KAZAN FEDERAL (VOLGA REGION) UNIVERSITY INSTITUTE OF FUNDAMENTAL MEDICINE AND BIOLOGY DEPARTMENT OF MORPHOLOGY AND GENERAL PATHOLOGY

Lecture 2 Respiratory system. Development





Respiratory system

is a biological system consisting of specific organs and structures used <u>for the</u> <u>process of</u> <u>respiration</u> in an organism

Breathing and Respiration

- BREATHING is the mechanical action of getting air in and out of the lungs.
- RESPIRATION is the chemical reaction that provides the energy that makes the organism function. It occurs in the cells, more precisely in the mitochondria (the powerplant of the cell).



Breathing	Cellular Respiration					
Definition						
Breathing involves the process of inhaling oxygen and exhaling carbon dioxide	Cellular respiration is the process of breaking down glucose to produce energy, which is then used by cells to carry out the cellular function.					
Process Occ	currence					
Breathing takes place in the lungs. Also involves the nose, mouth and pharynx	Respiration takes place in cells					
Type of Process						
Breathing is voluntary as well as an involuntary physical process. (For example, breathing during sleep is involuntary. Voluntary breathing is observed when we sing, speak, swim or for relaxation techniques)	Respiration is an involuntary chemical process.					
Production of	of Energy					
There is no production of energy in this process.	Energy is produced and released in the form of ATP.					
Cellular A	ctivity					
As it occurs outside cells, it is called the extracellular process. (Occurs between the organism and the external environment)	As it occurs inside cells, it is called the intracellular process.					
Enzyme used						
No enzymes are used during the process.	A large number of enzymes are used during the process.					
Associated Organs						
Breathing occurs through respiratory organs, including the nose, lungs, etc.	Respiration takes place in cells and cell organelles, including mitochondria, etc.					

Systema respiratorium





The inner surface of the airways is lined by the mucous membrane which is covered by *ciliated columnar epithelium* and contains numerous glands secreting the mucus.

Due to this the inspired air is <u>cleaned</u>, <u>humidified</u> and <u>warmed</u>.

The development of the respiratory system

The upper respiratory tract



Development of the face (from 4th to 8th weeks)

1. Development of the primitive mouth – stomodeum (beginning of the 4th week)

2. Rupture of oropharyngeal membrane (the 24th day)

- 3. Development of the nasal cavity (from the end of the 4th week)
- 4. Rupture of oronasal membrane (the 6th week)

5. Development of **paranasal air sinuses** from diverticuli of nasal walls during late fetal life & after birth



Sagittal section through a 25-day embryo Figure from Ten Cate's Oral Histology, Ed., Antonio Nanci, 6th edition



- The frontonasal process rises from the neural crest and covers the forebrain. It will give rise to two medial nasal processes and two lateral nasal processes.
- By the tenth week, the inter-maxillary process will form the nasal bridge and the philtrum of the upper lip.







- The tissues of the 1st (mandibular) pharyngeal arch originates from mesoderm and the neural crest.
- The 1st arch will give rise two mandibular processes and two maxillary processes (proximal part of the arch).
- The maxillary processes will later form to a pair of palatal processes.





Schematic of frontonasal region in embryological development.



- The maxillary prominences and median nasal prominences progressively migrate toward the midline.
- \succ The nose forms from fusion of the medial and lateral nasal prominences.
- The upper lip forms from the fusion of the medial nasal prominence and maxillary prominence on each side.
- The nasolacrimal grooves form as a gap between the lateral nasal prominence and the maxillary prominence

Rupture of buccopharyngeal membrane

- Fetus swallow amniotic fluid stimulation of growth of digestive system organs
- Organs of the respiratory system are isolated from fluid by epithelial cells growth ("stoper")



Rupture of buccopharyngeal membrane





Stomodeum

Oral cavity

Buccopharyngeal/oropharyngeal membrane \rightarrow Fauces Ectoderm \rightarrow Epithelial lining of oral cavity, teeth Ectoderm \rightarrow Parotid and submandibular salivary glands Endoderm (foregut) Epithelial lining of pharynx Endoderm (foregut) Sublingual salivary gland Ratke`s pouch \rightarrow Adenohypophysis

Prominence	Derivatives		
Frontonasal	Forehead, bridge of nose,		
	prominences		
Medial nasal	Philtrum, primary palate,		
	upper 4 incisors and		
	associated jaw		
Lateral nasal	Sides of the nose		
Maxillary (1st pharyngeal	Cheeks, lateral upper lip,		
arch)	secondary palate, lateral		
	upper jaw		
Mandibular (1st	Lower lip and jaw		
pharyngeal arch)			

Development of the primitive mouth It develops (Stomodeum)

from five facial primordia:

– Frontonasal prominence

– Paired maxillary prominences

– Paired mandibular prominences



Medial and Lateral Nasal Prominences form a boundary of Naris

Stomodeum and nasal placodes

Stomodeum (future oral cavity) Nasal placodes

-bilateral right and left oval thickenings of surface ectoderm, the end of the 4th week

Nasal placodes → Nasal pits → Nasal sacs

Nasal placodes

- divide frontonasal prominence into medial nasal and lateral nasal processes





Maxillary prominences and lateral nasal process fuse, between them remains nasolacrimal groove (nasolacrimal canal in future)





7-8th weeks – intensive growth of the medial nasal processes between maxillary prominences – formation of philtrum
fusion of medial nasal processes with maxillary prominences – formation of the upper lips





Medial nasal processes

Lateral nasal processes

Maxillary prominences

Mandibular prominences





The lateral aspect of external nose, nostrils

The maxillae, lateral parts of the upper lips, the hard palate

The mandible, lower lips

Development of the Palate



Development of nasal cavity and palate



- Rupture of oronasal membrane (6th week)
- Development of choana
- Development of primary and secondary palate

Development of nasal cavity and palate



Nasal septum, incisive bone & central part of upper lip develop from merged medial nasal prominences

Development of the palate and palate cleft



Normal







Anterior cleft only



Posterior cleft only





Congenital anomalies of middle face

1. Oblique cleft of the face (persistent nasolacrimal groove)

It connect mouth to medial palpebral angle of the orb

Nasolacrimal duct is present as open grove
 It results from failure of fusion of lateral nasal and maxillar
 prominences

2. Cleft of upper lip, superior alveolar arch and palate – It results from failure of fusion of medial nasal and maxillary prominences They could be unilateral or bilateral









Paranasal air sinuses



Anterior

-facial skull bones which contain air spaces
lined with mucous membrane
-make the skull light
-impart resonance to voice
-act as conditioning chambers for inspired air



- Sinuses appear on 12th week of gestation
- Rapid growth till 12-years after birth
- Growth together with facial skull bones
- Growth of maxillary sinus stops with eruption of last molars

Development of branchial apparatus (arches, pouches, grooves)



The 4th week - neural crest cells migrate through the mesenchyme to the future head and neck region, forming elevations of mesoderm on each side of the primitive pharynx



Pharyngeal arches



- a series of mesodermal outpouchings on both sides of the developing pharynx
- covered with:
- Ectoderm outside formation of pharyngeal clefts
- Endoderm inside formation of pharyngeal pouches

The 1st Pharyngeal arch (mandibular)

<u>Develop:</u>

- masticatory muscles
- m. mylohyoideus, m. digastricus (venter anterior)
- m. tensor veli palatini, m. tensor tympani
- Lips
- Jaws
- Palate
- Anterior 2/3 of the tongue
- Porus accusticus externus
- Membrana tympanica
- Malleus and incus
- External ear (anterior part)
- Innervated by trigeminal nerve (V)



Meckel`s cartilage – mandible

NBI Mandible buds are paired!



The 2nd Pharyngeal arch (hyoid)

- Innervated by facial nerve (VII)
- mimic muscles
- m. digastricus (venter posterior)
- m. stylohyoideus
- Stapes and m.stapedius
- Processus styloideus
- Hyoid bone
- Tonsilla palatina
- External ear (posterior part
- Anterior 2/3 of the tongue





The 3rd Pharyngeal arch

- Innervated by glossopharyngeal (IX) nerve
- muscles of the palate
- m. stylopharyngeus
- Hyoid bone
- Thymus
- Posterior 1/3 of the tongue





The 4th and the 6th Pharyngeal arches

- Innervated by vagal (X) nerve
- Muscles of the palate and pharynx
- Cartilages and muscles of the larynx
- Thymus
- Root of the tongue





Development of the tongue



Figure 12-3. Diagram showing the development of the tongue. (A) At week 5. (B) In the newborn.

Tongue parts	Tongue buds	Origin of the bud	Fusion	Innervation
Anterior 2/3 of the tongue	-Median bud -2 distal buds	Pharyngeal arch 1,2	Median sulcus	CN V, CN VII
Posterior 1/3 of the tongue	- Copula	Pharyngeal arches 3	Sulcus terminalis Foramen cecum	CNIX
Root of the tongue	- Hypobranchi al prominence	Pharyngeal arch 4,5		CNX

Development of the tongue



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Pathology of the tongue development

1. <u>Aglossia</u>

2. <u>Microglossia</u>, which is always combined with other defects and syndromes, like Moëbius syndrome

3. <u>Macroglossia</u>, which is commonly associated with cretinism, Down's syndrome, Hunter's syndrome, Sanfilippo syndrome and other types of mental retardation

4. <u>Accessory tongue</u>

5. Long tongue

6. <u>Cleft or Bifid tongue</u>, condition very usual in patients with the orodigitofacial syndrome

7. <u>Glossitis Rhombica Mediana</u>, a developmental malformation

8. Lingual thyroid.

Ankyloglossia

- Fixation of the tongue to the floor of the mouth, causing restricted movement.
- > CLINICAL FEATURES
- Speech disorders
- Deformities in occlusion
- Difficulties in swallowing
- It can be either complete ankyloglossia or partial ankyloglossia (tongue tie)
- <u>Complete ankyloglossia</u> occurs as a result of fusion between the tongue and the floor of the mouth. Can be surgically treated by frenulectomy.
- <u>Partial ankyloglossia</u> occurs as a result of short lingual fraenum or due to a fraenum which attaches too near the tip of the tongue. It is self corrective.





The development of the respiratory system

The lower respiratory tract



Development of the larynx - the 4th and the 6th Pharyngeal arches - Innervated by vagal (X) nerve

- Muscles of the palate and pharynx
- Cartilages and muscles of the larynx
- Thymus



Development of Laryngeal Inlet



Figure 11-3. Drawings illustrating successive stages in the development of the larynx. A, 4 weeks. B, 5 weeks. C, 6 weeks. D, 10 weeks. The epithelium lining the larynx is of endodermal origin. The cartilages and muscles of the larynx arise from mesenchyme in the fourth and sixth pairs of pharyngeal arches. Note that the laryngeal inlet or aditus changes in shape from a slitlike opening to a T-shaped inlet as the mesenchyme surrounding the developing larynx proliferates.

cartilages

Development of the trachea



Figure 11-1. Early development of respiratory system. (*A*) Lateral view of an embryo at day 25, showing the entire primitive gut tube. The area in the *rectangle* indicates the portion of foregut involved in respiratory development. This area is enlarged in *B*. (*B*) Relationship of the laryngotracheal diverticulum and foregut. *Curved arrows* indicate the movement of the tracheoesophageal folds.



Congenital anomalies of trachea

 Tracheoesophageal fistula – communication between trachea and esophagus



Congenital anomalies of trachea

2. Tracheal Stenosis (narrowing) and Atresia (closure)



Congenital anomalies of trachea

3. Tracheal diverticulum





From foregut develop:

- Esophagus
- Stomach
- Duodenum (proximal part)
- Liver, pancreas, gall bladder
- Respiratory tube

Blood supply – truncus coeliacus Sympathetic innervation – n. splanchnicus major Parasympathetic innervation – n.vagus



Tubular organ layers development

Epithelial lining and glands - Derived from endoderm

- Mucosa

Muscularis mucosae

Lamina propria

Derived from visceral mesoderm

- Submucosa

- Muscularis externa/cartilages

- Adventitia/Serosa



Five phases of development of the lungs



Development of the bronchi



embryo, 5 week



- 1 heart 2 – chorda 3 – brain vesicles and neural tube 4 – oesophagus 6 – stomach 7 – liver 8, 9 – midgut form yolk loop, 10 – hindgut 11 - cloaca 12 – cloacal membrane 13 – allantoise 14 – yolk stalk/duct 15 - coelom
 - b coelom

1. Embryonic Phase

The distal end of the lung bud bifurcates into the right and left primary bronchial buds, whereas the proximal end (stem) forms the trachea and larynx.

Primitive

Gut Tube

Respiratory

Diverticulum



- > By the fifth week of gestation, the primary bronchial buds form three secondary bronchial buds on the right side and two on the left
- Each secondary bronchial bud gives rise to ten tertiary bronchial buds on both sides, demarcating the end of the embryonic phase

42 days

Α.

D

Trachea

28 days

35 days

Bronchial

eft secondary bronchus

Right secondary bronchus

buds



2. Pseudoglandular phase

takes place during <u>between the sixth and sixteenth week</u> of gestation.
 The respiratory tree undergoes twelve to fourteen more generations of branching, resulting in the formation of <u>terminal bronchioles</u>.

➤This passageway will be lined with a specific type of respiratory epithelium, simple columnar epithelium (ciliated) transitioning to simple cuboidal epithelium (some cilia).





3. Canalicular phase

canalicular phase takes place during the <u>sixteenth and twenty-</u> <u>eighth week of gestation</u>.

Each terminal bronchioles further divide into <u>respiratory</u> <u>bronchioles</u>, which become surrounded with an increase in <u>vascularization</u>.





4. Saccular phase

- takes place between <u>the twenty-eighth and thirty-sixth week of</u> gestation.
- The respiratory bronchioles give rise to a final generation of terminal branches.
- These branches become invested in a dense network of capillaries, forming the <u>terminal sacs (primitive alveoli)</u> that are lined with type I and type II alveolar cells.





5. Alveolar phase

The alveolar phase is characterized by the maturation of the <u>alveoli</u>, a process that takes place during the end of fetal life and many years after birth.





Embryonic	Pseudoglandular	Canalicular	Saccular	Alveolar
×				ઙૺ૱
0 7 we	eks 17 w	eeks 27 w	eeks 36 we	ks 2 years
Trachea	 Terminal bronchiles 	 Respiratory bronchioli 	 Gas exchange 	Septation
 Right and left main bronchi Segmental bronchi 	 Pulmonary artery veins 	 Alveolar ducts Primitive alveoli Alveolar capillary barrier 	 Alveoli 	Multiplication of alveoli

Bronchopulmonary segments

- is a segment of lung tissue supplied by a tertiary (segmental) bronchu



Development of the human lung



Day 41-44

Week 9

Week 10

7 trachea; 1 Left main bronchus; 6 right main bronchus; others lobes



Type I pneumocytes – thin, flat cells that make up part of the blood-air barrier Type II pneumocytes – cells, that produce surfactant

Pulmonary surfactant

- a surface-active lipoprotein complex (phospholipoprotein) formed by type II alveolar cells. By adsorbing to the air-water interface of alveoli it reduces surface tension and prevents collapse of the lung (atelectasis) at the end of expiration.



normal alveolar sac with increased water-air contact - thank you surfactants!

collapsed alveolar sac with minimal water-air contact



Premature fetuses born between week 25 and 28 can survive with intensive care!

This is the earliest point at which fetus can survive.

Adequate vascularization and surfactant levels are the most important factors for the survival of premature infants!

Changes that occur after birth



After birth, the circulation of fetal blood through the placenta ceases: – Delivery of oxygenated blood to fetus via umbilical vein ceases–

Hypoxia of all tissues is increasing

 Respiratory centers of the brain stem are stimulated by carbon dioxide

- Inspiratory muscles contract, thoracic cage is expanded

- Expansion of the lungs and First Breath takes place
- Inspired air enters respiratory passageways, pushes the contained fluids out of the way and inflates the bronchial and respiratory trees
- Infant's lungs begin to function and newborn infant utters a loud cry

- IRDS usually occurs when the baby's lungs have not produced enough surfactant
- Surfactant is made up of proteins and fats, helps keep the lungs inflated and prevents them collapsing.
- A baby normally begins producing surfactant sometime between weeks 24 and 28 of pregnancy.
- Most babies produce enough to breathe normally by week 34.
- IRDS occurs most often in babies born before their due date, usually before 28 weeks of pregnancy.
- Less often, RDS can affect full-term newborns.

Infant Respiratory Distress Syndrome



Congenital abnormalities

- Congenital Lung Cysts
- Agenesis of Lungs or one Lung
- Lung Hypoplasia
- Accessory Lung
- Lobe of Azygos Vein





Agenesis of the right lung

Absence of nasal breathing

Consequences:

- Retarded development of the nose
- Inflammation of the nasal cavity
- Small chin
- Wrong position of the tongue
- Problems with speech and phonation
- Increased salivation
- Anterior position of the head problems with cervical part of the vertebral column
- Retarded physical development , passive – hypoxia
- Retarded mental development hypoxia of the brain
- Weak muscles of the lips changes in teeth position and malocclusion
- Temporomandibular joint disorders, etc.









Primary gut (foregut) —>Hollow organs (trachea, bronchi) Intraembryonic cavity —>Pleural cavity

Development of the pleura and pleural cavities



Pleura – serose membrane lining lungs and walls of the thoracic cavity
 - is derived from intraembryonic mesoderm

Lateral mesoderm forms two plates: somatic and splanchnic



EEM, extraembryonic mesoderm; YS, Yolk sac; NP, neural plate.

Intraembryonic body cavity(coelom) - Pleural cavity

Somatic mesoderm

Splanchnic mesoderm



Parietal pleura

Visceral pleura

Development of pleura


Development of the pleura and pleural cavities



Development of the pleura and pleural cavities



Expansion of the lung buds into the pericadioperitoneal canals. At this stage, the canals are in communication with the peritoneal and pericardial cavities.



Diaphragm develops from 4 sources: -1) Septum Transversum -2) Pleuroperitoneal Membranes (folds) -3) Dorsal Mesentery of Esophagus -4) Body Wall





The trachea is lined with pseudostratified ciliated columnar epithelium with goblet cells. This epithelium is derived from

1)Neuroectoderm 2)Endoderm 3)Ectoderm 4)Visceral mesoderm 5)Mesoderm of 4th and 6th pharyngeal arches Smooth muscle, connective tissue, and cartilage of primary bronchi are derived from which of the following sources?

1)Neuroectoderm
2)Endoderm
3)Ectoderm
4)Visceral mesoderm
5)Mesoderm of 4th and 6th pharyngeal arches



Components of blood-air barrier in the lungs are derived from which of the following sources?

1)Ectoderm only
 2)Visceral mesoderm only
 3)Visceral mesoderm and ectoderm
 4)Endoderm and ectoderm
 5)Visceral mesoderm and endoderm



The laryngotracheal tube initially is an open communication with the primitive foregut. Which of the following embryonic structures is responsible for separating these two structures?

1)Laryngotracheal tube
 2)Posterior esophageal folds
 3)Laryngoesophageal diverticulum
 4)Tracheoesophageal septum
 5)Bronchopulmonary segment

Pleura





Along the surface of the lung's root the visceral pleura is continuous with the parietal pleura lining the walls of the thoracic cavity and limiting the mediastinum from the sides.

Parietal pleura





Pleural cavity – slit-like space between the parietal and visceral pleurae







Pleural recesses (sinuses)

- Formed in the places where one part of the pleura is continuous with another part.
- They are reserve spaces of the right and left pleural cavities.
- When the pleura is inflamed, and the processes of the production and absorption of the serous fluid are disordered, the recesses may accumulate this fluid.

Costodiaphragmatic recess

 Where the costal part is continuous with the diaphragmatic part;
 The deepest one



Phrenicomediastinal recess

 Between the mediastinal and diaphragmatic parts of the pleura
 It is not very deep
 It is arranged in the sagittal plane





Costomediastinal recess

 Formed between the anterior portion of the costal part and the mediastinal part
 The smaller recess



recessus costomediastinalis

recessus costodiaphragmaticus

Vertebromediastinal recess

Where the mediastinal part of the pleura continues to cover the thoracic part of the vertebral column





SUFACE ANATOMY OF PLEURA



- Apex: lies one inch above the medial 1/3 of the clavicle.
- <u>Right pleura: The anterior margin</u> extends vertically from sternoclavicular joint to <u>6th costal cartilage.</u>
- Left pleura: The anterior margin extends from sternoclavicular joint to the <u>4th costal cartilage</u>, then deviates for about 1 inch to left at <u>6th costal</u> <u>cartilage</u> to form cardiac notch
- Inferior margin : passes around the chest wall, on the 8th rib in midclavicular line, 10th rib in midaxillary line and finally reaching to the last thoracic spine.
- Posterior margin : along the vertebral column from the apex to the inferior margin.

Mediastinum is a complex of the organs situated between the right and left pleural cavities



The mediastinum is limited

- anteriorly by the sternum
- posteriorly by thoracic vertebrae
- Interally by the right and left mainal parts of the parietal pleura
- <u>above</u> it extends to the superior thoracic aperture
- below it reaches the diaphragm





1.Superior mediastinum,

2. Inferior mediastinum, which is further partitioned into:

- \succ anterior,
- ➤ middle,
- \succ posterior mediastinum by the pericardial sac.





- Anterior mediastinum
- Middle mediastinum
- Posterior mediastinum

<u>The anterior mediastinum</u> is between the sternal body anteriorly and the anterior part of the costal pleura posteriorly.



- the internal thoracic vessels
- ✓ the parasternal, anterior mediastinal and prepericardial lymph nodes.





- Superior mediastinum
- Anterior mediastinum
- Middle mediastinum
- Posterior mediastinum

The middle mediastinum contains the heart with the pericardium, the roots of the great vessels, the roots of the lungs and the tracheobronchial lymph nodes. Also the phrenic nerves and pericardiophrenic vessels pass here.







Posterior mediastinum

<u>The posterior mediastinum</u> is bounded by the pericardium anteriorly: by the thoracic part of the vertebral column and ribs posteriorly.

It includes:

- ✓ the thoracic part of the descending aorta,
- ✓ azygos and hemiazygos veins,
- ✓ right and left sympathetic trunks,
- ✓ the vagus and splanchnic nerves,
- \checkmark lymphatic thoracic duct,
- the middle and inferior portions of the thoracic part of the oesophagus,
- ✓ the posterior mediastinal and prevertebral lymph nodes.



Thank you for your attention!

