

2. Blastogenesis. Implantation. Gastrulation. Notochord. Somites.

Upon fertilization

- restoration of the diploid number of chromosome
- individual karyotype (set of chromosomes) completed
- chromosomal determination of sex of the new individual (46 XX, 46XY)
- mitoses = cleavage
- zygote → blastomeres, until the day 4 still within the zona pellucida
 - 30 hours: 2 blastomeres
 - 40 hours: 4 blastomeres
 - 3 days 16 blastomeres = morula
- day 4
 - late morula → hatching from the ZP
 - cavities fusing into blastocoelom → blastocyst
- day 6: outer × inner blastomeres get specialized to:
 - trophoblast cells → later on gives rise to extraembryonic structures, fetal membranes
 - embryoblast → later on gives rise to epiblast and hypoblast (embryonic/animal pole)

Cleavage and gastrulation in man

- oocyte
 - oligolecithal (little yolk only)
 - isolecithal (even distribution of yolk)
- cleavage
 - total (the whole volume undergoes the cleavage)
 - equal (uniform size of blastomeres)
- gastrulation
 - Deuterostomia (Echinodermata, Hemochordata, Chordata)
 - delamination (migration of cell layers) instead of invagination

Morula and blastocyst

- day 3: 16 blastomeres = morula
- day 4:
 - hatching of the late morula
 - outer cell mass = trophoblast
 - inner cell mass = embryoblast
 - blastocoelom → blastocyst

Implantation (nidation)

- mostly in anterior or posterior uterine wall, in the cranial third of the uterine body
- cave: ectopic implantation (graviditas extrauterina - GEU)
- day 6-11
- adhesion of the trophoblast to the endometrium (secretory phase)
 - selectins produced by the trophoblast bind the oligosaccharides on the endometrial surface

- integrins produced by the trophoblast and the endometrial matrix (laminin, fibronectin)
- invasion of the syncytiotrophoblast (enzymes)

Abnormal implantation

- extrauterine (ectopic) pregnancy:
 - uterine tube (ampullar region, isthmus, pars uterina)
 - abdominal cavity, rectouterine (Douglas') pouch
 - internal orifice of the cervical canal → placenta previa
- abnormal blastocysts - 30-40%, approx. 50% blastocysts fail to develop
- cystic hydatidiform mole (trophoblast only, producing hCG)

Hypoblast and epiblast

- day 8: embryoblast differentiates into 2 layers:
 - hypoblast (adjacent to the blastocoel cavity)
 - epiblast
- day 8-9: reticular cell migrating from the cytotrophoblast into the blastocyst and producing matrix → extraembryonic (primary) mesoderm (mesenchyme)
 - extraembryonic coelom = cavity within the extraembryonic mesenchyme; it is surrounded by the exocoelomic Heuser's membrane
 - extraembryonic mesoderm becomes divided by the extraembryonic coelomic cavities into:
 - parietal layer = extraembryonic somatopleuric mesoderm
 - visceral layer = extraembryonic splanchnopleuric mesoderm

Amniotic and yolk vesicles and bilaminar embryonic disc

- embryoblast differentiates into two epithelial layers: epiblast (thicker) and hypoblast (thinner)
- each of two layers develops into a cavity within the extraembryonic mesenchyme
 - a cavity lined with epiblast is called amniotic vesicle (its bottom = ectoderm, its roof = amnioblasts)
 - a cavity lined with hypoblast is called yolk vesicle (its roof = primitive entoderm)
- the contact between the epiblast and the hypoblast is called the bilaminar embryonic disc (approx. 0,1-0,2 mm) and consists of two layers: ectoderm and entoderm (end of week 2)
- the walls of these vesicles contribute also to the embryonic membranes as follows:
 - chorion = extraembryonic mesenchyme + cytotrophoblast + syncytiotrophoblast
 - amnion = extraembryonic mesenchyme + amniotic ectoderm
- connecting stalk = extraembryonic mesenchyme connecting the embryonic disc with the trophoblast

Gastrulation = blastula reorganized into a trilaminar gastrula

- beginning of the week 3: primitive streak = thickened epiblast in the midline growing from the caudal pole
 - its cephalic end has a thickened primitive (Hensen's) node with a primitive pit
- hypoblast becomes thickened in two regions

- prechordal plate
 - buccopharyngeal region, induction of the telencephalon
- cloacal region
 - grown into allantois towards the connecting stalk
- the proper development of the primitive streak and primitive node is essential for:
 - further development of axial structures, such as notochord, neural tube, primitive gut
 - induction of brain vesicles (namely prosencephalon dividing into telencephalon and diencephalon)
 - establishing the right-to-left axis (laterality); abnormal laterality = complete or incomplete situs viscerum inversus (reverse or mirroring of major visceral organs)
- epiblast of the primitive streak proliferates, invaginates, migrates and forms the three germinative layers (week 3, craniocaudal gradient)

Gastrulation = formation of three germinative layers (trilaminar embryo)

- epiblast of the primitive streak
 - contributes to the ectoderm
 - migrates to the hypoblast and replaces it by forming the embryonic entoderm
 - migrates between the ectoderm and the entoderm, thus giving rise to embryonic (secondary) mesoderm
- the result of the gastrulation is trilaminar gastrula with ectoderm, mesoderm, and entoderm

Derivatives of the germ layers

- ectoderm: epidermis, nerve system, neural crest
- entoderm: lining of the GIT (except of ectodermal stomodeum and proctodeum) and its derivatives (hepatobiliary system, pancreas, larynx, tracheobronchial tree)
- mesoderm: urogenital system, most of the mesenchyme → connective tissues including skeleton, muscle tissue, circulation

Further development of the gastrula

- Primitive node forms a midline cord = the notochord
- The primitive streak gives rise to the rest of the intraembryonic mesoderm
 - including the cardiogenic mesoderm in front of the oropharyngeal membrane
- The primitive streak and node → the body axes are established
 - Gene expression patterns → left-right, anterior-posterior, ventral-dorsal

Formation of the notochord

- cells from the primitive (Hensen's) node and pit grow forwards to the prechordal plate = chordomesodermal (notochordal) process
- luminization of this process → notochordal canal of Lieberkühn
- the hypoblast is replaced by entoderm cells from the primitive streak
- the notochordal canal opens → the neurenteric canal connects temporarily the amniotic vesicle with the yolk vesicle
- the notochordal canal flattens → a notochordal plate
- a solid cord of cells from the notochordal plate = the notochord (chorda dorsalis)

- first, it originates cranially; later on, it develops also in the caudal region, as the Hensen's node shifts caudally
- underlies the neural tube
- becomes support and basis for the development of axial skeleton

Mesoderm and coelomic cavity

- the mesoderm germ layer originates during gastrulation and is organized into structures running parallel to the chordal plate
 - paraxial mesoderm: close to the notochord, becomes segmented into 42-44 pairs of somitic mesoderm
 - intermediate mesoderm: connects the paraxial and lateral plate mesoderm; it becomes luminized
 - in the cervical and thoracic regions, it undergoes segmentation and forms segments called nephrotomes
 - remains unsegmented in the caudal regions and it gives rise to nephrogenic blastema
 - gives rise to pronephros, mesonephros, metanephros, ureters, and gonads
 - lateral mesoderm: separates into two sheets (layers) that are separated by a cavity called intraembryonic coelomic cavity (coelom); these two sheets are:
 - somatopleuric mesoderm
 - dorsal somatic, i.e., parietal mesoderm
 - gives rise to lateral and ventral body wall including its muscles and parietal layer of serous membranes lined with mesothelium (future parietal pleural, peritoneal, and pericardiac membranes)
 - splanchnopleuric mesoderm
 - ventral splanchnic, i.e., visceral mesoderm
 - gives rise to the mesenteries, mesodermal layers of the digestive tube (but the epithelium of the gut originates from the entoderm) and to the visceral layer of serous membranes
- at first, the intraembryonic coelom is continuous with the extraembryonic coelomic cavity; later on, these spaces are separated by the expanding edges of amniotic vesicles
- the intraembryonic coelomic cavity later on separates into serous body cavities: peritoneal cavity, pleural, and pericardiac cavity
- in regions without mesoderm, the ectoderm comes in touch with the entoderm, which leads to perforation of these temporary contacts, namely:
 - oropharyngeal (oral) membrane
 - cloacal membrane
- proper formation of the mesoderm is essential for development of limb skeleton and limb muscles, vertebrae and paravertebral muscles, body muscles, for development of circulation system, urogenital system and other structures

Somites (embryonic body segments)

- during day 18-19, the paraxial mesoderm divides into segments = somites
- this is the first visible segmentation of body structures; later on, it is followed by segmentation of skeleton, muscles, blood vessels, and nerves

- starting cranially, the mesoderm condenses into somitomeres, which are primordia of the somites; this process propagates in the caudal direction
 - day 20: first occipital somites
 - until the end of week 5, approximately three pairs of new somites appear each day
- each somite consists of mesodermal epithelial layer and an inner cavity named somitocoel
- at the end of week 5, 42-44 pairs of somites are formed:
 - 5 pairs of occipital somites
 - 7 pairs of cervical somites
 - 12 pairs of thoracic somites
 - 5 pairs of lumbar somites
 - 5 pairs of sacral somites
 - 8-10 pairs of coccygeal somites
 - the first occipital somites disappear and fuse with the cranial basis; the last 5-7 caudal somites disappear
- the persisting 38-40 pairs of somites split into three parts; during this process, the somitic mesoderm produces extracellular matrix, thus turning into mesenchyme tissue
- each somite splits into three parts:
 - dermatome
 - the most lateral part of somite
 - dermatomes from various somites fuse into a continuous layer → dermis of the skin
 - myotome
 - the middle part of somite
 - epaxial part of myotomes remains segmented → primordia or paravertebral muscles
 - ventrolateral parts migrate into the body wall → thus becoming hypaxial muscles of the trunk
 - sclerotome
 - the medial part of the somite
 - becomes condensed around the notochord
 - each sclerotome divides into a cranial and a caudal half
 - the slit between these two halves is populated by mesenchyme and becomes the annulus fibrosus of the intervertebral disc (the nucleus pulposus remains from the notochord)
 - the caudal half of each sclerotome merges with the cranial half of the following sclerotome, thus forming vertebral bodies; the body of each vertebra originates from two halves of two adjacent somites
- somites of the paraxial mesoderm are still connected to the lateral mesoderm via intermediate mesoderm