

## 7. Development of digestive system I. Yolk sac. Primitive gut. Stomodeum. Teeth. Branchial clefts, pouches and arches. Tongue.

### Gut tube

- the roof of the yolk sac is cephalocaudally and laterally folded by the expanding amniotic vesicle → blindly ending entoderm-lined blind-ending cavity named primitive gut (archenteron)
- the vitelline duct (ductus omphaloentericus) connects the middle part of the primitive gut with the yolk sac
- both ends of the primitive gut are temporarily closed by membranes, which represent boundaries between entoderm and ectoderm
  - anteriorly, there is an oral (oropharyngeal) membrane (breaks down before week 4)
  - posteriorly, there is a cloacal membrane (breaks down after month 3)
- the primitive gut becomes divided into three parts:
  - **the foregut**, which develops into pharynx (extends from the oropharyngeal membrane to the respiratory diverticulum), oesophagus, stomach and cranial part of the duodenum; it extends caudally to the liver diverticulum; most of the caudal part of foregut is supplied by the coeliac artery
  - **the midgut**: begins caudal to the liver bud and extends to the junction of the right two-thirds and left third of the transverse colon (anastomosis between the superior and inferior mesenteric arteries (the arc of Riolan, medial colic and left colic artery)); most of the midgut is supplied by the superior mesenteric artery
  - **the hindgut**: extends from the left third of the transverse colon to the cloacal membrane; the hindgut is supplied mostly by the inferior mesenteric artery
- entoderm forms the epithelial lining of the digestive tract and gives rise to the epithelium of liver and pancreas
- the connective tissue and smooth muscle of the gut is derived from the visceral mesoderm
- the gut tube is connected to the dorsal and ventral body wall by mesenteries, which are double layers of splanchnopleuric mesoderm covered by peritoneal membrane
  - dorsal mesentery → forms the dorsal mesogastrium (the greater omentum), the dorsal mesoduodenum, the mesentery proper of the jejunum and ileum, the dorsal mesocolon
  - ventral mesentery originates from the septum transversum → forms the lesser omentum and the falciform ligament (between the liver and the ventral body wall)

### Stomodeum

- it is a primitive oral cavity derived from ectoderm
- its border to the entodermal pharynx is temporarily closed by the oropharyngeal membrane
- the rupture of the oropharyngeal membrane in the 4<sup>th</sup> week establishes an open communication between the oral cavity and the primitive gut (pharynx)
- develops into the oral epithelium, labial and dental lamina, ectodermal part of teeth (enamel), and epithelium of the anterior part of tongue
- thickens into the labiogingival lamina

- it forms a furrow named the labiogingival sulcus, thus separating the lips from the gingiva
- along both the upper and lower jaw, a horseshoe-shaped dental lamina originates from the surface epithelium; it splits into 5 dental buds in each quadrant
- the dental buds are connected with the oral epithelium and form the primordia of the ectodermal components of teeth
- the dental buds develop into caps with outer and inner dental epithelium (ameloblasts) and inner core (stellate reticulum), thus forming the enamel organ
- mesenchyme cells adjacent to the dental caps condense into the dental papilla
- the surface mesenchyme cells of the dental papilla interact with the inner dental epithelium and differentiate into preodontoblasts
- the outer (convex) dental epithelium is named the outer ameloblasts
- the inner (concave) dental epithelium is named the inner ameloblasts, which produce enamel proteins and long enamel prisms
- as the tooth grows, the remnants of the enamel organ temporarily persist on the surface of the enamel as the dental cuticle; this is lost shortly after tooth eruption
- the mesenchymal preodontoblasts differentiate into odontoblasts; each odontoblasts forms a projection named Tomes' fibre and produces dentin
- first, the primitive enamel and predentin are not mineralized; later on, they are mineralized with hydroxyapatite (and fluoroapatite) prisms
- the dental papilla develops into the tooth pulp
- the outer and the inner ameloblasts touch each other in the region of the future root, thus forming the epithelial root sheath (of Hertwig); in this region, no enamel is formed anymore; the projections of the root sheath will give rise to the roots
- the mesenchyme outside the root dentin differentiate into cementoblasts; these cells produce the cementum
- outside the cement layer, mesenchyme gives rise to the dental follicle, which differentiates into periodontal ligaments
- the eruption of deciduous teeth occurs between 6-24 months after birth
- during 3<sup>rd</sup> prenatal months, buds for the permanent teeth develop on the lingual/palatal aspect of the milk teeth
- just in front of the oropharyngeal membrane, the ventral ectoderm is elevated with proliferating underlying mesenchyme and forms a medial swelling named the tuberculum impar (see the development of tongue)
- dorsally and in front of the oropharyngeal membrane, the ectoderm of the stomodeum forms an outpocketing known as Rathke's pouch → it grows towards a downward extension of the diencephalon, the infundibulum (grown from the bottom of the 3<sup>rd</sup> brain ventricle)
  - the Rathke's pouch loses its connection with the oral cavity and fuses with the infundibulum during week 5, thus forming the hypophysis
  - the Rathke's pouch develops into the endocrine epithelium of the adenohypophysis (the anterior lobe of the hypophysis)
  - the pars tuberalis is a small extension of the anterior lobe, which grows along the stalk of the infundibulum
  - remnants of the cavity of the Rathke's pouch may persist as small cavities in the pars intermedia and pars tuberalis
  - the infundibulum differentiates into the stalk and the pars nervosa (the posterior lobe of the hypophysis = the neurohypophysis)

## Foregut

### – Pharynx

- in the week 4-5, temporarily structures named pharyngeal arches develop in the region of head and neck
- the entoderm of the pharynx forms lateral outpocketings named **pharyngeal pouches** (= branchial pouches); these give rise to a number of important organs:
  - 1<sup>st</sup> pouch: the tubotympanic recess → the auditory (Eustachian) tube, tympanic (middle ear) cavity and the inner epithelium of the tympanic membrane (eardrum)
  - 2<sup>nd</sup> pouch: the tonsillar fossa with the palatine tonsils
  - 3<sup>rd</sup> pouch: the inferior parathyroid glands and thymus (migrate caudally)
  - 4<sup>th</sup> pouch: (incorporates also remnants of the reduced 5<sup>th</sup> pouch): superior parathyroid glands, ultimobranchial body (splits into the parafollicular C-cells of the thyroid gland that produce calcitonin)
- the surface ectoderm invaginates against the wall of the pharynx into **pharyngeal (branchial) clefts**
  - 1<sup>st</sup> cleft: gives rise to the external auditory meatus, and the outer epithelium of the eardrum; cranially to the meatus, three auricular hillocks proliferate
  - 2<sup>nd</sup> cleft: caudally to the meatus, another three auricular hillocks proliferate; together with the hillocks mentioned above, they will give rise to the external ear
  - the 2<sup>nd</sup>-4<sup>th</sup> cleft form a temporary ectodermal cavity named the cervical sinus; mesenchyme (operculum) proliferating from the second (hyoid) arch overlaps the cervical sinus, which later on disappears; remnants of the cervical sinus may persist as lateral cervical cysts
- pharyngeal arches are bulging between the clefts and pouches
- neural crest cells migrate into the arches to contribute to skeletal components of the face
- each pharyngeal arch contains a mesenchyme connective tissue core, that develop into skeletal components (piece of bone or cartilage), a muscular component, a cranial nerve, and an arterial arch (see the table below)
- in the bottom of the pharynx, following organs develop: the tongue, the thyroid gland and the respiratory diverticulum (lung bud)
- **the tongue** originates from several parts:
  - two lateral lingual swellings (on the inner surface of the first pharyngeal arch)
  - one medial swelling named the tuberculum impar (in front of the oropharyngeal membrane)
  - the lateral lingual swelling fuse with the tuberculum impar and form the body of the tongue
  - behind the oral membrane, the ventral wall of the pharynx has a medial swelling named copula – this develops into the root of the tongue, which is already of entodermal origin
- **the thyroid**
  - it appears as an epithelial diverticulum in the midline of the pharyngeal entoderm behind the oropharyngeal membrane caudal to the tuberculum impar
  - it proliferates into a canal named thyroglossal duct, which descends in front of the hyoid bone and reaches its position in front of the trachea

- the mesenchyme of the 2<sup>nd</sup>-3<sup>rd</sup> pharyngeal arch interrupts the thyreoglossal duct
  - the remnants of the duct become the foramen caecum of the tongue
  - the thyroid develops two lateral lobes and a small median isthmus (a pyramidal lobe might be also present)
- **Oesophagus**
  - is separated from the respiratory diverticulum (the lung bud) with a tracheoesophageal septum
  - it lengthens with the descent of the heart and lungs
- **Stomach**
  - appears as a fusiform dilation of the foregut in week 4
  - rotates clockwise around its longitudinal axis
    - the left side faces then anteriorly (the left vagus nerves comes ventrally), the dorsal convexity becomes the greater curvature
    - the right side rotates posteriorly (the right vagus nerve runs posteriorly), the ventral convexity becomes the lesser curvature
  - then the stomach rotates also around its antero-posterior axis → the cardiac portion moves to the left; the pyloric portion moves to the right and upward
  - due to the rotation, the dorsal mesogastrium goes to the left, thus becoming the greater omentum; the ventral mesogastrium goes to the right and becomes the lesser omentum

#### **Developmental defects of the pharynx and stomodeum**

- disruption of migration of neural crest cells → ectopic localization of thymus and parathyroids in the mediastinum,
- lateral cervical cysts (branchial fistulas) anteriorly to the sternocleidomastoid muscle are remnants of the cervical sinus when the second arch fails to grow over the cervical sinus
- Pierre-Robin sequence: hypoplasia of the mandible → posteriorly placed and bulging tongue prevents the fusion of palatal processes of the maxilla → cleft palate
- accessory/aberrant thyroid tissue (glands, cysts) along the descending thyreoglossal duct in the midline of the neck
- remnants of the Rathke's pouch → accessory hypophyseal tissue in the wall of pharynx; craniopharyngioma tumor; pressure lesions of the optic chiasm

#### **Developmental defects of the foregut**

- oesophageal atresia (innate absence of the lumen) or secondary esophageal stenosis (narrowing) → amniotic fluid is not swallowed → polyhydramnion
- tracheoesophageal fistula = abnormal connection between the oesophagus and trachea when the tracheoesophageal septum fails to separate these two tubes
- oesophagus fails to lengthen → the stomach is pulled through the diaphragm = congenital hiatal hernia
- pyloric stenosis (hypertrophy of the circular pyloric sphincter muscle)

### Structures and derivatives of pharyngeal arches

Pharyngeal arch No.	Nerve	Arteries (derivatives of aortic arches)	Muscles	Skeleton (bone, cartilage or ligaments)
1. (mandibular)	V. trigeminal nerve	some part persists as the maxillary artery	Masticatory muscles (temporal, masseter, medial and lateral pterygoids)  mylohyoid, anterior belly of digastric, tensor veli palatini, tensor tympani	Premaxilla, maxilla, palatine, zygomatic, squamous part of temporal, Meckel cartilage, mandible, malleus, incus, anterior ligament of maleus, sphenomandibular ligament
2. (hyoid)	VII. facial nerve	some part persists as the stapedial and hyoid arteries	Facial (mimic) muscles  posterior belly of digastric, auricular muscles, stylohyoid, stapedius	Reichert cartilage, stapes, styloid process, stylohyoid ligament, lesser cornua and upper portion of body of hyoid bone
3.	IX. glossopharyngeal nerve	common carotid artery, proximal part of the internal carotid artery	Stylopharyngeus, constrictor pharyngis superior	Greater horn and lower portion of body of hyoid bone
4.	X. vagus nerve, superior laryngeal branch	Right: proximal part of the right subclavian artery  Left: aortic arch from the left common carotid to the left subclavian arteries	Levator veli palatini, middle and interior constrictors of pharynx, cricothyroideus	Thyroid cartilage, cuneiform cartilage
5.	does not develop and fuses with the adjacent arches			
6.	X. vagus nerve, recurrent laryngeal branch	Right: right pulmonary artery  Left: left pulmonary artery and ductus arteriosus	Intrinsic muscles of larynx	Cricoid cartilage, arytenoid and corniculate cartilages