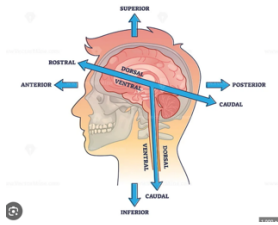


EMBRYOLOGY LECTURE 1

Development of the nose and Palate

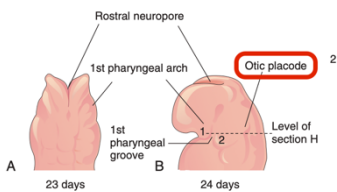


- General information to keep in mind:
 - We have **3 layers** :
 - **Endoderm** gives lining **epithelium**, ex: GI,RS lining.
 - **Mesoderm** gives bone, **cartilage, muscles, blood** and **lymph**.
 - **Ectoderm** gives **outer layers** like **skin**.
- Keep these locations in mind (picture on the left)

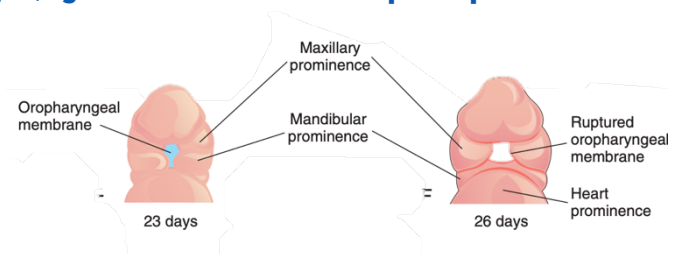
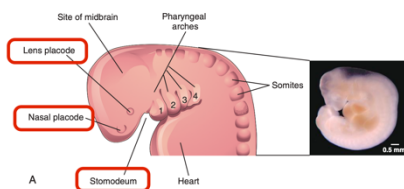
Development of the nose

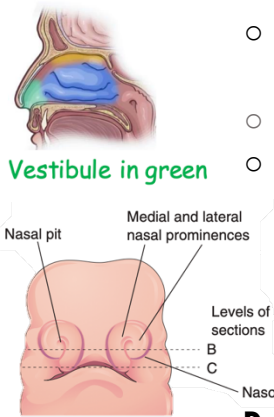
- At the **end of the fourth week**, **facial prominences** consisting **primarily of neural crest-derived mesenchyme** and **formed mainly** by the **first pair of pharyngeal arches** appear
- The **frontonasal prominence**, will **give a septum** formed by **proliferation of mesenchyme ventral to the brain vesicles**, constitutes the **upper border of the stomodeum**
- On both sides of the frontonasal prominence, local thickenings of the surface ectoderm, the nasal (olfactory) placodes, originate under inductive influence of the ventral portion of the forebrain

Terms to know:



- **Otic placode** : beginning of the **ear**.
- **Lens placode** : beginning of the **eye**.
- **Stomodeum** : related to **oral cavity** (extra info: depression in the ectoderm develops oral cavity)
- **Prominence: eminence**
- **Frontonasal prominence**: from **frontal bone descending** to the **nasal cavity**, to **form the septum of the nose**).
- **Nasal placode** makes **nostrils**.
- **Maxillary prominence** (upper jaw) , **grow toward the midline**, **participates in forming the upper lip**.
- **Mandibular arch** (lower jaw).

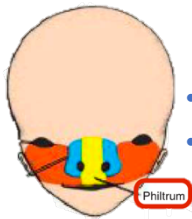
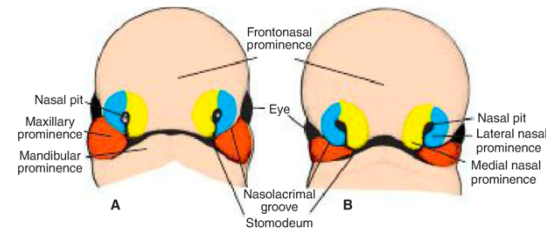




- During the **fifth week**, the **nasal placodes invaginate** to form **nasal pits (nostril)**, then **Invagination** of cells gives **vestibule**.
- In so doing, they create a ridge of tissue that surrounds each pit and forms the nasal prominences.
- The **prominences** on the **outer edge** of the **pits** are the **lateral nasal prominences**; those on the **inner edge** are the **medial nasal prominences**
 - The **lateral nasal placode** will give the **lateral wall** of the **nose**
 - The **medial nasal placode** will give the **septum** and **anterior wall** of the **nose**

- During the **following 2 weeks**, the **maxillary prominences continue to increase in size**
- Simultaneously, they grow medially, compressing the medial nasal prominences toward the midline
- Subsequently the cleft between the medial nasal prominence and the maxillary prominence is lost, and the two fuse

- **Medial nasal prominence** gives:
 - 1-**tip of the nose**.
 - 2-**septum**.
 - 3- **medial part of upper lip**.



- **Maxillary prominence** gives **lateral part of upper lip**.
- If **fusion fails to occur between medial nasal prominence and maxillary prominence**, **cleft will be formed**.
- **Philtrum: vertical depression of the upper lip**

- The **nose is formed from five facial prominences**
 1. **Frontal prominence**: gives rise to the **bridge**; and **nasal septum**
 2. merged **Medial nasal prominences**: provide the **crest** and tip
 3. **Lateral nasal prominences**: form the **sides (alae)**
 4. **Maxillary prominence**
 5. **Mandibular prominence**
- **Olfactory pit** forms the **nostril** and then **becomes deeper** to form a **blind sac** (the **vestibule**), [so **Olfactory pit** → **invagination of mucosa** → **vestibule**].

Summary:

TABLE 15.2 Structures Contributing to Formation of the Face

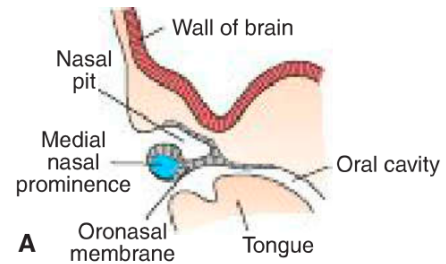
Prominence	Structures Formed
Frontonasal ^a	Forehead, bridge of nose, medial and lateral nasal prominences
Maxillary	Cheeks, lateral portion of upper lip
Medial nasal	Philtrum of upper lip, crest and tip of nose
Lateral nasal	Alae of nose
Mandibular	Lower lip

^a The frontonasal prominence is a single unpaired structure; the other prominences are paired.

Nasal Cavities

1. During the **sixth week**, the **nasal pits deepen** considerably, **partly** because of **growth** of the **surrounding nasal prominences** and **partly** because of their **penetration** into the **underlying mesenchyme**, [**nasal pit deepen the mucosa → cavity**].

The **oronasal membrane** in the picture that it is in the **position of the hard palate** which **separates the oral cavity from the nasal cavity**.

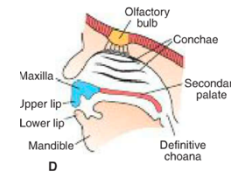


2. At **first** the **oronasal membrane (floor of the nose)** separates the **pits** from the **primitive oral cavity** by way of the **newly formed foramina**, the **primitive choanae**
Firstly, oronasal membrane rupture, when **formation of the septum (1ry palate)** begins, which will **separate both cavities**.

These choanae lie on each side of the midline and immediately behind the primary palate.

3. Later, with formation of the secondary palate and further development of the primitive nasal chambers the **definitive choanae** will **lie** at the **junction** of the **nasal cavity** and the **pharynx (nasopharynx)**.

Remember : conchae, which is extension of bones in the lateral wall of the nose where the superior and middle are from ethmoid bone, and inferior are from maxilla.



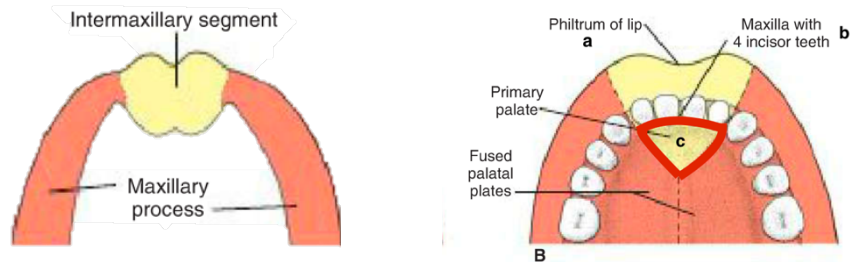
Paranasal air sinuses

- **Paranasal air sinuses develop** as **diverticula** of the **lateral nasal wall** and **extend into** the **maxilla, ethmoid, frontal, and sphenoid bones**.
- They **reach** their **maximum size during puberty** and **contribute** to the **definitive shape** of the **face**.
 - **Each sinus** has a **duct opening** in the **lateral wall** of the **nose**.
 - In the **development**, the **proliferation begins from the opening of lateral wall of nasal cavity**.
 - **Proliferation of cells → duct formation → continues through the cranial bone - forming a cavity → sinus formation**.
 - **Sinus is very small** in shape **at the beginning**, but **with the development** of the **face at puberty**, **Paranasal sinuses reach** its **maximal size**.

Primary palate

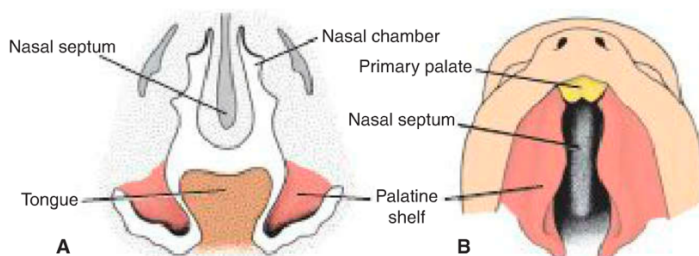
- As a result of **medial growth** of the **maxillary prominences**, the **two medial nasal prominences merge** not only at the surface but also at a **deeper level**.
- The **structure formed** by the two merged prominences is the **intermaxillary segment**
- It is **composed of** :
 - (a) a **labial component**, [coming from the nasal part, completed by the intermaxillary segment] which **forms the philtrum** of the **upper lip**;
 - (b) an **upper jaw component**, which carries the **four incisor teeth**;
 - (c) a **palatal component**, which **forms the triangular primary palate**, 1ry palate from Intermaxillary segments form maxillary prominence [the part labeled by laser in the picture].

The **intermaxillary segment** is **continuous** with the **rostral portion** of the **nasal septum**, which is **formed by the frontal prominence**.

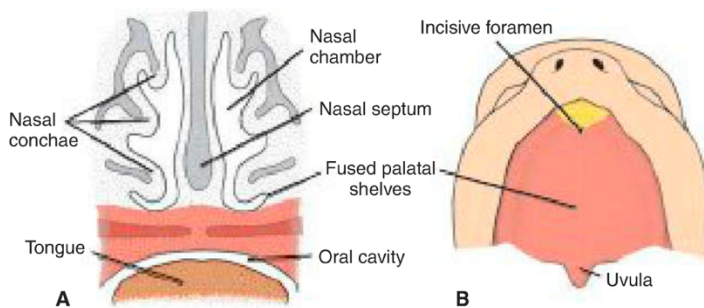


Secondary Palate

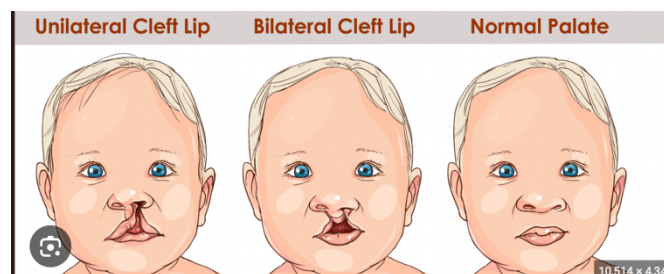
- The **main part** of the **definitive palate** is **formed** by **two shelflike outgrowths** from the **maxillary prominences**.
- These **outgrowths**, the **palatine shelves**, **appear** in the **sixth week** of development and are **directed obliquely downward** on **each side** of the **tongue**
 - The **Palatine shelves** which are **outgrowths** from the **two sides** of the **maxillary prominence**, **grow medially** and **directed above** the **tongue to form the hard palate** (secondary palate).
 - **Secondary shelves meet** in the **midline**.
 - Logically: **secondary palate** is **formed above** the **tongue**.
 - There is a **fusion between primary** and **secondary palate** in **midline**.
 - **Incisive foramen** will be **formed between 1ry & 2ry palates** :
 - forming **connection between oral cavity** and **nasal cavity**
 - formed due to **fusion between primary** and **secondary palate**
 - **Septum** of the **nose** is **descending downwards** (which **meets** and **fuses** with the **secondary palate** at the **midline**).



- In the seventh week, however, the palatine shelves ascend to attain a horizontal position above the tongue and fuse, forming the secondary palate
- **Anteriorly**, the **shelves fuse** with the **triangular primary palate**, and the **incisive foramen** is the **midline landmark between the primary and secondary palates**
- At the same time as the palatine shelves fuse, the nasal septum grows down and joins with the cephalic aspect of the newly formed palate
 - **If 1ry & 2ry palate fusion fails → cleft (unilateral or bilateral).**
- **2 folds grow posteriorly** from the **edge** of the **palatine process** to **form the soft palate and the uvula**.
- The **union** of the **2 folds** of the **soft palate occurs** during the **8th week**



- The **2 parts of the uvula fuse** in the **midline** during the **11th week (failure of this fusion would result in a cleft formed between uvula , uvula appears as it is divided into 2 parts)**
- **Unilateral cleft lip** can **extend to the nose**, (a cleft lip might be unilateral or bilateral / complete or incomplete)

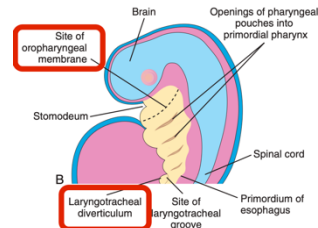


Respiratory System

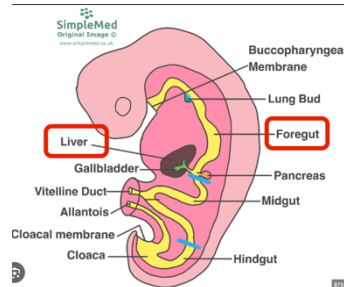
Primitive gut

○ Development of the **primitive gut** and its **derivatives** is in **four** sections:

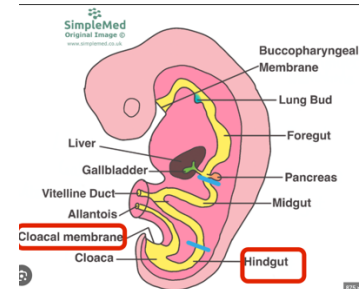
(a) The **pharyngeal gut/pharynx**, extends from the **buccopharyngeal membrane** to the **tracheobronchial diverticulum**



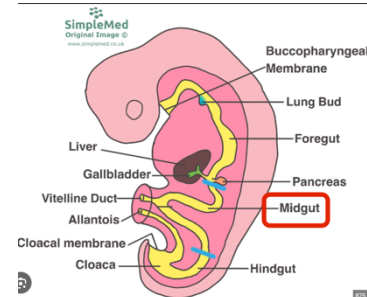
(b) The **foregut** lies **caudal** to the **pharyngeal tube** and **extends** as far **caudally** as the **liver outgrowth (Mid duodenum)**.



(c) 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** in the **adult**.

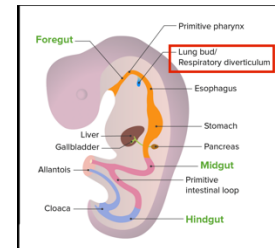


(d) The **hindgut** extends from the **left third of the transverse colon** to the **cloacal membrane**, (ends at **Upper half of the anal canal**)



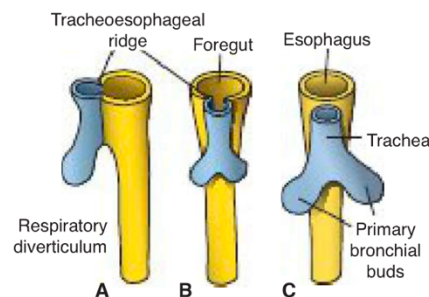
Respiratory diverticulum

- When the **embryo** is **approximately 4 weeks old**, the **respiratory diverticulum (lung bud)** **appears** as an **outgrowth** from the **ventral wall** of the **foregut**
 - **Proliferation** of **cells** makes the **lung bud** [which **represents** the **beginning** of **trachea formation**]



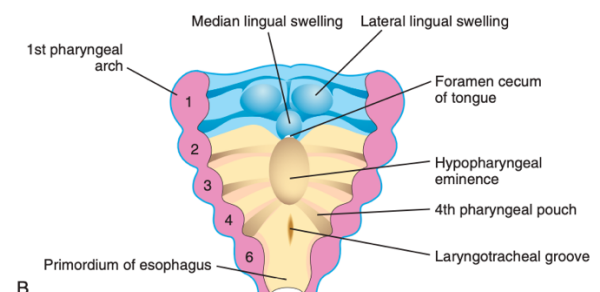
- The **location** of the **bud** along the **gut tube** is **determined by signals** from the **surrounding mesenchyme**, including **fibroblast growth factors (FGFs)** (**stimulates cells for proliferation**) that **instruct** the **endoderm**
- The **epithelium** of the **internal lining** of the **larynx**, **trachea**, and **bronchi**, as well as that of the lungs, is **entirely of endodermal origin**.
- The **cartilaginous**, **muscular**, and **connective tissue components** of the **trachea** and **lungs** are **derived** from **splanchnic mesoderm surrounding the foregut**.
 - Remember that Mesoderm has 2 types (splanchnic [lining]& somatic)

- Initially the lung bud is in open communication with the foregut
- When the **diverticulum expands caudally**, **two longitudinal ridges**, the **tracheoesophageal ridges**, **separate** it from the **foregut**
- Subsequently, when **these ridges fuse** to **form** the **tracheoesophageal septum**, the **foregut** is **divided** into a **dorsal portion**, the **esophagus**, and a **ventral portion**, the **trachea** and **lung buds**



- The **respiratory primordium maintains** its **communication** with the **pharynx through** the **laryngeal orifice**

- **Larynx originate** from **4,6 pharyngeal arches**.
- The **inlet** of the **larynx connects between** the **GI** and **RS**.



Esophagus

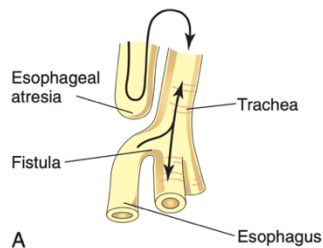
- At first the esophagus is short
- But with **descent of the heart and lungs** it **lengthens** rapidly
- The **muscular coat**, which is **formed** by **surrounding splanchnic mesenchyme**, is **striated** in its **upper two-thirds** and **innervated** by the **vagus** the **muscle coat** is **smooth** in the **lower third** and is **innervated** by the **splanchnic plexus (autonomic)** .

Anomalies of the trachea and esophagus

Tracheoesophageal fistula (TEF)

- Abnormalities in partitioning of the esophagus and trachea by the tracheoesophageal septum result in esophageal atresia with or without tracheoesophageal fistulas
- These defects occur in approximately in 1/3000 births, and 90% result in the upper portion of the esophagus ending in a blind pouch and the lower segment forming a fistula with the trachea
- Predominantly affect male infants

The case in the picture having **proximal atresia (blind-end)** and **distal fistula** is the **most common case** representing **90% of cases**.



Baby with Tracheoesophageal fistula will have :

1-**Vomiting** while **breast feeding**, because the blind end, the Esophagus is blocked, food can't reach the stomach.

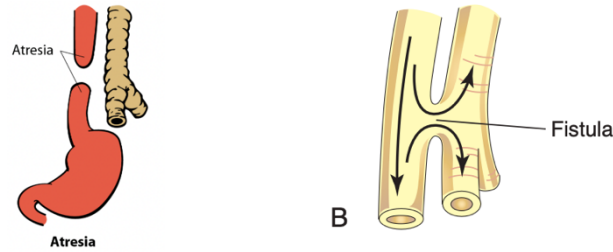
2-**abdominal distension, while crying**, air can reach the stomach by the distal part of the Esophagus which is connected to the trachea.

3-**pneumonia**, gastric contents travel to trachea to lungs, through the distal part of the Esophagus which is connected to the trachea.

4-**polyhydramnios** (extra amniotic fluid before birth) , [oligohydramnios is the opposite world] , normally amniotic fluid travel to the oral cavity to GI tract and leave with urine, but fistula impedes this pathway.

Sereen Draghmeh

- Isolated esophageal atresia and H-type TEF without esophageal atresia each account for 4% of these defects.



- Other variations each account for approximately 1% of these defects.
- TEF is the most common anomaly in the lower respiratory tract
- These **abnormalities** are **associated** with **other birth defects**, including **cardiac abnormalities** [**Falot's tetralogy & atrial, ventricular septal defect**], which **occur in 33% of these cases**.

•Complications with tracheoesophageal fistula:

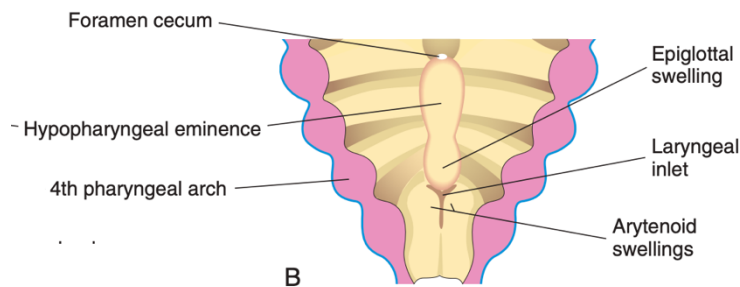
- In this regard **TEFs** are a **component of** the **VACTERL association** (Vertebral anomalies, Anal atresia, Cardiac defects, Tracheoesophageal fistula, Esophageal atresia, Renal anomalies, and Limb defects)
- a collection of defects of unknown causation, but occurring more frequently than predicted by chance alone.

Tracheal atresia (Rare) and stenosis

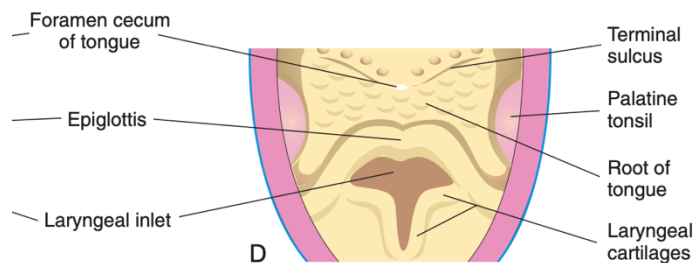
- Are uncommon anomalies and usually associated with one of the varieties of TEF
- In some case a **web tissue may obstructs the airflow (incomplete tracheal atresia)**

Larynx

- The **internal lining** of the **larynx originates** from **endoderm**, but the **cartilages** and **muscles originate** from **mesenchyme** of the **fourth and sixth pharyngeal arches**
- As a result of **rapid proliferation** of this **mesenchyme**, the **laryngeal orifice changes** in **appearance from a sagittal slit to a T-shaped opening**
(at the beginning of larynx formation the shape changes)



- Subsequently, when mesenchyme of the two arches transforms into the thyroid, cricoid, and arytenoid cartilages, the characteristic adult shape of the laryngeal orifice can be recognized



- **After larynx cartilage formation** → proliferation of mesenchymal cells which
 - **fill the larynx** → canalization → cavity which has 2 ventricles and a sacculle
- At about the time that the cartilages are formed, the laryngeal epithelium also proliferates rapidly resulting in a temporary occlusion of the lumen.
 - **Subsequently, vacuolization** and **recanalization produce** a pair of **lateral recesses**, the **laryngeal ventricles**

- These **recesses** are **bounded** by **folds** of **tissue** that **differentiate into** the **false and true vocal cords**.
 - Remember: Above the ventricle we have the false vocal cord, and below it the true vocal cord.
- Since **musculature** of the **larynx** is **derived** from **mesenchyme** of the **fourth and sixth pharyngeal arches**, **all laryngeal muscles are innervated by branches of the tenth cranial nerve, the vagus nerve**
- The **superior laryngeal (gives external laryngeal nerve)** nerve **innervates derivatives** of the **fourth pharyngeal arch (cricothyroid)**, and the **recurrent laryngeal nerve innervates derivatives** of the **sixth pharyngeal arch**

Anomalies of the larynx

Laryngeal atresia

- **Laryngeal atresia** is a **rare anomaly** and **cause obstruction** of the **upper fetal airway**
- **Also known as congenital high airway obstruction syndrome (chaos)**
- **Distal to the atresia or stenosis** the **lung** are **enlarged (to compensate the obstruction)** and **capable of producing echoes (echogenic)**
- **Also the diaphragm (instead of the copula)** is **flattened or inverted** and **fetal ascites (fluid in abdominal cavity)** and **hydrops (accumulation of serous fluid)** is **present**
- Prenatal ultra-sonography permits diagnosis. **Eco test**