Embryology of the Respiratory System

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Development of Pharyngeal (Branchial) Arches

These arches **appear in the fourth and fifth weeks of development** and contribute to the characteristic external appearance of the embryo. Branchial arches consist of bars of mesenchymal tissue separated by deep clefts, the **Pharyngeal (Branchial) Clefts**. **Pharyngeal pouches** are outpocketings appear along the lateral walls of the pharyngeal gut (the most cranial part of the Foregut), they appear simultaneously with development of the arches and clefts. The Pharyngeal Pouches penetrate the surrounding mesenchyme, but do not establish an open communication with the external clefts.

Pharyngeal Arches contribute to formation of Neck and Face. **At the end of the fourth week the centre of the face is formed by Stomodeum surrounded by the first pair of pharyngeal arches**
Development of Pharynx

Mesoderm

Ectoderm

Endoderm

Pharyngeal arches (5)

Pharyngeal pouches (4)

Pharyngeal cleft (4)

Oropharyng Memb

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Coronal section in the pharynx

- Phar. Arch
- Phar. Cleft
- Phar. Pouch

Pharyngeal arches

neural tube
neural crest
pharynx
pharyngeal arches
Components of Pharyngeal arch
Each pharyngeal arch consists of
1- A core of mesenchymal tissue derived from Paraxial and Lateral Plate Mesoderm, It gives origin to muscles of the face and neck. The core receives some Neural Crest Cells which migrate into the arches and contribute to skeletal components of the face
2- The core is covered on the outside by surface Ectoderm
3- On the inside of the core there is epithelium of Endodermal origin

Each Pharyngeal Arch has its own
1- Muscular components
2- Cartilaginous component
3- Cranial Nerve Components
4- Arterial Component
Pharyngeal arches are six in number, but the 5th arch degenerates and replaced by the 6th arch.
<table>
<thead>
<tr>
<th>Pharyngeal arch gives rise to</th>
<th>Muscular contributions[^3]</th>
<th>Skeletal contributions</th>
<th>Nerve supply</th>
<th>Artery supply</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st (also called &quot;mandibular arch&quot;)</td>
<td><strong>Muscles of mastication</strong>, anterior belly of the <strong>digastric</strong>, <strong>mylohyoid</strong>, <strong>tensor tympani</strong>, <strong>tensor veli palatini</strong></td>
<td><strong>Maxilla, mandible</strong> (only as a model for mandible not actual formation of mandible), the <strong>incus</strong> and <strong>malleus</strong> of the middle ear, also <strong>Meckel's cartilage</strong></td>
<td><strong>Trigeminal nerve</strong> (V2 and V3)</td>
<td><strong>Maxillary artery, external carotid artery</strong></td>
</tr>
<tr>
<td>2nd (also called the &quot;hyoid arch&quot;)</td>
<td><strong>Muscles of facial expression</strong>, <strong>buccinator</strong>, <strong>platysma</strong>, <strong>stapedius, stylomylohyoid</strong>, posterior belly of the <strong>digastric</strong></td>
<td><strong>Stapes, styloid process, hyoid (lesser horn and upper part of body), Reichert's cartilage</strong></td>
<td><strong>Facial nerve</strong> (VII)</td>
<td><strong>Stapedial artery, hyoid artery</strong></td>
</tr>
<tr>
<td>3rd</td>
<td><strong>Stylopharyngeus</strong></td>
<td><strong>Hyoid (greater horn and lower part of body), thymus, inferior parathyroids</strong></td>
<td><strong>Glossopharyngeal nerve</strong> (IX)</td>
<td><strong>Common carotid, external carotid</strong></td>
</tr>
<tr>
<td>4th</td>
<td><strong>Cricothyroid muscle</strong>, all intrinsic muscles of <strong>soft palate</strong> including <strong>levator veli palatini</strong></td>
<td><strong>Thyroid cartilage</strong>, superior parathyroids, <strong>epiglottic cartilage[^4]</strong></td>
<td><strong>Vagus nerve</strong> (X), <strong>superior laryngeal nerve[^5]</strong></td>
<td>Right 4th aortic arch: <strong>subclavian artery</strong> Left 4th aortic arch: <strong>aortic arch</strong></td>
</tr>
<tr>
<td>6th</td>
<td>All intrinsic muscles of <strong>larynx</strong> except the <strong>cricothyroid muscle</strong></td>
<td><strong>Cricoid cartilage</strong>, <strong>Arytenoid cartilages</strong>, <strong>corniculate cartilage[^4]</strong></td>
<td><strong>Vagus nerve</strong> (X), <strong>recurrent laryngeal nerve[^5]</strong></td>
<td>Right 6th aortic arch: <strong>pulmonary artery</strong> Left 6th aortic arch: <strong>pulmonary artery</strong> and <strong>ductus arteriosus</strong></td>
</tr>
</tbody>
</table>
Derivatives of Pharyngeal Pouches (4)

1st- Middle ear cavity  
Auditory tube

2nd- Palatine tonsils  
Tonsillar fossa

3rd- Inferior Parathyroid gland

4th- Ultimobranchial body (Parafollicular cells of thyroid gland) and Superior parathyroid gland

Derivatives of Pharyngeal Clefts (4)

1- External auditory meatus  
Epithelium of the eardrum

2-, 3-, 4- Cervical sinus
A. Development of the pharyngeal clefts and pouches. The second arch grows over the third and fourth arches, burying the second, third, and fourth pharyngeal clefts. B. Remnants of the second, third, and fourth pharyngeal clefts form the cervical sinus, which is normally obliterated. Note the structures formed by the various pharyngeal pouches.
Pharynx

- Posterior nasal aperture
- Nasopharynx
  - Pharyngeal tonsil
  - Opening of pharyngotympanic tube
- Uvula
- Oropharynx
  - Palatine tonsil
  - Lingual tonsil
- Laryngopharynx
- Esophagus
- Frontal sinus
- Sphenoid sinus
- Cribiform plate of ethmoid bone
- Nasal cavity
  - Superior concha
  - Middle concha
  - Inferior concha
  - Nostrils (nares)
- Hard palate
- Soft palate
- Tongue
- Hyoid bone
- Larynx
  - Epiglottis
  - Thyroid cartilage
  - Vocal fold
  - Cricoid cartilage
- Trachea

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Development of the nasal cavity
The developmental precursors of the nose are the neural crest cells, which commence their caudal migration toward the midface around the fourth week of gestation. Two nasal placodes develop inferiorly in a symmetrical fashion. Nasal pits divide the placodes into medial and lateral nasal processes. The medial processes become the nasal septum, philtrum, and premaxilla of the nose, whereas the lateral processes form the sides of the nose.
The nasal pits deepen during week 6 due to the growth of the surrounding nasal swellings, also their penetration into the underlying mesenchyme. Each primitive nasal cavity (nasal pits) grow dorsocaudally in a position which is ventral to the developing brain. Each primitive nasal cavity first, is separated from the primitive oral cavity by oronasal membrane which soon breaks down and allows the nasal and oral cavities to communicate with each other via the primitive choanae, which lie posterior to the primary palate. After the secondary palate develops, the choanae will be located at the junction of the nasal cavities and the pharynx. Secondary palate develops when the lateral palatine processes of the maxillae fuse with each other, and with the nasal septum, the oral and nasal cavities are again separated. This also separates the nasal cavities from each other.
The superior, middle, and inferior conchae develop as elevations on the lateral nasal wall of each nasal cavity. The ectodermal epithelium in the roof of the nasal cavities becomes specialized for olfaction (olfactory mucosa).

Development of nasal cavity
Inferior to the nasal complex, the stomodeum, or future mouth is formed. The **premaxilla (medial process of placodes)** is a pair of small cranial bones at the very tip of the upper jaw. The premaxilla fuses with the maxilla and usually termed as the incisive bone.

By 10 weeks, differentiation into muscle, cartilage, and bony elements occurs. Failure of these carefully orchestrated events in early facial embryogenesis may result in multiple potential anomalies, including choanal atresia,
Development of paranasal air sinuses
Paranasal air sinuses develop as a series of diverticula from each nasal cavity, they penetrate the maxillary, frontal, ethmoidal and sphenoid bones. They are lined by extensions of the nasal mucoperiosteum. This process begins prenatally, paranasal sinuses are small at birth, enlarge mainly during the eruption of the second dentation and reach their adult size soon after puberty.

The natural ventilation-rate of a sinus with a single sinus opening, is extremely slow. Such limited ventilation may be protective for the sinus, as it would help prevent drying of its mucosal surface and maintain a near-sterile environment with high carbon dioxide concentrations and minimal pathogen access. Composition of gas content in the sinuses is similar to the venous blood, with high carbon dioxide and lower oxygen levels compared to breathing air.
Paranasal air sinuses

- Aerated at birth
  - Maxillary sinuses

- Age 6-7
  - Frontal
  - Sphenoidal sinuses

- Puberty- approx 17-18 yrs
  - Ethmoid
Development of Respiratory system
At age of 4 weeks, at the end of the pharynx and beginning of oesophagus, at the ventral wall of the foregut, **Respiratory diverticulum (Lung bud)** appears between the 4\textsuperscript{th} and 6\textsuperscript{th} branchial arches.

**Tracheoesophageal septum** gradually develops and separates the diverticulum from the dorsal part, the foregut (oesophagus). In this way, the foregut is divided into ventral portion the **Respiratory Primordium** and dorsal portion, the **Oesophagus**.

At the beginning, the oesophagus is short but it lengthens rapidly with descent of the heart and lung.
The respiratory primordium maintains its communication with the pharynx through the Laryngeal orifice.

The epithelial lining of the larynx, trachea, bronchi and lungs is of <strong>endodermal origin</strong>. The cartilages, muscles and connective tissue of Larynx, trachea and lungs are derived from <strong>splanchnic (visceral) mesoderm surrounding the foregut</strong> (mesenchyme of the 4th and 6th Pharyngeal arches).
Development of Larynx

Anatomy of Larynx

[Diagram showing the anatomy of the larynx, including the hyoid bone, epiglottis, thyroid cartilage, cricothyroid muscles, cricoid cartilage, trachea, false vocal cords, true vocal cords, ventricle, and laryngeal sinus.]
Development of larynx

Development of larynx starts with the appearance of **Arytenoid swellings** on both sides of the **tracheobronchial diverticulum**.

- **Epithelial lining** of larynx originates from **endoderm**.

  **Laryngeal cartilages and muscles** originates from mesenchyme of the **forth and sixth Pharyngeal arches**.

  The mesenchyme proliferates to produce **paired arytenoid swellings**.

  The **laryngeal cartilages** develop within the arytenoid swellings from the cartilage bars of the branchial arches

  **The epiglottis** develops from the caudal half of the **hyopbranchial eminence**, a derivative of branchial arches III and IV
During growth of larynx, the laryngeal orifice changes from sagittal slit to a T-shaped opening and then to an adult shaped orifice when laryngeal cartilages have developed.
The aperture of Larynx remains occluded until the 3rd month of intrauterine life, this is due to the rapid proliferation of laryngeal epithelium which results in a temporary occlusion of the lumen. Subsequently, recanalization takes place, during this process two lateral recesses are formed, the **laryngeal ventricles**. Laryngeal ventricles are bounded by folds of tissue that differentiates into **vestibular (false) and true vocal cords**.

**Epiglottis** – develops from the **Hypobranchial eminence**.

**Thyroid cartilage** – develops from the ventral ends of 4th pharyngeal arch.

**Cricoid cartilage and tracheal cartilages** – develop from the 6th pharyngeal arch during the 6th week of intrauterine life.
Development of Trachea, Bronchi and Lungs

As the Tracheobronchial bud (lung bud) separated from the foregut, it forms the trachea and two lateral swellings, the bronchial buds. In the fifth week these swellings form the right and left main bronchi.

The right bronchus divides into three secondary bronchi and the left bronchus divides into two.

During further development, the left secondary bronchi divide and form ten Tertiary (Segmental) Bronchi and the right bronchi form eight, thus the Bronchopulmonary Segments of adult lung are formed.
Division of bronchi continue up till the fetal age of six months at which about 17 generations of subdivision have formed before the bronchial tree reaches its final shape. However, an additional six divisions take place during postnatal life. While the bronchial tree is developing, the lungs assume a more caudal position.
During the growth of the lung in a caudal and lateral direction, it expands into the body cavity on both sides of the foregut, this process helps in dividing the body cavity into three parts, peritoneal, pericardial and pleural cavities. The visceral mesoderm, which covers the outside of the lung develops into Visceral Pleura, while the parietal (somatic) mesoderm layer, lining the body wall from the inside develops into Parietal Pleura. The space between the visceral and parietal layers is called, the pleural cavity.
Development of body cavities

Lung

Layers of Pleura

Somatic (parietal) mesod

Splanchnic (visceral mesod)

Pleuropericardial folds fuse in the mid-line and separate the pleural and pericardial cavities

As the lungs grow the mediastinal pleural expands anteriorly and surrounds the pericardium

Fibrous layer formed from fibrous tissue from embryonic body wall and mediastinal pleura

Inner serosal layer (visceral) forms from splanchnic mesoderm

Outer serosal layer (parietal) forms from somatic mesoderm

Dorsal mesocardium regresses as heart develops

Embryonic body wall tissue invaginates between layers of somatic mesoderm

Splanchnic layer of mesoderm

Somatic layer of mesoderm

Ectoderm

Endoderm

Primitive heart tube forms within splanchnic mesoderm

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Development of body cavities

- Foregut
- Pericardial cavity
- Lung bud
- Pleuro-pericardial fold
- Phrenic nerve
- Common cardinal vein
- Heart
Maturation of the lungs
Up to the 6th month, the bronchi keep dividing and the vascular supply increases steadily. After age of 26 weeks, the cuboidal cells that line the Respiratory bronchioles change into thin flat cells (**type 1 alveolar epithelial cells**). These cells line spaces known as **terminal sacs** or **primitive alveoli** which are surrounded with blood and lymph capillaries.
During the seventh month, there is sufficient number of capillaries which enable the premature infant to survive if born at this age.
**During the last two months of pregnancy and for some years after birth**, the number of primitive alveoli increases greatly and their lining cells become thinner.
Subsequently, the surrounding capillaries are enabled to protrude into these thin walls and **mature alveoli** are formed. **Mature alveoli** are not present before birth.
**Type II Alveolar Epithelial Cells**

In addition to the flat alveolar cells, another cell type appears **at the end of the sixth month**. These cells are called **Type II Alveolar Epithelial Cells**, they **produce Surfactant**. This material is a phospholipid-rich fluid, it lowers the surface tension at the air-alveolar interface by forming a phospholipid coat on the alveolar membranes.

Before birth the lungs are filled with **fluid** that contains
1- High chloride concentration
2-Little amount of protein
3-Mucous
4-Surfactant

The amount of surfactant increases during the last two weeks before birth.
Type I and type II alveolar cells
At the beginning of respiration, the lung fluid is desorbed except for the surface coat. This coat prevents the collapse of the alveoli during expiration by reducing the surface tension at the air-blood capillary interface.

Insufficient surfactant in the premature baby causes Respiratory Distress Syndrome (Hyaline membrane Disease) The lungs continue growing during the first 10 years after birth, this is achieved through an increase in the number of respiratory bronchioles and alveoli.

At birth, only-sixth of the adult number of alveoli are present.
Congenital Anomalies of Respiratory System
Respiratory Distress syndrome
Tracheoesophageal Fistula

C. Double fistula
D. Fistula without esophageal atresia
E. Esophageal atresia without fistula
F. Aplasia of trachea (lethal)

G. Stricture of trachea
H. Absence of cartilage
I. Deformity of cartilage
J. Abnormalities of bifurcation
congenital diaphragmatic hernia

Normal newborn anatomy

Part of small intestine has herniated through the diaphragm
congenital lobar emphysema
Left side congenital pulmonary atresia
congenital cystic adenomatoid malformation of the lung