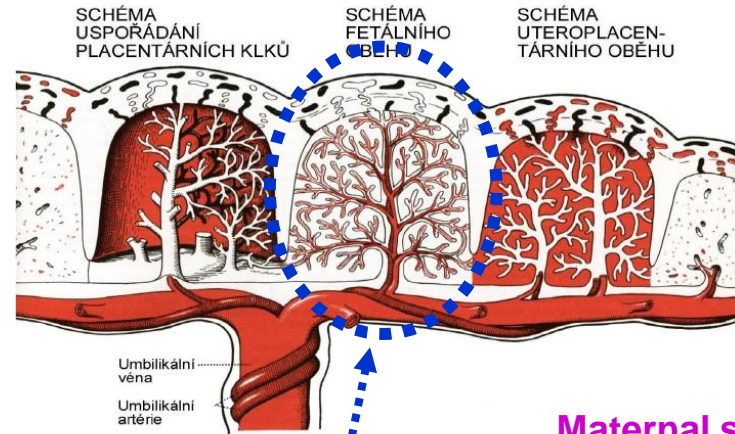


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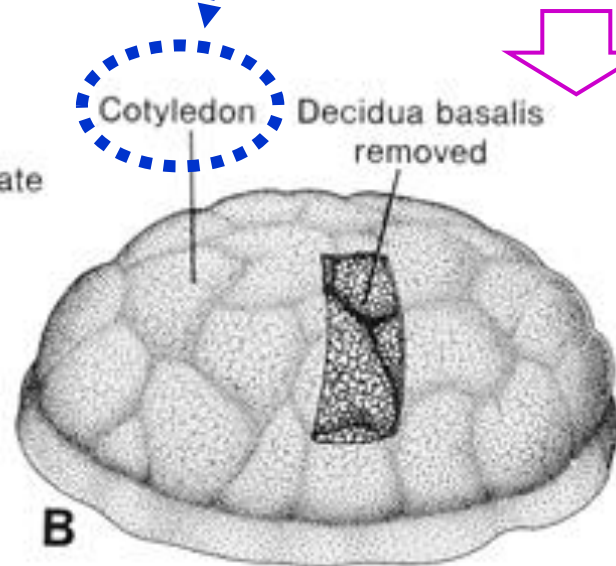
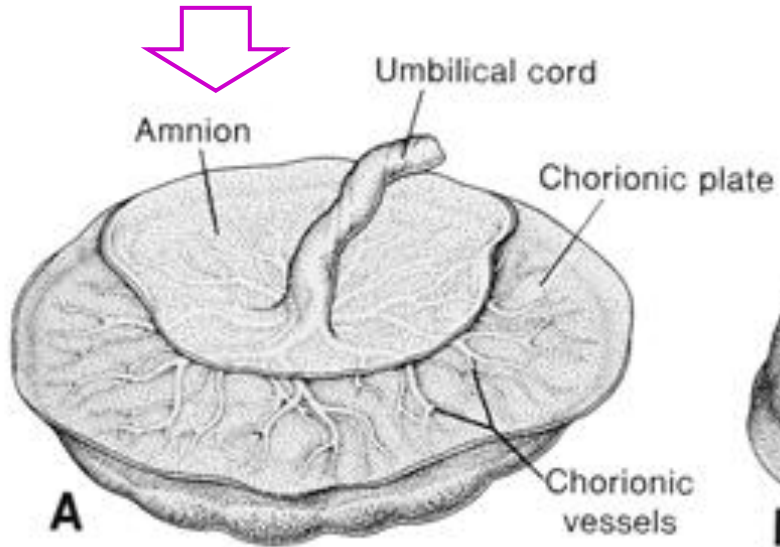
since month 5 cytotrophoblast loses its continuity

Placenta - cotyledons

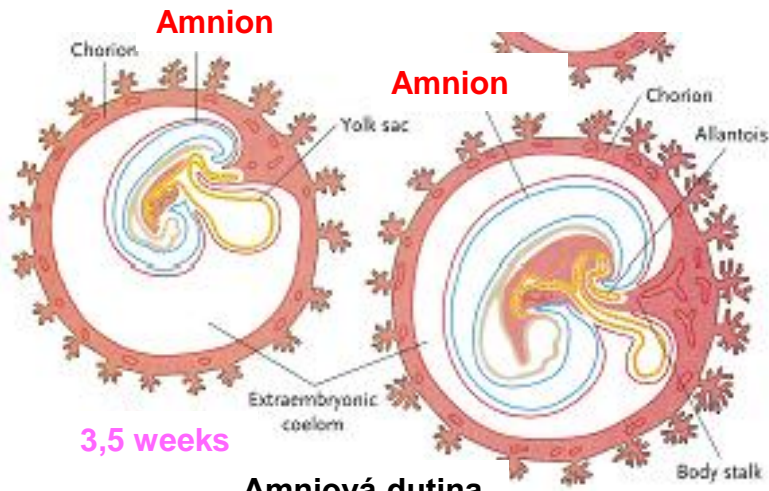


Fetal surface

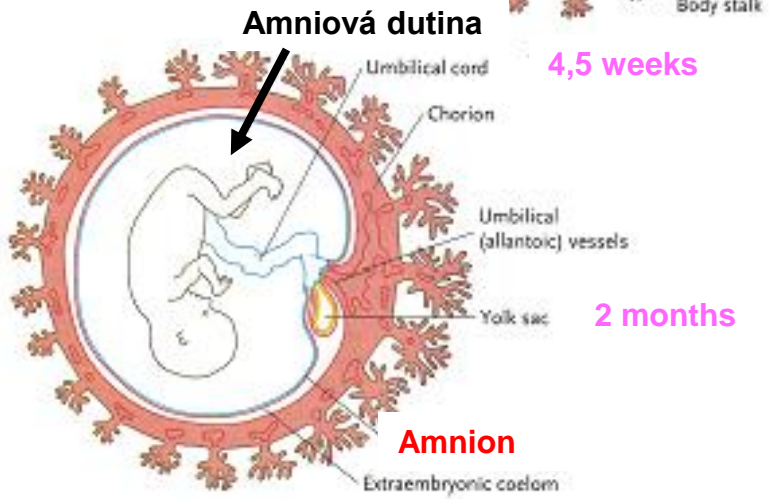
Maternal surface



Placenta – umbilical cord 1

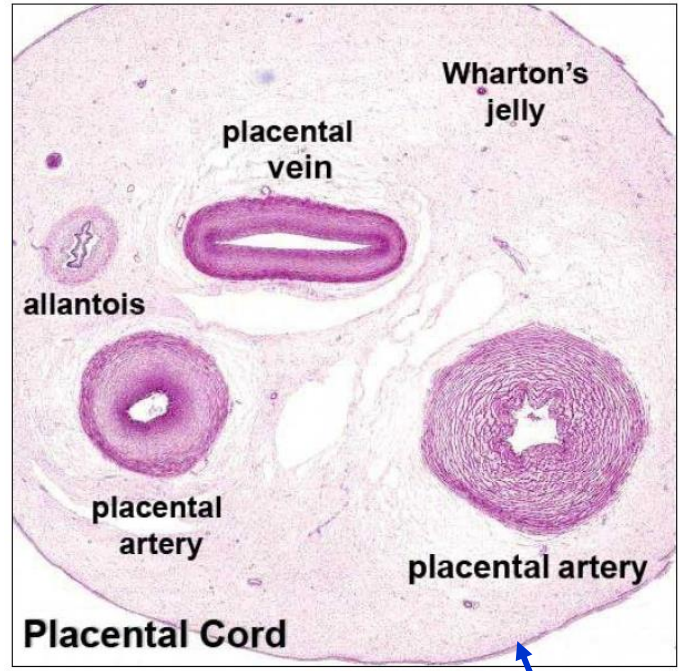


3,5 weeks

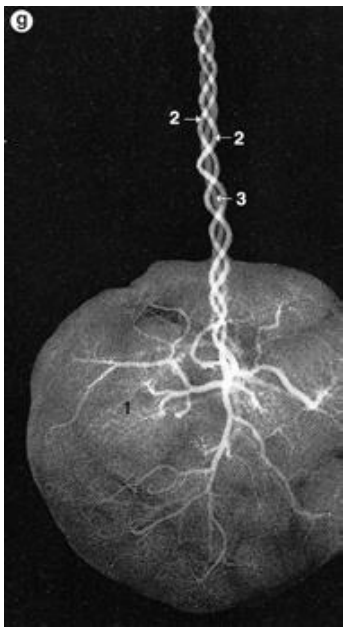


4,5 weeks

2 months

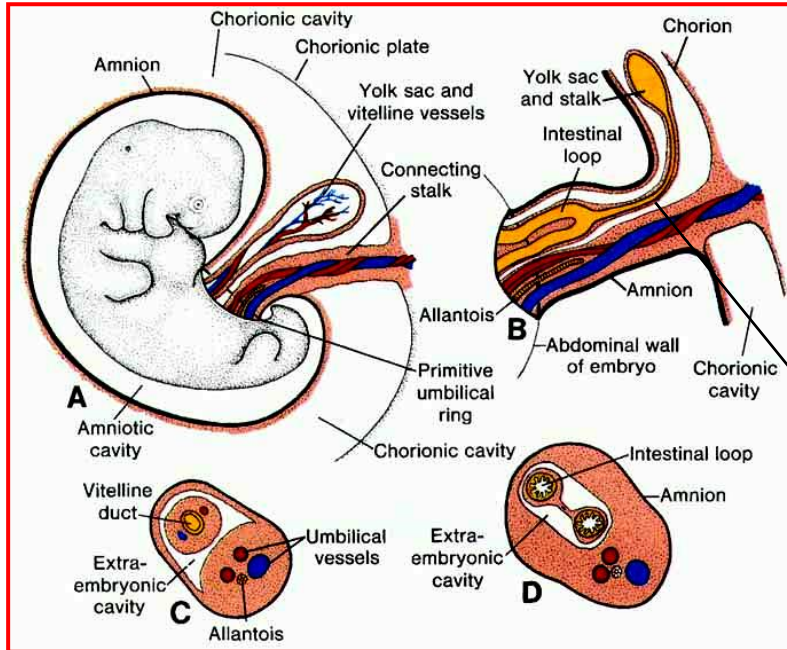


Amnionic ectoderm



- diameter 1,5 to 2 cm
- length 50 to 60 cm
- 1x vein + 2x artery (spiral organization)
- Wharton's jelly – loose connective tissue

Placenta – umbilical cord 2



1-Connecting stalk:

Allantois

Umbilical vessels (two arteries & one vein), they all embedded in

Wharton's jelly (extra embryonic mesoderm)

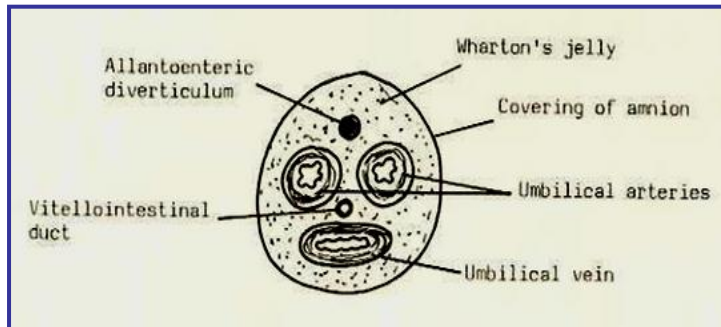
2-Yolk stalk (Vitello-intestinal duct):

(Ductus omphaloentericus)

A narrow, elongated duct which connects gut to yolk sac

It contains **Vitelline Vessels**

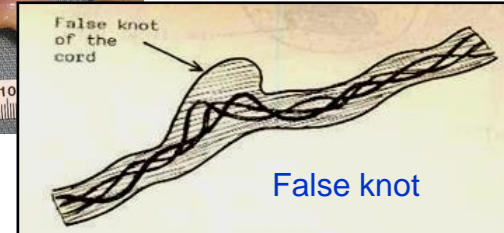
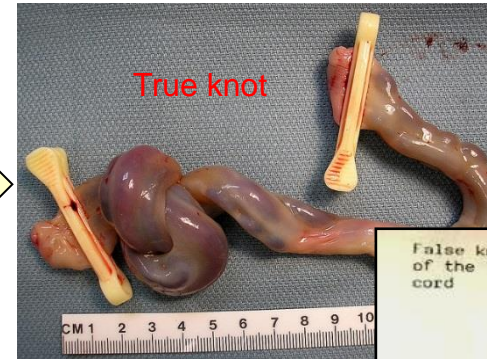
(Later on , it is obliterated and the vitelline vessels disappear).



Umbilical cord - anomalies

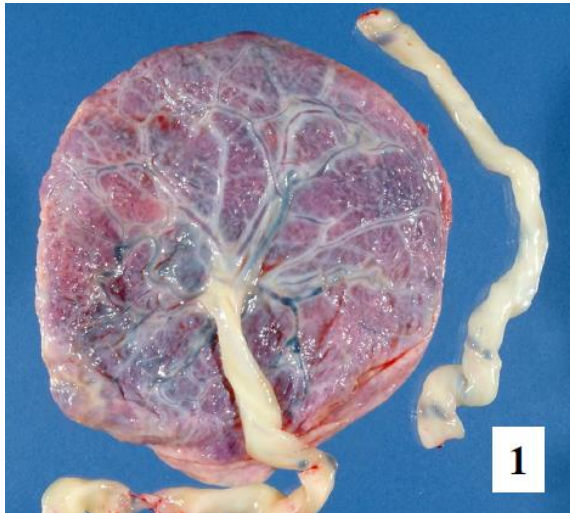
- Short umb. cord < 40 cm
- Long umb. cord > 60 cm
- Absence of one artery – fetal hypotrophy

True knot
Fetal strangulation
Umbilical prolapsus

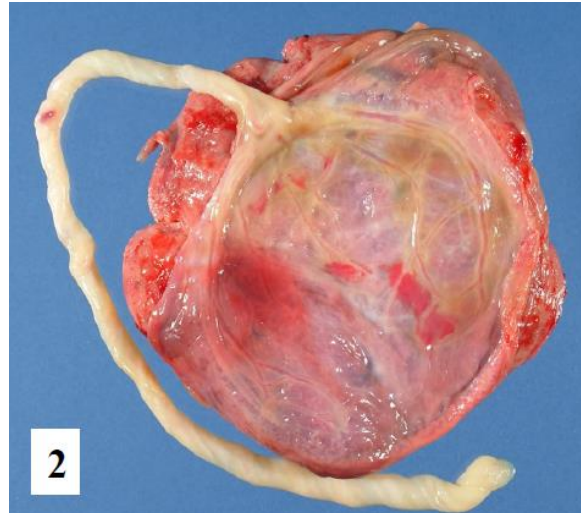


Attachment of umbilical cord to placenta

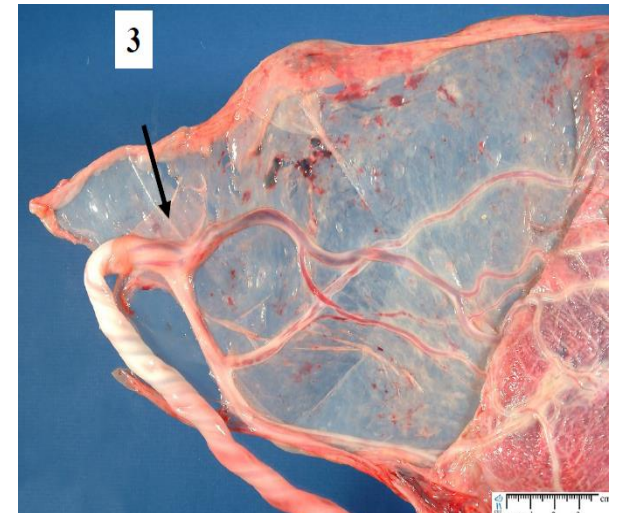
Insertio centralis (norm)



Insertio marginalis



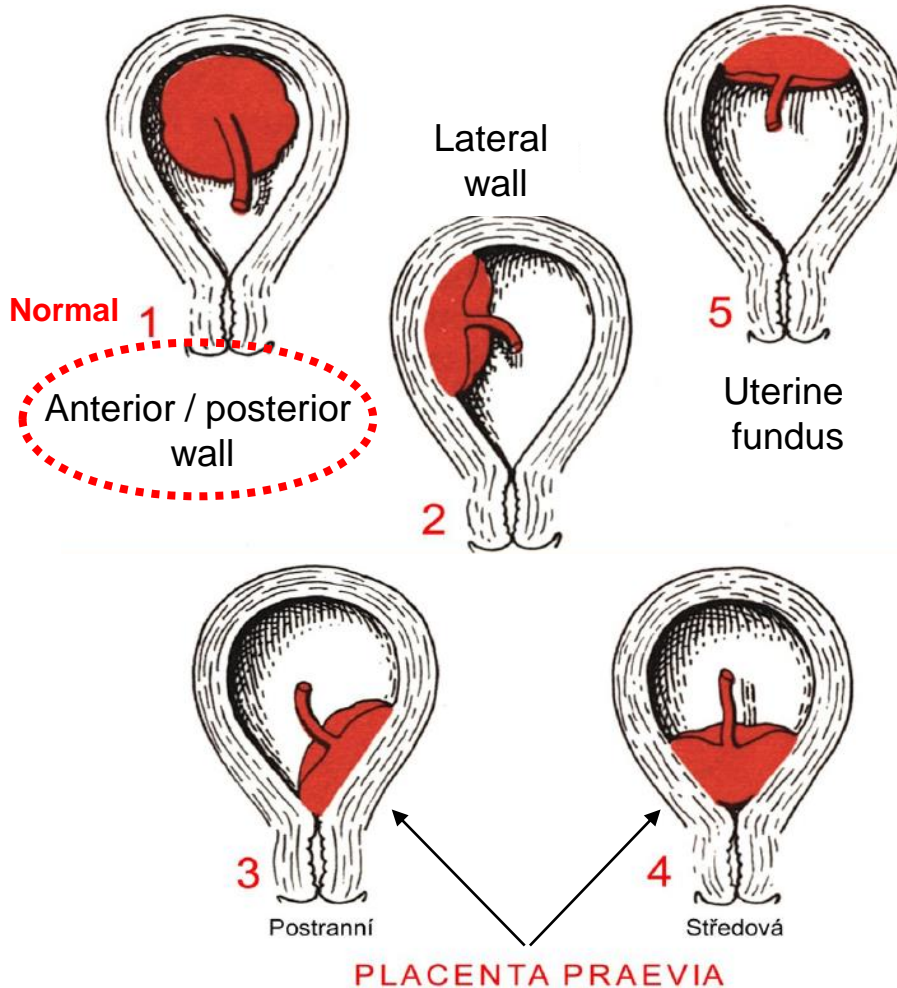
Insertio veluminosa (to chorion laeve)



Placenta – anomalies 1

Location of placenta in uterus

(1 to 5 according to frequency)



Attachment of placenta

(related to myometrium)

- **Placenta accreta**

attached to myometrium

- **Placenta increta**

grown into myometrium

- **Placenta percreta**

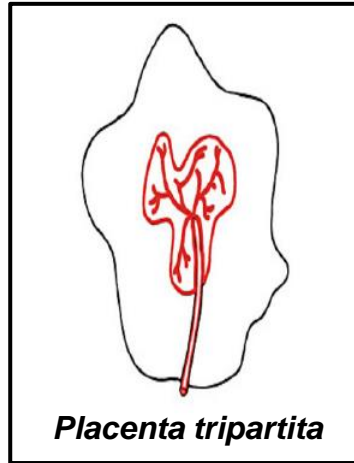
grown through myometrium

Placenta – anomalies 2

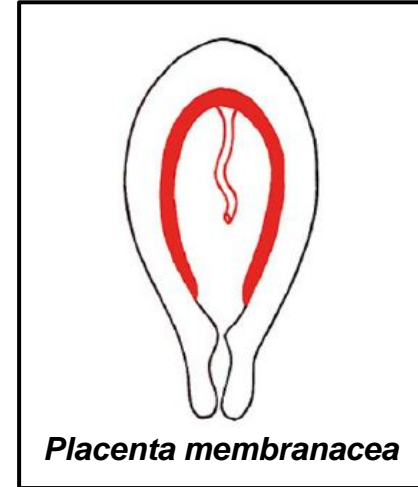
Shape and formation of placenta



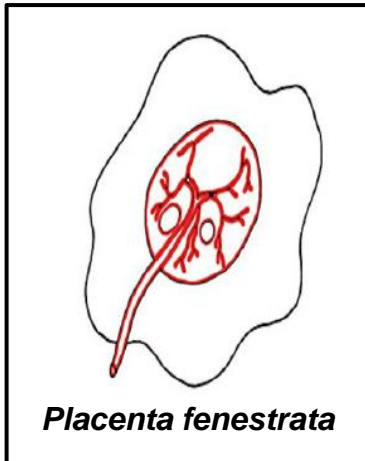
Normal placenta



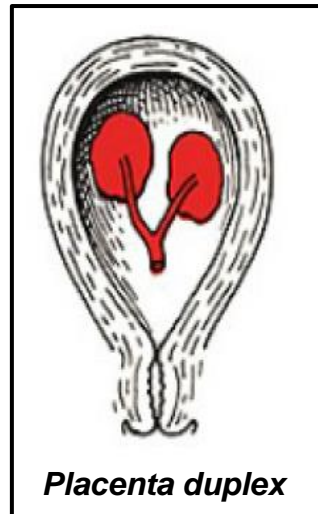
Placenta tripartita



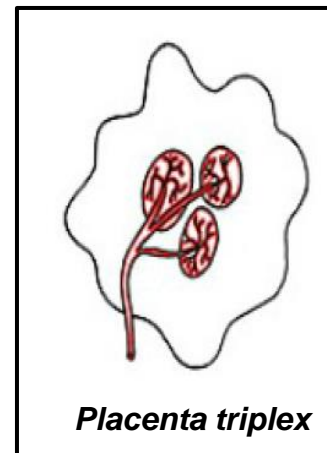
Placenta membranacea



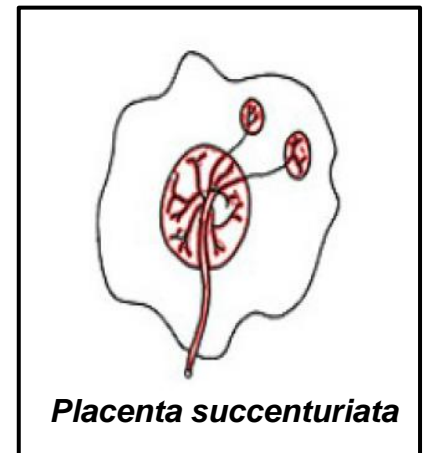
Placenta fenestrata



Placenta duplex



Placenta triplex



Placenta succenturiata

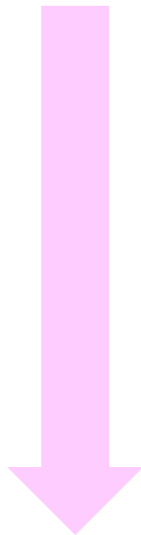
Placenta – multiparous pregnancy 1

TWINS

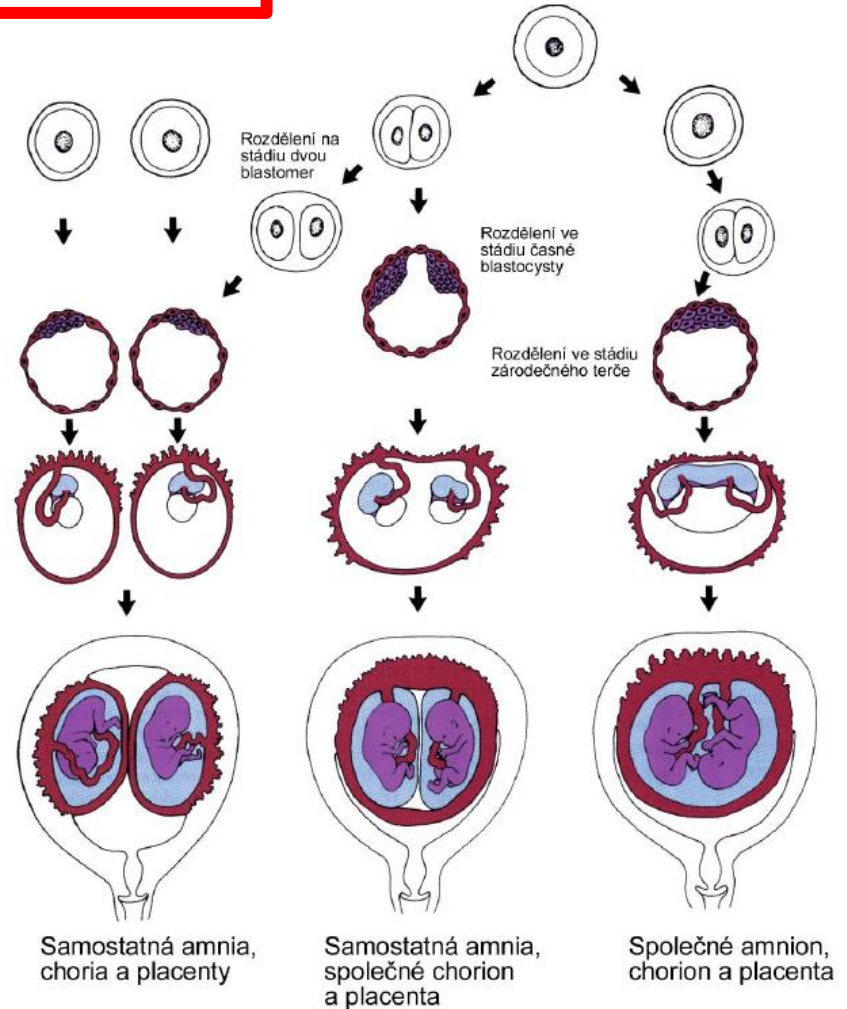
Dizygotic

Monozygotic

2 oocytes + 2 sperms

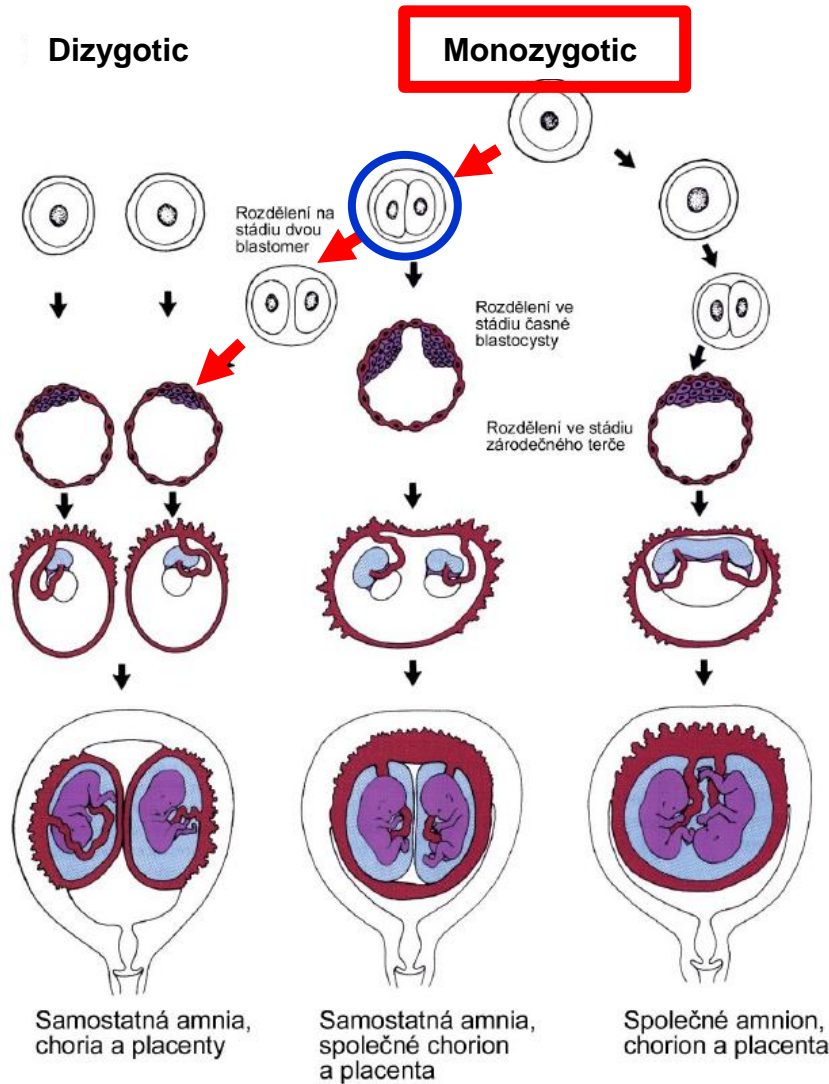


2x amnion + 2x chorion + 2x placenta



Placenta – multiparous pregnancy 2

TWINS



1 oocyte + 1 sperm

Embryo splits at 2-cell stage

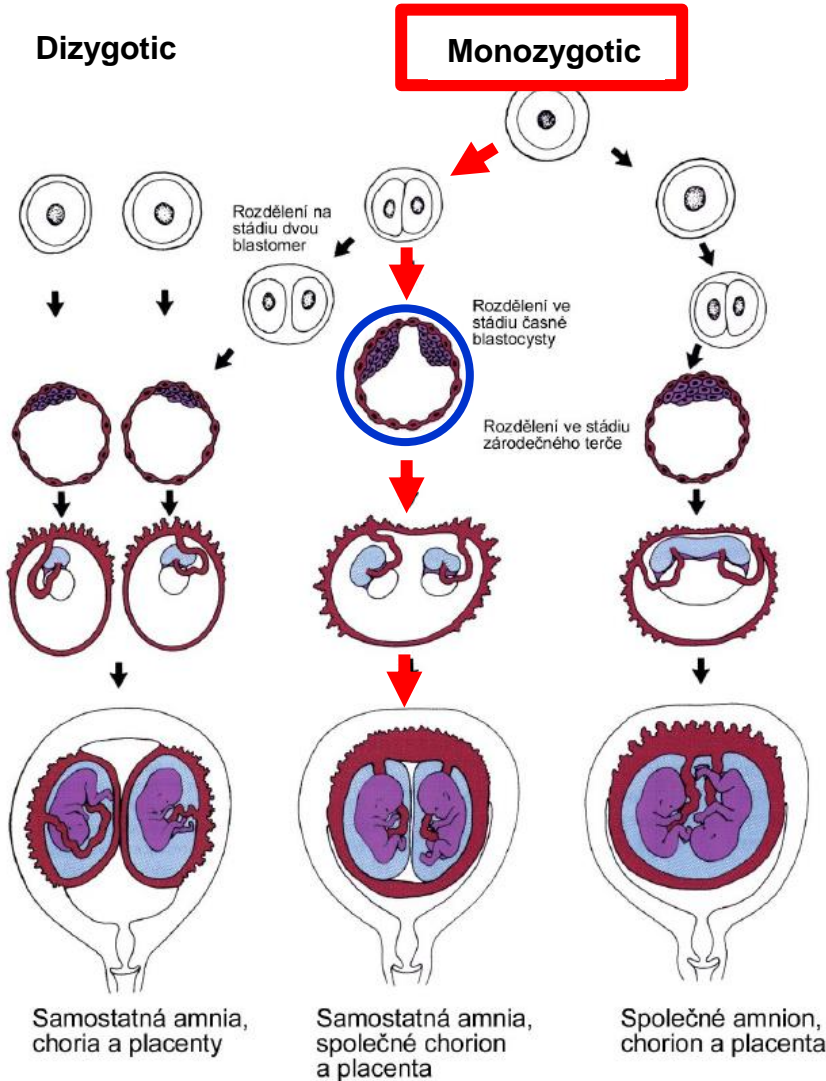
2x amnion + 2x chorion + 2x placenta

(as dizygotic twins)

Placenta – multiparous pregnancy 3

TWINS

Most frequent twins – 65 %



1 oocyte + 1 sperm

Embryo splits at blastocyst stage

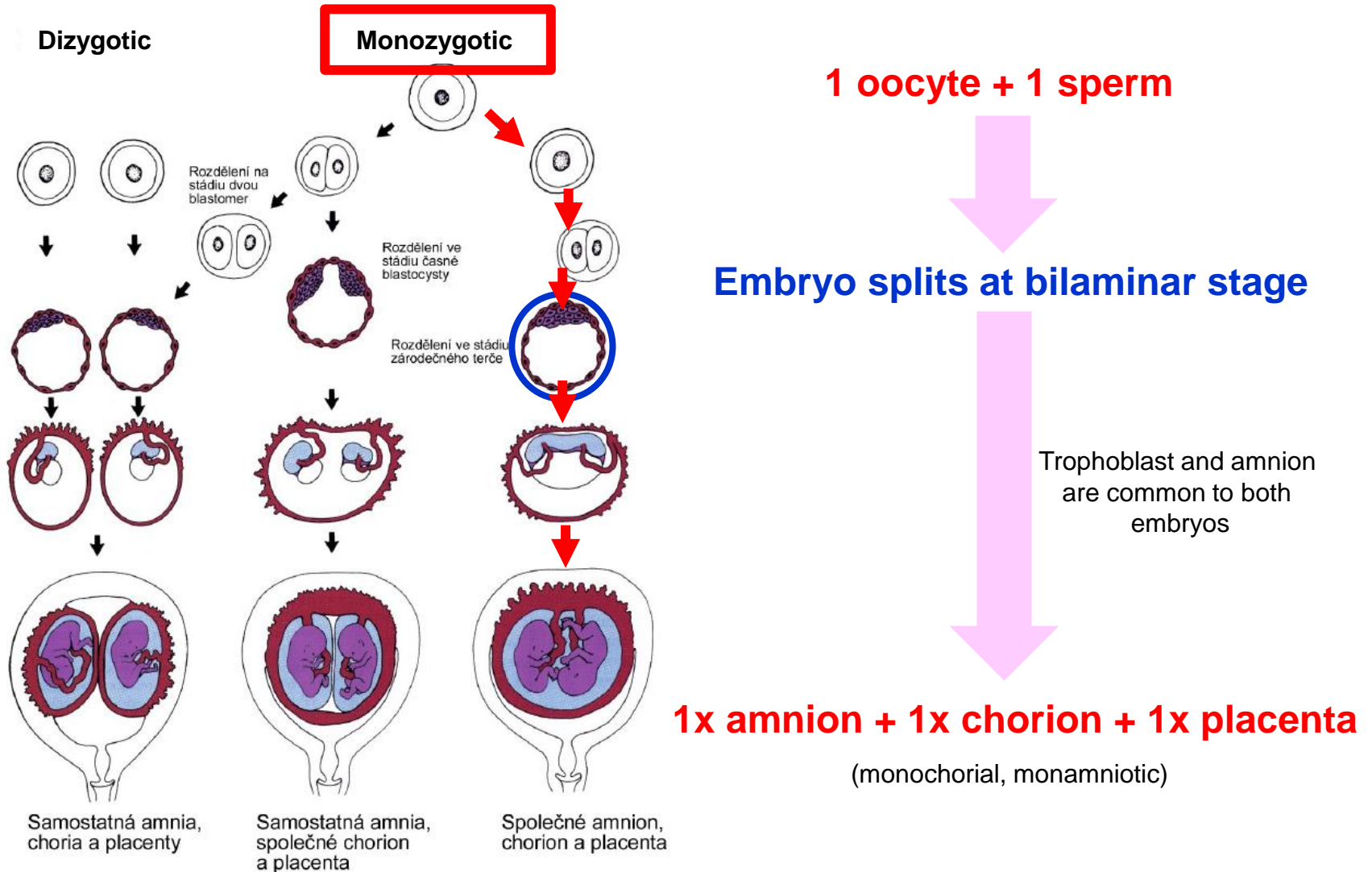
Trophoblast common to both embryos

2x amnion + 1x chorion + 1x placenta

(monochorial, diamniotic)

Placenta – multiparous pregnancy 4

TWINS



Thank you for your attention !

**Questions and comments at:
ahampl@med.muni.cz**